RESEARCH PAPER

Clinical Implications Of Patient Adherence And Pharmacological Knowledge In Methadone Maintenance Therapy: Evidence From A Major Treatment Center In Vietnam

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ABSTRACT

Objective: This study aimed to evaluate the clinical adherence rates and pharmacological understanding of Methadone Maintenance Treatment (MMT) among opioid-dependent patients. The findings provide critical evidence for optimizing therapeutic delivery and enhancing long-term treatment outcomes at specialized facilities. **Methods:** A mixed-methods cross-sectional study was conducted in 2020, involving 98 patients undergoing MMT for at least one month at the Methadone treatment facility of the Do Luong Medical Center in Nghe An provice, Vietnam. Adherence was clinically defined as zero missed doses within the preceding month, in accordance with the Vietnam Ministry of Health guidelines. **Results:** The therapeutic adherence rate was relatively hight at 77.6%, while 22.4% of the cohort demonstrated non-adherence. Primary barriers to adherence included occupational constraints (52.2%) and underlying health complications (30.4%), and the remaining group of patients who did not specify the reasons for discontinuing treatment (17.4%). Regarding pharmacological knowledge, a significant majority (91.8%) correctly identified Methadone's properties, and 98% understood its duration of action. Notably, 100% of participants recognized potential adverse drug reactions (ADRs), such as constipation (84.7%) and decreased libido (81.6%). However, a critical knowledge gap was identified regarding the required duration of MMT, with 88.8% of patients providing incorrect responses. While patients with higher adherence knowledge were 2.32 times more likely to remain compliant (95% CI: 0.82-6.55), the correlation was not statistically significant ($p > 0.05$). **Conclusion:** Although adherence rates are relatively high, the identified gaps in long-term treatment duration knowledge and occupational barriers necessitate targeted counseling interventions. Strengthening the synergy between healthcare providers and family support systems is essential to maintain steady-state drug delivery and prevent relapse.

Keywords: Methadone Maintenance Treatment (MMT), Therapeutic Adherence, Pharmacological Knowledge, Opioid Substitution Therapy, Patient Outcomes.

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INTRODUCTION

Globally, Opioid Substitution Therapy (OST) using Methadone, a synthetic mu-opioid receptor agonist, has been established since the 1960s as a gold-standard pharmacological intervention for opioid dependence [1-4]. From a clinical pharmacology perspective, Methadone is characterized by its high oral bioavailability and an extended elimination half-life, typically ranging from 24 to 36 hours [2], [5]. This unique pharmacokinetic profile allows for a steady-state plasma concentration with once-daily dosing, effectively suppressing withdrawal symptoms and neutralizing the euphoric effects of illicit opioids through cross-tolerance. In Vietnam, the pilot Methadone Maintenance Treatment (MMT) program, initiated in 2008, has demonstrated significant clinical efficacy in controlling heroin addiction and reducing HIV transmission [5-7]. However, the therapeutic success of MMT is highly contingent upon strict adherence to the prescribed dosing regimen. Interruption in drug delivery or inconsistent dosing can lead to sub-therapeutic plasma levels, triggering withdrawal syndromes and increasing the risk of relapse. Therefore, understanding the pharmacological nature of the medication and maintaining a consistent delivery schedule are critical factors for long-term patient stabilization. The MMT facility at the Do Luong Medical Center in Nghe An province, Vietnam established in 2015, serves as a pivotal center for managing opioid-dependent cohorts. Despite the clinical benefits of Methadone, patient adherence is often compromised by various factors, including a lack of pharmacological understanding and socioeconomic barriers. Specifically, misconceptions regarding the

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duration of MMT and the management of adverse drug reactions (ADRs) can significantly undermine the stability of the treatment. While previous studies have focused on the social aspects of addiction, there is a need to evaluate adherence through the lens of patient knowledge regarding the drug's pharmacological action and the consequences of missed doses. This study, titled **"Clinical Implications of Patient Adherence and Pharmacological Knowledge in Methadone Maintenance Therapy (MMT)"** was conducted analyze the status of treatment adherence and the depth of patients' pharmacological understanding. The findings aim to provide a scientific basis for optimizing drug delivery protocols and enhancing the clinical management of opioid-dependent patients.

METHODS

Study Design and Setting: A cross-sectional descriptive study, utilizing a convergent mixed-methods approach (integrating quantitative and qualitative data), was conducted in 2020. The study was situated at the Methadone Treatment Facility of the Do Luong Medical Center in Nghe An Province, Vietnam - A primary regional hub for Opioid Substitution Therapy (OST).

Participant Selection and Sampling: The study utilized a total population sampling method, recruiting all patients currently enrolled in the Methadone Maintenance Treatment (MMT) program. To ensure data stability, inclusion criteria were restricted to patients who had been undergoing maintenance therapy for a minimum duration of one month. A total of 98 patients met the criteria and were included in the final analysis.

Assessment of Therapeutic Adherence: Adherence was evaluated based on the clinical guidelines established by the Vietnam Ministry of Health [5]. For the purpose of this study, adherence was operationalized as a binary variable: Adherence (Zero missed doses within the 30-day period preceding the study) and Non-adherence (Any instance of missed medication within the same period).

Instrumentation and Knowledge Assessment: A structured survey instrument was developed, referencing the Ministry of Health's 2010 MMT guidelines and validated international adherence scales [5]. The tool assessed three primary domains of pharmacological and clinical knowledge:

1. **General Pharmacology of Methadone:** Understanding the drug's definition, mechanism, and properties.
2. **Clinical Treatment Protocols:** Knowledge of the duration of MMT effects and long-term treatment requirements.
3. **Adherence Protocols:** Awareness of the risks associated with non-adherence and the clinical procedures for dose adjustment or program re-entry.

"General Knowledge" was defined as "Achieved" only if the participant provided correct responses across all three domains.

Statistical Analysis: Data were processed using specialized statistical software. Descriptive statistics, including frequencies and percentages, were used to characterize the cohort's adherence status and knowledge levels. To investigate the relationship between patient knowledge and adherence behaviors, Odds Ratios (OR) with 95% Confidence Intervals (CI) were calculated. A p-value < 0.05 was considered the threshold for statistical significance.

RESULTS.

Sociodemographic Characteristics of the Cohort: The study population (N = 98) was predominantly male (99.0%) and only 1.0% being female, with a mean age of 37.9 ± 7.8 years (The youngest patient participating in treatment was 19 years old, the oldest was 52 years old). A significant majority (80.6%) were aged 30 or older. Educational attainment was relatively low, with 41.9% of participants having not completed upper secondary school. Despite these factors, 87.8% of the cohort maintained active employment, and 65.3% were married.

Therapeutic Adherence Status

Table 1. The status of missed doses in the past a month

Content		Number	Percentage (%)
Adherence to treatment (no missed doses in a month)		76	77.6
Non-adherence to treatment		22	22.4
Number of consecutive days of missed doses in a month	From 01-03 consecutive days	18	18.4
	From 04-05 consecutive days	2	2.0
	Over 05 consecutive days or more	2	2.0
Reasons for missed doses in	Forgot	0	0.0

the past a month	Unable to arrange work	12	52.2
	Health reasons	7	30.4
	Unclear reasons	4	17.4

Table 1 shows that the clinical adherence rate to the MMT protocol was 77.6% (no missed doses in the preceding month). Conversely, 22.4% of patients demonstrated non-adherence. Among the non-adherent group, 18.2% missed doses for four or more consecutive days, requiring potential clinical dose titration or program reintegration. The primary barriers to adherence were identified as: Occupational Constraints (52.2% of non-adherent patients were unable to coordinate work schedules with facility hours), Health Complications (30.4% cited physical health issues as the reason for missed doses), and Undisclosed Factors (17.4% did not provide a specific rationale for treatment interruption).

Pharmacological and Treatment Knowledge

Table 2. Patients' knowledge about the Methadone treatment program

Content		**Number**	**Percentage (%)**
Definition of Methadone	Correct	90	91.8
	Incorrect	8	8.2
Duration of Methadone's effects	Correct	96	98.0
	Incorrect	2	2.0
Benefits of Methadone treatment	Able to name 1 benefit	0	0.0
	Able to name 2 benefits	4	4.1
	Able to name 3 benefits	21	21.4
	Able to name 4 benefits	10	10.2
	Able to name 5 benefits	13	13.3
	Able to name 6 benefits	39	39.8
	Able to name 7 benefits	11	11.2
Duration of Methadone treatment	Correct	11	11.2
	Incorrect	87	88.8
Reasons for having to come to the facility to take medication daily	Incorrect	0	0.0
	1 correct reason	2	2.0
	2 correct reasons	36	36.7
	3 correct reasons	42	42.9
	4 correct reasons	18	18.4
Aware that Methadone causes side effects	Yes	98	100
	No	0	0.0
Able to name side effects of Methadone	Constipation	83	84.7
	Dry mouth, tooth decay	66	67.3
	Increased sweating	66	67.3
	Sleep disorders	60	61.2
	Nausea, vomiting	40	40.8
	Itching	28	28.6
	Decreased sexual desire	80	81.6
	Other	6	6.1

The results in **Table 2** show that Patient understanding of the MMT program was high in several domains, all patients were able to name 2 to 7 benefits of MMT treatment, but revealed critical gaps in others **(Table 2):** Mechanism and Duration is 91.8% correctly defined Methadone, and 98.0% understood its 24-hour therapeutic window; Adverse Drug Reactions (ADRs) is 100% of participants were aware that MMT can cause side effects. Most frequently reported knowledge included constipation (84.7%), decreased libido (81.6%), and dry mouth (67.3%); Duration of Therapy is a significant knowledge deficit was observed regarding the length of treatment, with 88.8% of patients providing incorrect responses.

Table 3. The status of patients' knowledge about treatment adherence

Content		**Number**	**Percentage (%)**
Definition of treatment adherence	Correct	75	76.5
	Incorrect	23	23.5

Harms of non-adherence to treatment	Answered 1 correct harm	13	13.3
	Answered 2 correct harms	72	73.5
	Answered 3 correct harms	12	12.2
	Did not know	1	1.0
Aware that dose reduction is necessary after stopping medication	Correct	63	64.3
	Incorrect	35	35.7
Aware that program termination is necessary after stopping medication	Correct	60	61.2
	Incorrect	38	38.8

Table 3 shows that 76.5% of patients correctly understood the definition of treatment adherence, and 12.2% of patients could fully name 03 harms of non-adherence to treatment (withdrawal symptoms, heroin relapse, potential use of other opioids). 64.3% of patients understood that if they miss doses for 04-05 consecutive days, the dose should be reduced by half, and 61.2% of patients understood that if they miss doses for more than 30 days, they must leave the program.

Correlation between Knowledge and Adherence (Factors Influencing Adherence):

Table 4. Factors influencing the relationship between knowledge about the MMT program, knowledge about MMT treatment adherence, and MMT treatment adherence

Factor		Treatment adherence		OR (95% CI)	P
		Yes	No		
Knowledge about the MMT program	Achieved	6	3	0.54	>0.05
	Not achieved	70	19	0.12-2.37	
Knowledge about MMT treatment adherence	Achieved	61	14	2.32	>0.05
	Not achieved	15	8	0.82-6.55	

Statistical analysis was performed to evaluate the impact of knowledge on adherence behaviors **(Table 4).** While patients with an "Achieved" level of adherence knowledge demonstrated a higher likelihood of compliance (OR = 2.32; 95% CI: 0.82–6.55), this association did not reach statistical significance ($p > 0.05$); No significant correlation was found between general MMT program knowledge and adherence rates ($p > 0.05$).

DISCUSSION

Therapeutic Adherence Status

The study observed a treatment adherence (meaning they did not miss any doses in the past a month) rate of 77.6% **(Table 1)** which is relatively higher than reported in several previous international cohorts [2], [4], possibly due to differences in the time of evaluation and data collection between studies, patients who have maintained treatment have a higher adherence rate than patients who are beginning treatment, and this elevated adherence suggests a robust integration of patients into the MMT framework at this facility. However, the 22.4% non-adherence rate remains a clinical concern. From a pharmacological perspective, Methadone requires a consistent daily intake to maintain a steady-state plasma concentration. The finding that 52.2% of non-adherent patients cited occupational constraints as a primary barrier highlights a significant systemic challenge such as the conflict between rigid facility dispensing hours and the socioeconomic reintegration of the patient, which can be explained by the nature of work requiring travel or frequent work with specific hours, causing patients to miss treatment doses. Next, health problems accounted for 30.4%, due to some patients having poor health and being unable to come to the facility for medication as prescribed, or even due to oversleeping or being too engrossed in work, causing them to miss the facility's working hours. The remaining 17.4% of patients did not specify the reasons for discontinuing treatment; most of these patients did not want to disclose why they had missed treatment. There were no cases of non-adherence to treatment due to forgetting. In the context of drug delivery technology, this emphasizes the need for more flexible delivery models, such as take-home doses or extended-release formulations, to minimize the risk of sub-therapeutic troughs and subsequent relapse.

Beside, there are 2 patients missing medication from 4-5 consecutive days and also 2 patients missing medication for more than 5 days; Of course, according to the treatment regimen of the Vietnam Ministry of Health [5], these patients will have their dose adjusted or restarted. Although this rate is not high, these patients need to be noted, the reasons need to be clearly understood, appropriate solutions need to be given to overcome the situation, and regular counseling is needed to provide necessary and appropriate support, [8], [9], [10].

Pharmacological and Treatment Knowledge

Understanding methadone and understanding the purpose of treatment are the first requirements for patients when they are admitted to treatment, right from the beginning of the first group counseling session. When admitted to treatment, and especially before starting the dose, patients have been instructed by counselors and treating physicians on general knowledge in methadone treatment to maximize the effectiveness of methadone treatment for patients addicted to opioids. A profound discrepancy was identified between general awareness and deep pharmacological understanding. While nearly all patients understood the 24-hour duration of Methadone's effects (98%) and identified its benefits, a staggering 88.8% possessed incorrect knowledge regarding the total duration of the MMT program **(Table 2)**. This "knowledge-action gap" is critical; patients often mistakenly believe that MMT is a short-term detoxifying agent rather than a long-term maintenance therapy. This misconception may lead to premature self-discontinuation once the acute symptoms of opioid withdrawal subside. Furthermore, the 100% awareness rate regarding Adverse Drug Reactions (ADRs), but specifically regarding constipation (84.7%) and decreased libido (81.6%) is significant **(Table 2)**. In clinical pharmacology, unmanaged ADRs are a leading cause of treatment attrition. The high awareness recorded here suggests that while patients are informed of the risks, they require more intensive clinical support to manage these physiological burdens to ensure long-term compliance with the delivery protocol. The reason for the high percentage of patients with incorrect understanding about the duration of Methadone treatment may be that patients participating in group education before treatment did not listen carefully to the counseling of counselors and treating physicians about Methadone treatment being a long-term treatment, sometimes lifelong. Through investigation, some patients mistakenly believe that after stable maintenance treatment without heroin relapse, patients can reduce the dose and leave the program without relapsing into opioid use. To ensure patients have a clear understanding of Methadone, counseling and treatment staff need to emphasize these contents in group sessions and individual counseling. Most patients in this study were well aware of the benefits of participating in treatment, such as: drug detoxification, reduced costs due to drug use, reduced transmission of HIV, hepatitis B, C.... while some previous studies have shown that the most commonly known benefits are drug detoxification, reduced transmission of infectious diseases and reduced law violations [7]. Regarding knowledge of Methadone treatment adherence, the percentage of patients with correct understanding of the definition of treatment adherence is 76.5% **(Table 3)**, and the percentage of patients knowing at least a harm of non-adherence to treatment is high, at 99.0% **(Table 3)**, which is higher than many studies. However, the percentage of correct understanding of Methadone treatment adherence is much lower than the correct understanding of the treatment program. The percentage of patients knowing the time to stop medication to adjust the dose (64.3%) and knowing the time to stop medication to leave the program (61.2%) is still low **(Table 3).**

Correlation between Knowledge and Adherence (Factors Influencing Adherence):

Although patients with higher adherence knowledge were 2.32 times more likely to comply with the regimen, the lack of statistical significance ($p > 0.05$) suggests that knowledge alone is an insufficient predictor of behavior; Nevertheless, enhancing knowledge about MMT treatment adherence may still potentially help improve MMT adherence. **Table 4** shows that Adherence in MMT is a multifactorial construct influenced by pharmacological, socioeconomic, and psychological variables. Therefore, interventions must move beyond simple information dissemination toward a comprehensive patient-centered support model involving both family and healthcare providers [9-11]. From the research results, to optimize the efficacy of Methadone delivery and enhance patient outcomes, the following clinical strategies are recommended as follows: Enhanced Counseling, reforming educational sessions to emphasize the long-term nature of MMT and the pharmacological rationale behind maintenance therapy; Family members and those supporting patients' treatment need to fully participate in group sessions to have a clear understanding of knowledge about Methadone treatment and treatment adherence, so that they can better support patients in treatment; The patient need to fully participate in counseling sessions and group education to have a correct and complete understanding of information related to Methadone treatment; ADR Management, monitor and support patients when they experience side effects during treatment. Implementing proactive clinical monitoring for common side effects like constipation and sexual dysfunction to prevent treatment dissatisfaction; Closely coordinate with the treatment facility to have measures to supervise and remind patients in adhering to treatment. Further analyze the reasons for non-adherence to treatment to have appropriate measures to reduce the rate of treatment discontinuation; Focus on better educating, reminding, and supervising unemployed patients, patients experiencing side effects during treatment, and patients using heroin and other illegal addictive substances during treatment; Methadone treatment facilities need to coordinate and connect with counseling channels and job introduction for unemployed patients; And the systemic flexibility, developing dispensing protocols that accommodate the working schedules of patients to ensure uninterrupted medication delivery.

CONCLUSION

The study results show that the rate of patient adherence to treatment is quite high, at 77.6%, while 22.4% of patients do not adhere to treatment for various reasons, with the leading reason being the inability to arrange work, followed by health problems, and the group of patients who do not specify the reasons for discontinuing treatment. Regarding knowledge of Methadone treatment, 91.8% of patients have correct knowledge about Methadone, 98% of patients understand the correct duration of MMT's effects, 100% of patients have knowledge that Methadone treatment can cause side effects, and all patients can name 2 to 7 benefits of MMT treatment. However, 88.8% of patients have incorrect knowledge about the duration of MMT treatment.

Although knowledge about MMT treatment adherence has a 2.32 times higher likelihood of treatment adherence compared to not having knowledge about MMT treatment adherence, no influence of Methadone treatment knowledge on patient treatment adherence has been detected. In conclusion, to achieving superior therapeutic adherence, patients need support from many sources, requires a synergy between patient education, family support, and flexible healthcare systems to maintain the pharmacological stability essential for successful opioid recovery.

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