# Effect of Therapy Reminder Application on Treatment Adherence in Adults with Beta-Thalassemia Major: A Randomized Clinical Trial

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## What's Known

- Non-adherence to treatment is a major concern for chronic disease patients.
- Mobile applications (apps) enhance adherence in various conditions, such as thalassemia.
- Many medication reminder apps do not support the Persian language.

#### What's New

- The ThalaME app enhances treatment adherence specifically for Persian-speaking thalassemia patients.
- The ThalaME app has potential for broader adoption and could be proposed to the World Thalassemia Organization for global use.

## **Abstract**

**Background:** Non-adherence to treatment in patients with beta-thalassemia major (BTM) presents a significant challenge in effective disease management. This study aimed to assess the effect of a therapy reminder application (app) on treatment adherence in adult patients with BTM in Mashhad in 2024.

**Methods:** A randomized clinical trial was conducted in 2024 at a thalassemia clinic affiliated with Mashhad University of Medical Sciences (Mashhad, Iran). Participants were randomly assigned to the intervention and control groups, using permuted block randomization, with concealed allocation. The intervention group used the ThalaMe therapy reminder app for 8 weeks (February-July 2024), while the control group received standard care. Medication adherence was measured using the Morisky Medication Adherence Scale (MMAS-8) and the Chronic Disease Treatment Adherence Questionnaire (CDTAQ) before and after the intervention. Statistical analysis was conducted using SPSS software, using paired *t* tests or Wilcoxon signed-rank tests for within-group comparisons and independent *t* tests or Mann-Whitney U tests for between-group comparisons. P<0.05 was considered statistically significant.

**Results:** The study included 76 adult patients with BTM, equally distributed between the intervention and control groups (n=38 each). Baseline measurements showed no significant differences between groups in either MMAS-8 scores (P=0.75) or CDTAQ scores (P=0.11). The MMAS-8 was inversely scored, with lower scores indicating higher adherence. Following the 8-week intervention period, the group using the ThalaMe app demonstrated significantly better adherence outcomes (1.05±0.78) than the controls (2.92±1.4, P<0.001). The intervention group had significantly higher CDTAQ scores (185.5±8.07) than the control group (151.79±27.08, P<0.001).

**Conclusion:** The therapy reminder app significantly enhanced medication adherence and treatment management in patients with BTM, while simultaneously enhancing patient and family engagement through counseling.

Trial registration number: IRCT20240222061079N1

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Keywords • Thalassemia • Patient compliance • Medication adherence • Treatment adherence and compliance • Telemedicine

## Introduction

Beta thalassemia major (BTM) represents the most severe form of thalassemia, characterized by insufficient beta-globin chain synthesis in hemoglobin. This condition shows particularly high prevalence across the "thalassemia belt" regions, including the Mediterranean countries, North and West Africa, the Middle East, the Indian subcontinent, and Southeast Asia.<sup>1, 2</sup> By 2020, Iran had approximately 18,600 BTM patients, ranking first globally in the ratio of patients to population. The disease is usually diagnosed around 6 months of age, and the most effective treatment involves lifelong red blood cell transfusions and iron chelation therapy.<sup>3</sup>

Strict adherence to blood transfusion and iron chelation therapy is vital for preventing complications in thalassemia. Inadequate transfusions worsen anemia and increase the risk of cardiac failure, while insufficient iron chelation leads to iron deposition in vital organs, causing organ dysfunction. Secondary complications, such as delayed growth, infertility, diabetes, endocrine issues, and infections, can further harm the patient's health. Following treatment protocols is essential to prevent these complications and improve outcomes.3,4 Adherence to treatment refers to the patient's compliance with medical instructions. long-term therapies, the continuous use of medications and frequent follow-up visits can lead to decreased adherence.5,6

Approximately 30% to 50% of chronic patients fail to take their medications as prescribed,7 which results in health complications, poor clinical outcomes, and increased healthcare costs.8 Motivational interviewing, education, and counseling all help to improve treatment adherence; however, they are time-consuming, expensive, and need physical presence. Easy-to-implement solutions are essential for chronic disease management. Reminder (apps) help track treatment, applications enhance patient awareness, and improve adherence, thereby gaining attention for chronic disease management.9 Medication reminder apps promote treatment adherence and are available both online and offline. They might be interactive, connecting patients with healthcare providers, or non-interactive, providing a more straightforward user experience. 10, 11 These apps assist patients in adhering to treatment plans by delivering reminders, providing medication education, and increasing awareness. Advanced features include progress tracking, appointment scheduling, side effect recording, and the ability to communicate with healthcare providers. These

strategies improve adherence and enhance clinical outcomes.8, 12 Jonassaint and colleagues proposed designing a medication reminder app for patients with BTM, focusing on patients aged 18 and older, to track medication use and provide regular reports.9 Meanwhile, Badawy and colleagues concluded that studies are required to explore the effectiveness of computer and mobile technology interventions to improve disease management and adherence to iron chelation therapy in young patients over 18 with complications from the disease.<sup>13</sup> A medication reminder app is critical for thalassemia patients who receive blood transfusions every 21 days and require iron chelation therapy on a regular basis. It can remind people of blood transfusion times, iron chelation therapy schedules, and doctor appointments. Additionally, the patient can keep track of the side effects of medications or treatments and report them to the doctor, allowing for a more consistent treatment plan and potentially fewer difficulties.13, 14

The effectiveness of medication reminder apps in improving treatment adherence among thalassemia patients remains unclear due to limited evidence. However, given the high pill burden and complex regimens in BTM, such apps may offer significant benefits by helping patients follow medical instructions, enhancing their participation in care, improving clinical outcomes and quality of life, and potentially reducing healthcare costs.13 Currently, most available treatment reminder apps designed for thalassemia patients are only available in English, creating accessibility barriers for populations. Persian-speaking Additionally, while the reporting feature is a crucial element, Iranian patients cannot utilize these capabilities in non-Iranian apps due to payment restrictions. To address these limitations, the present study was designed as a randomized controlled clinical trial to investigate the impact of a treatment reminder app on medication adherence in adults with BTM in Mashhad in 2024.

# Patients and Methods

The study protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences (code: IR.MUMS.NURSE. REC.1402.116). The trial was registered in the Iranian Registry of Clinical Trials (IRCT20240222061079N1).

# Aim and Design

This randomized controlled clinical trial evaluated the efficacy of a therapy reminder app on treatment adherence in adult patients with

BTM employing control and intervention groups, in Mashhad, in 2024. The study was conducted in three phases: app design and development, app validation and evaluation, and clinical trial implementation using a pre-test/post-test design

Participants were randomly allocated to either intervention (app users) or control groups, with adherence outcomes compared between groups.

## Setting

Participants were selected from Sarvar Specialty Polyclinic, the largest thalassemia clinic affiliated with Mashhad University of Medical Sciences, Iran. This study was conducted from February 2024 to July 2024.

#### Inclusion and Exclusion Criteria

Eligible participants were adults (≥18 years) with a confirmed diagnosis of BTM who were actively receiving blood transfusions and iron chelation therapy at Sarvar Clinic. All participants possessed an Android smartphone (version 5 or higher) with a minimum of 88 MB available storage space and demonstrated sufficient Persian/ English proficiency to use the app. Participants were excluded if they had psychiatric disorders or hearing/vision impairments (due to the need to perceive the app's visual and auditory alarms). Written informed consent was obtained from all the enrolled participants in the study.

The exclusion criteria were as follows: patients currently using any medication reminder system (e.g., dedicated apps or phone calendar alerts); patients who changed their phone platform (e.g., switching from an Android to iOS,) which did not support the app; participants who reported non-use of the app during two consecutive researcher phone calls; patients who voluntarily withdrew from the study. Patients who did not respond to the researcher's phone calls after the intervention initiation; and patients who passed away during the study period.

# Study Outcomes

The primary outcomes of the study were treatment adherence and medication adherence, which were assessed using the Treatment Adherence Questionnaire for Chronic Disease (TAQCD),<sup>15</sup> and the Morisky Medication Adherence Scale (MMAS-8).<sup>16</sup>

## Tools/Instruments

The Mobile App Usability Questionnaire (MAUQ), developed by Zhou and colleagues, was used to assess app usability and patient satisfaction.<sup>17</sup> This 18-item questionnaire assessed three domains, including ease of use, interface, satisfaction, and usefulness.

The responses were rated on a seven-point Likert scale, where higher scores indicate better usability.<sup>17</sup> Since no Persian studies reported the content validity ratio (CVR) and content validity index (CVI) for this instrument, these were calculated using Lawshe's method.<sup>18</sup> Ten experts rated each item's necessity using a three-point Likert scale, and the CVR was then calculated using formula:<sup>18</sup>

$$CVR = \frac{ne - \frac{N}{2}}{\frac{N}{2}}$$

In this formula, N represents the total number of experts, and ne indicates the number of experts who selected the "essential" option. According to Lawshe's table and the evaluation of 10 experts, the minimum acceptable CVR was 0.62. In this study, the CVR values ranged from 0.79 to 1, confirming their acceptability.18 To assess the questionnaire's validity, the CVI proposed by Waltz and Bausell was used. For CVI assessment, experts rated each item's relevance on a four-point scale: not relevant, needs major revision, relevant but needs minor revision, and completely relevant. The CVI was calculated by dividing the number of experts who selected options 3 or 4 by the total number of experts:19

$$CVI = \frac{\text{The number of experts who rated the item as 3 or 4}}{\text{Total number of experts}}$$

According to the test guideline interpretation, a CVI score higher than 0.79 was considered appropriate, a CVI score between 0.70 and 0.79 required revision, and scores below 0.70 were unacceptable.19 The results of the CVI evaluation indicated that the CVI ranged from 0.87 to 1, which confirmed that all items had appropriate content validity. For reliability assessment, a test-retest method was applied. where 10 participants completed the MAUQ again after a two-week interval. The Cronbach's alpha reliability coefficient was 0.95, which was comparable with the Cronbach's alpha reported in Mortezaei's study in Iran (0.976).20 The final evaluation is categorized as: unacceptable (0-49.9%), relatively acceptable (50-74.9%), and acceptable(75-100%). All items were considered acceptable for inclusion in the MAUQ.

The MMAS-8 included seven dichotomous (Yes/No) questions and one Likert-scale question. Questions 1-7 were scored 1 for "Yes" and 0 for "No," with question 5 being reverse-scored. Question 8 was scored from 0 (Always) to 1 (Never), yielding a total possible score of 0-8, where lower scores indicated better adherence. The scale demonstrated 80.3% classification

accuracy for blood pressure control adherence, with 93% sensitivity and s 53%pecificity.¹6 The internal consistency of the MMAS-8, measured by the Kuder-Richardson 20 (KR-20) coefficient, was 0.767.²¹ For the Persian version, all items showed acceptable validity metrics: CVR≥0.75, CVI>0.79, and impact score>1.5. These results confirmed that all items met the inclusion criteria for the scale.²²

The CDTAQ, developed by Modanloo, consisted of 40 items assessing seven adherence domains: commitment to treatment, willingness to participate, ability to adapt to life. integration of treatment into life, insistence on treatment, treatment commitment, and executive strategies. Responses were recorded on a sixpoint Likert scale ranging from "Completely" (5 points) to "Not at all" (0 points), with items 33-40 (excluding item 36) reverse-scored. Higher total scores indicated better adherence. The questionnaire demonstrated strong psychometric properties, with a CVI of 0.914 and Cronbach's alpha of 0.921. In the Persian version, all items met validity thresholds (CVR≥0.51; CVI>0.79), their appropriateness for scale confirming inclusion.15

The MARS-Fa, developed by Barzegari, evaluated apps based on five criteria: Engagement (5 items), Functionality (4 items), Aesthetics (3 items), Information Quality (7 items), and App Subjective Quality (4 items), using a five-point Likert scale. The scale also allows for the inclusion of six additional custom criteria for more comprehensive evaluation. The scores were categorized as: 0-49.9% unacceptable, 50-74.9% relatively acceptable, and 75-100% acceptable. In Barzegari's study, the Cronbach's alpha was reported as 0.84.<sup>23</sup> For the Persian version of MARS, all items demonstrated acceptable validity values (CVR≥0.59; CVI>0.79).<sup>24</sup>

## Sample Size

The sample size was determined based on a study by Najafi and colleagues, which examined the impact of a smartphone-based app on medication adherence in patients with heart failure. The sample size was calculated to be 34 individuals per group using the following formula. After accounting for a potential 10% dropout rate, the final sample size was determined to be 38 participants per group.

$$n = \frac{\left(Z_{\left(1 - \frac{\alpha}{2}\right)} + Z_{\left(1 - \beta\right)}\right)^{2} \left(Sd_{1}^{2} + Sd_{2}^{2}\right)}{d^{2}}$$

 $\alpha$ =0.05,  $\beta$ =0.1

(Mean and standard deviation of Morisky in the test group)= $\mu_1\pm S_1=7.27\pm0.67$ 

(Mean and standard deviation of Morisky in the control group)= $\mu_2\pm S_2$ =6.67±0.91

## Randomization Process

In this study, participants were randomly assigned to the intervention group (code A) or control group (code B) using the permuted block randomization method. The blocks consisted of four sequences of AB and BA, and their random sequence was generated using the "permutations" and "random" libraries in Python version 3 (developed and maintained by the Python Software Foundation [PSF], USA).26 When an AB block was selected, the first participant was assigned to group A (intervention), and the second participant to group B (control). Allocation sequences were concealed in sealed envelopes opened sequentially during patient visits. In the end, each group consisted of 38 participants.

## Study Conditions

This study was conducted in three sequential stages: app design and development, app validation and evaluation, and clinical trial implementation.

Stage 1: Application Design and Development

The development process began with a comprehensive literature search across PubMed, Scopus, Magiran, and SID databases, along with app stores (App Store and Google Play), using targeted keywords to identify the needs and expectations for the app.

The search strategy in PubMed was as follows: (("application"[Title/Abstract] "app" [Title/Abstract] OR "apps" [Title/Abstract] OR "mobile" [Title/Abstract] OR "cellular phone" [Title/ Abstract] OR "cell phone" [Title/Abstract] OR "mHealth" [Title/Abstract] OR "smartphone" [Title/ Abstract]) AND ("review" [Publication Type] OR "systematicreview"[Filter])AND(("adheren\*"[Title/ Abstract] OR "nonadheren\*"[Title/Abstract] OR "complian\*"[Title/Abstract] OR "concordan\*" "refusal"[Title/Abstract] [Title/Abstract] OR "refuse"[Title/Abstract]) AND [Publication Type] OR "systematic review" [Filter])))AND(review[Filter]ORsystematicreview [Filter]).

After compiling a list of expectations, they were validated by medical experts for cultural and clinical appropriateness for Iranian patients. Subsequently, the app was designed and developed by a software engineering team. This resulting Android app, named ThalaMe, was developed as an offline solution with six core modules (user profile, medication registration, doctor visits, laboratory tests, clinical symptoms, and reporting). Besides,

it has the capability to send medication reminders and generate PDF outputs.

# Stage 2: Validation and Evaluation of the Application

The app was evaluated by five specialists (one nursing PhD, one pharmacologist, one hematologist, and two informatics experts) using the Application Rating Scale, receiving an average score of 7.81±0.75, indicating acceptable quality. Both white-box and black-box testing methods were employed to assess performance and security. A pilot evaluation was conducted with 10 thalassemia patients to gather feedback for app improvements.

## Stage 3: Conducting the Clinical Trial

Following ethical approval, the researcher collected data at Sarvar Clinic. Eligible patients referred by the head nurse were screened, provided consent, and randomly assigned to either the intervention (app) or control group using a block randomization method with opaque envelopes. Both groups completed demographic and adherence questionnaires before the intervention. While full blinding was not feasible, the data analyst remained blinded to group assignments to minimize bias.

# Intervention Group Procedures

The treatment reminder app was installed and

tested on the intervention group smartphones by the first author, who also provided comprehensive usage instructions. The Patients' capability and willingness to use the app were assessed both before and after installation. Since the app was installed on the day of blood transfusion visits, follow-up support was provided the following day. Throughout the 8-week intervention period (February -July 2024), weekly check-ins ensured proper app utilization, with technical assistance offered as needed.

## Control Group Procedures

The control group received standard care without access to the medication reminder app. To prevent contamination, researchers avoided disclosing any information about the app. After 8 weeks, control group participants were questioned about the potential use of other reminder apps. Both groups completed the CDTAQ and MMAS-8 questionnaires at the end of the study.

## Statistical Analysis

To account for potential non-adherence and missing data in RCTs,<sup>27</sup> the sample size was increased by 10%, and per-protocol analysis was employed, which excluded protocol violators and cases with missing data.<sup>28</sup> Data were analyzed using SPSS software (version 16.0; SPSS Inc., Chicago). The normality was assessed using the Kolmogorov-Smirnov test.

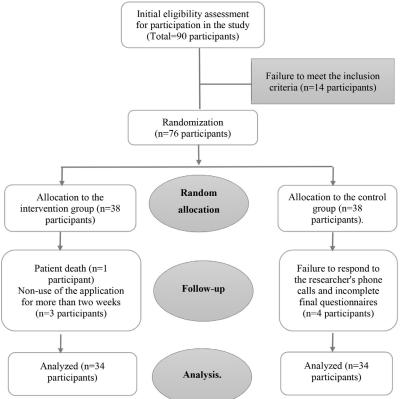


Figure 1: This figure represents the CONSORT flow diagram of the study.

Table 1: Characteristics of participants in the control at Variables		Intervention Group	Control group	P value	
		(n=34)	(n=34)		
		Frequency n (%)	Frequency n (%)		
Sex	Female	22 (64.7)	17 (50)	0.22ª	
COA	Male	12 (35.3)	17 (50)	0.22	
Marital status	Single	20 (58.8)	17 (50)	0.46a	
Wartar Statas	Married	14 (41.2)	17 (50)	0.10	
Job status	Unemployed	16 (47.1)	13 (38.2)	0.46a	
oob status	Employed	18 (52.9)	21 (61.8)	0.40	
Education level	Elementary	1 (2.9)	2 (5.9)	0.31 <sup>b</sup>	
Eddodtion level	Middle school	5 (14.7)	9 (26.5)	0.01	
	Diploma	14 (41.2)	8 (23.5)		
	Associate Degree	6 (17.6)	6 (17.6)		
	Bachelor's degree	7 (20.6)	6 (17.6)		
	Master's degree	0	3 (8.8)		
	PhD	1 (2.9)	0		
Economic	Less than enough	18 (52.9)	19 (55.0)	0.64 <sup>b</sup>	
situation <sup>e</sup>	Enough		, ,	0.04	
	More than enough	15 (44.1)	15 (44.1) 0		
Hoalth incurence	No Insurance	1 (2.9)		0.28 <sup>b</sup>	
Health insurance		1 (2.9)	0 6 (17.6)	U.20°	
	Rural Insurance Healthcare Services Insurance	2 (5.9)	6 (17.6)		
		16 (47.1)	12 (35.3)		
	Social Security Insurance	11 (32.4)	15 (44.1)		
	Bank Melli Insurance	1 (2.9)	0		
0 1:1:	Armed Forces Insurance	3 (8.8)	1 (2.9)	0.405	
Comorbidity	Cardiac disease	5 (14.7)	3 (8.8)	0.43 <sup>b</sup>	
	Endocrine disease	1 (2.9)	1 (2.9)		
	Renal disease	1 (2.9)	1 (2.9)		
	Vision disease	3 (8.8)	1 (2.9)		
	Hearing disease	1 (2.9)	1 (2.9)		
	Hepatic disease	1 (2.9)	1 (2.9)		
	Pulmonary disease	0	1 (2.9)		
	Endocrine-Renal	2 (5.9)	2 (5.9)		
	Cardiac-Endocrine	7 (20.6)	8 (23.5)		
	Cardiac-Endocrine-Hepatic	5 (14.7)	9 (26.5)		
	Cardiac-Pulmonary-Hepatic	4 (11.8)	3 (8.8)		
	Cardiac-Hepatic-Renal	4 (11.8)	3 (8.8)		
Chelator type	NanoJade	4 (11.8)	3 (8.8)	0.55 <sup>b</sup>	
	Desferal	1 (2.9)	1 (2.9)		
	Osveral	3 (8.8)	4 (11.8)		
	JadeNew	1 (2.9)	1 (2.9)		
	Defriprone+Desfonac	13 (38.2)	13 (38.2)		
	Defriprone+Desferal	12 (35.3)	11 (32.4)		
Number of drugs	1	6 (17.6)	3 (8.8)	0.54 <sup>b</sup>	
	2	3 (8.8)	8 (23.5)		
	3	5 (14.7)	3 (8.8)		
	4	6 (17.6)	8 (23.5)		
	5	5 (14.7)	7 (20.6)		
	6	7 (20.6)	5 (14.7)		
	7	0	0		
	8	2 (5.9)	0		
Variables		Median (Min-Max)	Median (Min-Max)	P value	
Age (year)		27 (18-42)	27 (18-44)	0.54°	
Age of starting che	elator therapy (year)	2.5 (1-12)	2 (1-17)	0.22°	
	gnosis (month) (mean±SD)	6.02±2.5	6.2±1.54	0.17 <sup>d</sup>	
-	I packs per month (mean±SD)	1.88±0.53	2±0.8	0.25 <sup>d</sup>	

a: Chi square test. b: Fisher's exact test. c: Mann-Whitney U test. d: Independent *t* test. e: Economic situation was assessed through a self-reported measure where participants were asked, "How would you describe your economic situation?" They could choose from three options: 1. Less than enough, 2. Enough, or 3. More than enough. This classification reflects participants' personal perception of their income relative to their basic needs.

The Chi square test was used to analyze the categorical variables, and *t* tests or Mann-Whitney U tests were employed to analyze the quantitative data. Within-group comparisons were conducted using paired *t* tests or Wilcoxon signed-rank tests. P<0.05 was considered statistically significant. The implementation process is presented in figure 1.

## Results

Table 1 provides demographic characteristics and treatment-related variables for both study groups.

As shown in table 2, the control group demonstrated no significant changes in MMAS-8 (P=0.75) or CDTAQ scores (P=0.11) over the two-month study period. In contrast, the intervention group showed statistically significant improvements in both measures, including a reduction in MMAS-8 scores (P<0.001) and an increase in CDTAQ scores (P<0.001).

Table 3 demonstrates that the intervention yielded significant improvements in both medication and treatment adherence, as evidenced by a marked reduction in MMAS-8 scores and a substantial increase in CDTAQ scores (both P<0.001). In contrast, the control group showed only marginal, non-significant changes in adherence measures.

# Discussion

Consistent with the first objective of determining the therapy reminder app's effect on medication adherence in adults with thalassemia major, the results of the present study showed lower medication adherence scores (indicating better adherence due to reverse scoring) in the app group than the control group. These findings were in agreement with multiple studies demonstrating apps' positive effects on treatment adherence. For instance, Poorcheraghi and colleagues demonstrated that after 8 weeks of using the app, medication adherence significantly increased in the intervention group.<sup>29</sup> Similarly, Torkabad and colleagues<sup>30</sup> and Santo and colleagues<sup>31</sup> reported improved adherence in their intervention groups. Furthermore, Morawski and colleagues<sup>32</sup> and Chawsamtong and colleagues<sup>33</sup> provided similar findings regarding the impact of apps on treatment adherence and the reduction of serum ferritin levels in thalassemia patients. However, Spetz and colleagues found no significant difference in medication adherence between the control and intervention groups after one year,34 which contrasted with the findings of the present study. This discrepancy might be due to differences in the study populations and the timing of adherence measurement (12-month follow-up after 12-week intervention) versus our 8-week evaluation period. The differences in the study design and methods likely account for the varied outcomes.

In line with the second objective of assessing the therapy reminder app's effect on treatment adherence in adults with thalassemia major, the findings of the present study indicated higher treatment adherence in the app group than in the control group. These findings were supported by a previous study by Abu-El-Noor and colleagues, which reported that the intervention group showed significantly improved treatment adherence than the control

Variables		Intervention group (n=34)	Control group (n=34)	P value between groups	
		mean±SD	mean±SD		
MMAS-8 <sup>e</sup>	(Before the intervention)	2.9±1.05	2.85±1.53	0.88°	
	(2 months after the intervention)	1.05±0.78	2.92±1.4	<0.001 <sup>d</sup>	
	P value within groups	<0.001a	0.75 <sup>b</sup>	-	
CDTAQ <sup>f</sup>	(Before the intervention)	155.88±18.92	153.23±28.08	0.65°	
	(2 months after the intervention)	185.5±8.07	151.79±27.08	<0.001 <sup>d</sup>	
	P value within groups	<0.001a	0.11 <sup>b</sup>	-	

a: Wilcoxon signed-rank test; b: Paired *t* test; c: Independent *t* test; d: Mann-Whitney U test; e: Morisky medication adherence scale (MMAS-8); f: Chronic disease treatment adherence questionnaire (CDTAQ)

Table 3: Comparison of changes in mean MMAS-8 and CDTAQ scores in the two groups before and after the intervention										
Variable	Control group	Intervention	Between-groups differences							
	changes (n=34)	group changes(n=34)	Mean differences (SEM)	Effect size Δ «Cohen's d"	95% confidence interval	P value <sup>a</sup>				
MMAS-8, mean±SD	0.067±1.26	-1.845±1.47	-1.912 (0.33)	-1.39	(-1.917,-0.855)	<0.001				
CDTAQ, mean±SD	-1.44±5.11	30.61±18.40	32.058 (3.27)	2.37	(1.744,2.992)	<0.001				

a: Independent t test

group.<sup>35</sup> Additionally, Karaaslan and colleagues reported an increase in chemotherapy adherence scores among cancer patients in the intervention group.<sup>36</sup> Furthermore, Jiménez and colleagues conducted a systematic review and concluded that mobile apps effectively enhance treatment adherence in adults, with app users showing significant improvements in adherence to treatment.<sup>37</sup>

Non-adherence to treatment remains a significant challenge in chronic disease management, particularly for thalassemia major patients, often resulting in suboptimal clinical outcomes. While traditional adherence interventions frequently prove ineffective, mobile apps present a scalable alternative. Existing apps such as MediSafe, Rxmind Me, Med Helper, and Pill Reminder offer standard features including medication reminders, dosage tracking, and drug information. The ThalPal app (developed by Dr. Ouyang and Dr. Kohlbry) provides medication reminders and response tracking,38 though it lacks Persian language support. In contrast, the ThalaME app, introduced in this study, delivers comparable functionality in Persian, making it suitable for recommendation to the World Thalassemia Organization to support Persianspeaking patients in Iran, with potential benefits for both treatment adherence and quality of life.

In this study, patients received instructions for installing and using the app, with weekly follow-ups to address any issues. Most patients used Android phones, though some did not use smartphones. For patients whose first appointment was on their blood transfusion day, follow-up calls were made the next day. A limitation of the study was the 8-week duration, and longer-term results might yield better outcomes.

## Conclusion

This study demonstrated that the ThalaMe app increased adherence to therapy in adults with BTM. Interventions that improve medication adherence are an integral part of managing thalassemia patients. The ThalaMe app could assist patients in better managing their medication timing and administration methods.

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staff at Sarvar Clinic, and the Thalassemia Association of Khorasan Razavi Province for their valuable contributions.

# **Authors' Contribution**

F.M: Study design, carrying the out implementation, data analysis, and reviewing the manuscript; M.A: Study design, carrying out the implementation, data analysis, and drafting; Z.B: Study design, and reviewing the manuscript. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest: None declared.

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