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Original Research

Long-term impact of pillbox use on medication adherence in patients with type 2 diabetes mellitus

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Abstract

Background: This follow-up study assessed the long-term impact of pillbox use on medication adherence in type 2 diabetes mellitus (T2DM) patients over two years. **Method:** A cross-sectional study consisting of 52 participants was divided into two groups: pillbox (intervention) and non-pillbox (control). Adherence was measured using the pill count method, and clinical outcomes such as blood glucose levels were recorded. **Results:** Results revealed that the pillbox group had significantly higher adherence rates over time, with adherence increasing from 94.01% initially to 96.67% after two years. In contrast, adherence in the non-pillbox group declined from 88.62% to 88.26%. Postprandial blood glucose control improved significantly in the pillbox group (141.38 mg/dl to 129.88 mg/dl), whereas the non-pillbox group experienced an increase (137.96 mg/dl to 145.69 mg/dl). Fasting and random blood glucose levels did not show statistically significant changes. The analysis identified education and occupation as important predictors of adherence, while factors such as age, gender, comorbidities, and medication changes showed marginal or non-significant effects. **Conclusion:** These findings suggest that pillbox interventions can effectively improve long-term medication adherence and postprandial blood glucose control in T2DM patients, particularly when considering sociodemographic factors like education and occupation. Further research should explore the broader implications of these findings for diabetes management and potential strategies to improve adherence in diverse patient populations.

Keywords: long-term adherence, pillbox, predictors

INTRODUCTION

Adherence to prescribed medication is a crucial component of effective disease management, especially for chronic conditions such as type 2 diabetes mellitus (T2DM)[1]. Medication adherence refers to the extent to which patients take their medications as prescribed by their healthcare providers[2]. High levels of adherence are associated with better clinical outcomes, including improved glycemic control, reduced risk of diabetes-related complications, and overall enhanced quality of life[3–5]. Conversely, poor adherence can lead to suboptimal clinical outcomes, increased healthcare costs, and higher morbidity and mortality rates[6–9].

Type 2 diabetes mellitus is a chronic metabolic disorder characterized by insulin resistance and relative insulin deficiency, leading to elevated blood glucose levels[10]. The long-term complications of poorly managed diabetes include cardiovascular diseases, nephropathy, retinopathy, and neuropathy[10]. According to the International Diabetes Federation, the prevalence of diabetes is rising globally, with Indonesia ranking among the top countries with the highest number of diabetes cases[11]. This rising prevalence underscores the need for effective strategies to improve medication adherence and, by extension, diabetes management.

In a study conducted at the Public Health Center (PHC) Lubuk Kilangan in Padang City, a pill count method was employed to assess medication adherence among patients with T2DM. The research compared the adherence levels of two groups of patients: those who used pillboxes and those who did not. The results indicated a significant difference in adherence between the two groups, with the pillbox group demonstrating higher adherence levels. Specifically, the study found that 96.15% of patients using pillboxes adhered to their medication regimen, compared to 76.92% in the non-pillbox group[5,12].

The pillbox, also known as a pill organizer, is a simple yet effective tool designed to help patients manage their medication intake[13]. It provides a visual and practical aid for organizing daily doses, thereby reducing the likelihood of missed or incorrect doses. The initial study's findings suggest that the use of pillboxes can significantly enhance medication adherence in patients with T2DM[5]. However, while these results are promising, they represent only a snapshot in time.

To build on these findings, the current follow-up study aims to evaluate the long-term impact of pillboxes on medication adherence in the same cohort of patients. This follow-up research is essential to determine whether the initial improvements in adherence are sustained over a more extended period and to understand the factors that influence long-term adherence.

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The primary objective of this follow-up study is to assess the sustained impact of using pillboxes on medication adherence among patients with type 2 diabetes mellitus over an extended period. Specifically, the study aims to evaluate the long-term adherence levels in patients using pillboxes and compare the adherence levels from the initial study period to the follow-up period to assess any changes or trends. By achieving these objectives, the study seeks to provide comprehensive insights into the effectiveness of pillboxes as a long-term adherence strategy for patients with T2DM. This information can inform healthcare providers and policymakers about the potential benefits of incorporating pillboxes into diabetes management programs and guide the development of targeted interventions to improve medication adherence in this population.

METHOD

Research design

This research employed a longitudinal follow-up design over 2 years to evaluate the long-term impact of using pillboxes on medication adherence in patients with type 2 diabetes mellitus (T2DM). The study focused on a population comprising patients with T2DM registered at PHC Lubuk Kilangan in Padang City. The sample included those T2DM patients who had participated in the initial study, ensuring continuity and enabling assessment of changes in adherence over time. The study design has constraints, including not addressing behavioural factors like motivation and forgetfulness, limiting insights into adherence. It lacks a detailed exploration of predictive factors such as education and occupation and provides a brief discussion of outliers, leaving anomalies underexplored. Additionally, the single-site design restricts generalizability, reducing the applicability of findings to broader populations or healthcare settings.

Population and sample

To calculate the sample size from a small population, especially when the total population is only 52 people, the initial sample size is first determined using the equation: , Z^2 is the Z-score value corresponding to the desired confidence level (1.96 for a 95% confidence level)[14]. The variable p represents the proportion of the population expected to have a specific characteristic (if unknown, it can be assumed to be 0.5). The term e^2 refers to the desired margin of error (0.05 for a 5% error. After that, the number of participants is adjusted to the population size using the formula finite population correction (FPC): . In this case, there are only 52 populations, so using a 95% confidence interval and a 5% error, there would be 46 participants. This number was then divided into two groups, intervention and control so the minimum number in each group is 23 participants.

Inclusion and exclusion criteria

The study included patients with type 2 diabetes mellitus (T2DM) who were 18 years or older, had participated in the initial study, and were willing to continue the research for the second year. Patients who had serious complications or other medical conditions that could impact medication adherence, as well as those who were unable to communicate or provide accurate information about their medication use, were excluded from the study.

Type of pillbox

A pillbox was designed for safe and organized medication storage. It has 21 compartments, each equipped with rubber seals for airtight protection and constructed from lightproof material to prevent exposure to light and humidity, ensuring medication stability. The ergonomic design allows easy access to individual compartments without disturbing others, enhancing user comfort.

Patient training

Patients were trained to fill compartments based on their medication schedules, ensuring adherence and minimizing errors. This intervention is particularly beneficial for managing chronic diseases, preserving medication efficacy, and promoting systematic and practical medication management.

Variables

Several variables were analyzed in this research. The dependent variables were medication adherence, measured by the pill count method, and random blood glucose levels. The independent variable was using a pillbox (yes/no). Confounding variables included age, gender, duration of diabetes, education level, social support, number and type of medications taken, and underlying disease.

Procedures

The data collection began with a baseline assessment, which collected demographic data, medical history, and initial medication adherence levels. During this phase, pillboxes were provided to the intervention group. The follow-up assessment measured medication adherence throughout 2 using the pill count method to ensure consistent and accurate adherence tracking. This research was only carried out at two points. Next, the adherence percentage was calculated by dividing the remaining drugs by the number of days of drug consumption[5].

Statistical analysis

This study's statistical analysis methods include descriptive and inferential approaches. Descriptively, the study will outline the demographic and clinical profiles of both the intervention and control groups while also calculating medication adherence rates at baseline (1 month) and 2-year (24 months). Inferential analyses will utilize several methods: the Mann-Whitney test to compare medication adherence between the intervention and control groups at each assessment point and logistic regression to identify factors significantly influencing long-term medication adherence[15]. These approaches collectively aim to provide a comprehensive understanding of the effectiveness and factors impacting medication adherence in patients using pillboxes to manage type 2 diabetes mellitus.

RESULTS

The research began by describing the baseline sociodemographic characteristics of both the control group

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(non-pillbox) and the intervention group (pillbox) in patients with type 2 diabetes mellitus (T2DM) at PHC Lubuk Kilangan. Differences in adherence levels were analyzed between the first month and the end of the two-year follow-up period to assess long-term adherence patterns. Clinical outcomes between the pillbox and non-pillbox groups were compared to determine the effectiveness of the intervention, next to decide on factors influencing adherence levels in the T2DM population, including demographic, clinical, and treatment-related variables.

Table 1. presents the baseline sociodemographic characteristics of the control (non-pillbox) and intervention (pillbox) groups, providing an overview of key factors such as age, gender, education level, employment status, and comorbidities in each group before the intervention. These characteristics are essential for understanding the comparability between the groups at the start of the study.

Table 1: Baseline sociodemographic of control (non-pillbox) and intervention (pillbox) groups.

Characteristic	Pillbox (N = 26)		Non Pillbox (N=26)		Total (N=52)		*p-value*
	N	%	N	%	N	%	
Age, year (Mean±SD)	56.54 ±9.05		63.04 ± 5.723		52	100	0.006[a]
30-39	1	3.8	0	0	1	1.9	0.006[b]
40-49	4	15.4	1	3.8	5	9.6	
50-59	13	50	7	26.9	20	38.5	
60-69	5	19.2	14	53.8	19	36.5	
≥70	3	11.5	4	15.4	7	13.5	
Gender							
Men	6	23.1	5	19.2	11	21.2	0.736[c]
Women	20	76.9	21	80.8	41	78.8	
Education level							
Not attending school	1	3.8	3	11.5	4	7.7	0.431[c]
Elementary	15	57.7	14	53.8	29	55.8	
Junior high school	5	19.2	3	11.5	8	15.4	
Senior high school	2	7.7	5	19.2	7	13.5	
University	3	11.5	1	3.8	4	7.7	
Occupation/ Work							
Homemaker	16	69.6	28	63.64	44	65.67	0.431[b]
Driver	0	0	1	3.8	1	1.9	
Trader	1	3.8	1	3.8	2	3.8	
Private sector	0	0	1	3.8	1	1.9	
Civil servant	0	0	1	3.8	1	1.9	
Unemployed	4	15.4	3	11.5	7	13.5	
Underlying diseases							
Hypertension	13	50	10	38.5	23	44.2	0.107[b]
Hypertension +heart disease	0	0	2	7.7	2	3.8	
Hypertension + gout	1	3.8	2	7.7	3	5.8	
Hypertension + hyperlipidemia	1	3.8	2	7.7	3	5.8	
Hyperlipidemia	1	3.8	0	0	1	1.9	
Hyperlipidemia + gout	5	19.2	1	3.8	6	11.5	
Osteoarthritis	0	0	2	7.7	2	3.8	
Tuberculosis	1	3.8	0	0	1	1.9	
None	4	15.4	7	26.9	11	21.2	

[a] = Compare-means;
[b] = Fisher exact test
[c] = Chi-square;

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The groups differ significantly in age, with the non-pillbox group being older. Gender, education level, occupation, and underlying disease distributions show no significant differences between the two groups. The mean age of the pillbox group is 56.54 ± 9.05 years, while the non-pillbox group is 63.04 ± 5.72 years. This is statistically significant difference (p=0.006), suggesting that the non-pillbox group is significantly older. The age distribution shows that more participants in the non-pillbox group are older ranges (60-69 and ≥70), while the pillbox group has a larger proportion in the 50-59 age group. While gender distribution also shows no significant difference, as both groups are predominantly female (76.9% in the pillbox group and 80.8% in the non-pillbox group, p=0.736)

Hypertension is the most common condition in both groups, affecting 50% of the pillbox group and 38.5% of the non-pillbox group. Combined conditions (e.g., hypertension with heart disease or gout) are more common in the non-pillbox group, although this is not statistically significant difference (p=0.107). Notably, 21.2% of participants in the non-pillbox group have no underlying diseases, compared to 15.4% in the pillbox group.

The differences in medication adherence levels between the initial first month and the end of the second-year follow-up, as seen in Table 2, highlighted changes in adherence over time for both the control and intervention groups. This comparison provides insights into the long-term impact of the pillbox intervention on patient adherence.

The adherence levels between the pillbox and non-pillbox groups exhibited clear differences over time. Initially, the pillbox group demonstrated a higher average adherence (94.01 ± 8.43) compared to the non-pillbox group (88.62 ± 15.83), although this was not statisticaly significant difference (p=0.067). This indicates that participants using the pillbox were slightly more consistent with their medication regimens at the start of the study. Still, there was greater variability in adherence within the non-pillbox group. After two years, adherence in the pillbox group improved to 96.67 ± 2.59, while adherence in the non-pillbox group decreased slightly to 88.26 ± 8.51. This difference was statistically significant (p=0.000), suggesting that the pillbox intervention effectively helped sustain or increase medication adherence, while the non-pillbox group experienced a decline. Although the initial difference was not significant, by the two-year follow-up, the pillbox group had significantly higher adherence, highlighting the intervention's positive impact.

The research data are also presented in a box plot to clarify the differences in compliance levels between groups in the 2-year follow-up (Figure 1).

The boxplot in Figure 1. illustrates a comparison of adherence percentages between two groups, the intervention and the control groups, at two distinct time points: initial and final adherence. In the intervention group, adherence levels were consistently high, with the median approaching 100% and most data falling within the 80%-100% range, though one outlier was observed at 45%. After the intervention, the distribution of adherence remained stable, with no significant changes, as the median stayed near 100%. On the other hand, the control group showed a wider range of adherence levels, with a lower median than the intervention group, though still within the 80%-100% range. Two notable outliers were recorded at 12% and 13%. In the final adherence assessment, the control group experienced a slight decline in adherence compared to the initial measure, with the median remaining around 80% and one outlier at 12%. In summary, the intervention group exhibited consistently higher and more stable adherence levels than the control group, both before and after the intervention, with fewer outliers. In contrast, the control group displayed more adherence variability, with a few individuals showing significantly lower levels. Overall, the intervention appeared effective in maintaining high adherence, while the control group experienced a slight decline.

Sticking to prescribed medication is directly linked to overall health and well-being. Table 3 shows the differences in clinical outcomes between the pillbox and non-pillbox groups, comparing key health indicators such as blood glucose levels.

Over a 2-year follow-up period, the clinical outcomes for fasting blood glucose, 2-hour postprandial blood glucose, and random blood glucose were compared between the pillbox and non-pillbox groups. The pillbox group experienced a slight increase in fasting blood glucose from 112.50 mg/dl to 113.81 mg/dl. In contrast, the non-pillbox group decreased from 122.62 mg/dl to 111.04 mg/dl, though this was not statistically significant difference (p=0.527). In terms of 2-hour postprandial blood glucose, the pillbox group showed a substantial reduction from 141.38 mg/dl to 129.88 mg/dl, while the non-pillbox group's levels increased from 137.96 mg/dl to 145.69 mg/dl. This change was statistically significant (p=0.000), indicating improved postprandial glucose control in the pillbox group. For random blood glucose, the pillbox group experienced a minor

Table 2: Differences in adherence levels in the initial first month and the end of the second-year follow-up

Adherence level	Groups	$\bar{X}$±SD	SE	95%CI		p-value
				min	max	
Initial	Pillbox	94.01±8.43	1.65	57.5	100	0.067[a]
	Non-Pillbox	88.62±15.83	3.1	28.33	100	
2-year follow-up	Pillbox	96.67±2.59	0.51	90	100	0.000[a*]
	Non-Pillbox	88.26±8.51	1.67	62.5	99.17	

[a] = Mann Whitney
[*] = Significant level <0.05

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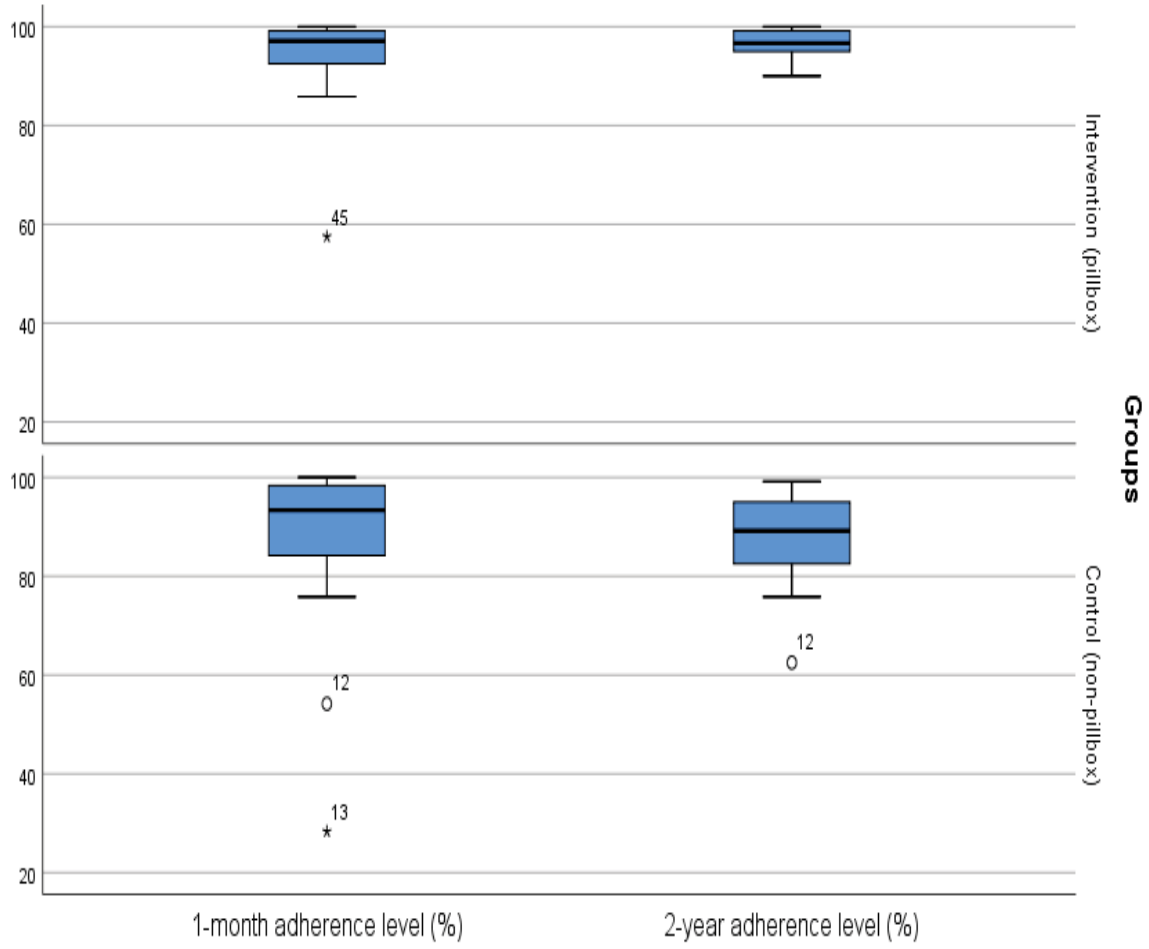

Figure 1. Differences in adherence levels in the initial first month and the end of the second-year follow-up in boxplot.

Table 3: Differences in clinical outcomes in the pillbox and non-pillbox groups

Clinical outcome	Groups	Initial (mean±SD) (mg/dl)	2-year follow-up (mean±SD) (mg/dl)	p-value
Fasting blood glucose	Pillbox	112.50±9.98	113.81±17.55	0.527[a]
	Non-Pillbox	122.62±25.30	111.04±14.96	
2-h Post prandial blood lucose	Pillbox	141.38±11.42	129.88±9.56	0.000[a*]
	Non-Pillbox	137.96±20.17	145.69±8.28	
Random blood glucose	Pillbox	133.73±6.63	132.31±7.54	0.107[a]
	Non-Pillbox	149.65±22.11	136.23±9.46	

[a] = Mann Whitney
[*] = Significant level <0.05

decrease from 133.73 mg/dl to 132.31 mg/dl, while the non-pillbox group had a more notable drop from 149.65 mg/dl to 136.23 mg/dl. However, this was not statistically significant difference (p=0.107). Overall, the pillbox group demonstrated substantial improvement in postprandial blood glucose control, whereas fasting and random blood glucose changes between the groups were not statistically significant. By categorizing the adherence groups into decrease, stable, and increase groups with the increase group as a reference, factors were obtained that are estimated to influence changes in adherence, as seen in Table 4.

In this model, the most significant predictors of medication adherence are education (p = 0.018) and occupation (p = 0.044), indicating that an individual's educational background and employment status notably impact their adherence levels. Additionally, there are marginally significant effects for comorbidities (p = 0.074) and changes in the number of medications (p = 0.058), suggesting that these factors may

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Table 4: Factors influencing adherence levels in the T2DM population at PHC Lubuk Kilangan

Likelihood Ratio Tests

	Model Fitting Criteria	Likelihood Ratio Tests		
Effect	**-2 Log Likelihood of Reduced Model**	**Chi-Square**	**df**	**Sig.**
Intercept	30.738[a]	0	0	
Age	34.704	3.965	2	0.138[d]
Gender	30.738	0	2	1.000[d]
Age groups	40.972	10.234	8	0.249[d]
Education	49.24	18.501	8	0.018[b]
Occupation	52.232	21.494	12	0.044[b]
Underlying disease	55.499	24.761	16	0.074[c]
Change in the drug name	30.738[a]	0	0	-
Change in the number of drug consumption	36.442	5.704	2	0.058[c]
Change in regimen/ drug dose	31.927	1.188	4	0.880[d]

[a] Reduced model is equivalent to the final model, omitting the effect does not increase the degrees of freedom.
[b] Significant
[c] Marginally significant
[d] Non-significant

influence adherence. However, further investigation is required to confirm their roles. On the other hand, age, gender, age group, medication name change, and dosage/regimen change do not show statistically significant effects on adherence. Overall, education and occupation are key factors influencing adherence, while other predictors appear to have less impact.

DISCUSSION

Several critical aspects warrant discussion in examining the data from this study to fully understand the implications of the findings, starting with age disparity, sociodemographic patterns, clinical outcomes, and factors that influenced adherence value. The significant age difference between the pillbox and non-pillbox groups (p=0.006) suggests the need to explore how age might influence adherence and clinical outcomes. Age and number of medications may affect pillbox use, but adherence does not differ between groups[16]. Several studies agree with these results, including research related to drug compliance in geriatric patients with cardiovascular disorders[17] . The use of pillboxes can also reduce the cost of doctor visits. The pillbox, combined with tailored messages, resulted in better self-reported mental health during the intervention and fewer higher-cost care encounters at 12 months without increasing office visits[18]. However, older individuals might be in the non-pillbox group. Older individuals might be in the non-pillbox group for several reasons: older adults often experience cognitive decline and multiple chronic conditions which can make it challenging to manage complex medication regimens, including the use of pillboxes[19]; physical limitation and lack of familiarity or comfort with pillboxes[16]. Other studies revealed older adults tend to benefit more from pillboxes, especially when these devices are tailored to their needs[17,20]. Middle-aged adults also use pillboxes effectively, particularly when managing complex medication regimen[16]. Younger adults are less likely to use pillboxes; when they do, the impact on adherence is less significant[21]. Overall, pillboxes are a valuable tool for improving medication adherence, particularly among older populations.

Although gender, education, occupation, and comorbidities did not significantly differ between groups, several studies have their findings. Gender differences in medication adherence are inconsistent, with some studies showing poorer adherence in women for certain conditions like hypercholesterolemia and type 2 diabetes, while others show no significant difference[5,22–24]. Higher education levels generally correlate with better medication adherence, although some studies report mixed results[22,23,25]. Employment status has a mixed impact on adherence. Employed individuals may have lower adherence due to time constraints, while others show better adherence, possibly due to better access to healthcare resources[23,26].

The two groups demonstrated differing results over the two-year follow-up period regarding clinical outcomes. While fasting blood glucose slightly increased in the pillbox group (from 112.50 mg/dl to 113.81 mg/dl) and decreased in the non-pillbox group (from 122.62 mg/dl to 111.04 mg/dl), these changes were not statistically significant (p=0.527). However, significant differences were observed in 2-hour postprandial blood glucose, with the pillbox group showing a marked decrease (from 141.38 mg/dl to 129.88 mg/dl), whereas the non-pillbox group's levels increased (from 137.96 mg/dl to 145.69 mg/dl, p=0.000). Random blood glucose levels also significantly declined in the non-pillbox group, though this was not statistically significant difference (p=0.107). Overall, the pillbox group significantly improved postprandial blood glucose, suggesting better control over time. There was a significant increase in adherence in the pillbox group after two years (p=0.000) and a decline in the non-pillbox. However, several

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factors contributed to the decrease in adherence in the control group. Forgetfulness, low patient's feeling of responsibility, long duration of sleep, and presence of a handicapped or small child in care are significant factors contributing to non-compliance[27]. In addition, Refilling medicine and intentional nonadherence in taking medicine subscale contributed to changes in compliance in the non-pillbox group[28].

The notable enhancement in post-prandial blood glucose levels is quite promising. The Pillbox group highlighted several important clinical benefits of the intervention. Some studies suggest that pillbox interventions improve medication adherence and quality of life in diabetes mellitus patients, while other studies indicate that they did not change clinical outcomes**.** Pillbox use is associated with a significant reduction in blood sugar levels in type 2 diabetes patients[12]**.** The use of pillboxes, combined with educational interventions by pharmacists, significantly improves medication adherence in diabetes patients[28,29], and enhances the quality of life in geriatric patients with type 2 diabetes mellitus[6,30,31]. However, the impact on broader clinical outcomes, such as disease control for multiple conditions, is less clear, with some studies showing no significant change in clinical outcomes despite improved adherence[32].

Education and occupation emerged as significant predictors of adherence (p=0.018 and p=0.044), while factors like age and gender did not. Several studies found an educational intervention can improve patients' knowledge, adherence, and quality of life, but knowledge level is not associated with increased adherence[29,33]. Education enhances health literacy, which is closely linked to effective disease management, including better adherence to medication[34].

Strength and limitation

The research presented adherence data clearly, using statistical to highlight the pillbox intervention's significance. It comprehensively analyses adherence levels and clinical outcomes, linking these to the intervention's impact. A visual aid (boxplot) enhances comprehension, while the logical structure makes the analysis easy to follow. However, the draft lacks depth in exploring predictive factors like education and occupation more thoroughly. The discussion of outliers is brief, and implications for practice are missing. Additionally, the research did not address behavioral factors such as motivation and forgetfulness, which are critical limitations as they may significantly influence adherence and clinical outcomes.

CONCLUSION

The pillbox intervention significantly improved postprandial blood glucose control and medication adherence over two years, while fasting and random blood glucose levels remained unchanged. Adherence increased in the pillbox group and decreased in the non-pillbox group, highlighting the intervention's effectiveness. Education and occupation were key predictors of adherence, emphasizing sociodemographic influences. Although factors like comorbidities and medication changes showed some impact, further research is needed. The study lacked detail on unexplained clinical outcomes and adherence outliers. Future research should explore behavioral factors and practical applications to improve adherence, especially for patients with low health literacy or complex regimens.

AUTHOR'S CONTRIBUTION

NF was the principal investigator on this research and wrote the first draft. YOS and PPP helped collect data. YOS calculates the adherence score. NF performed statistical analysis. All authors accept the final draft.

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ETHICAL CONSIDERATION

Ethics consideration was obtained from the Health Research Ethics Committee Faculty of Pharmacy Universitas Andalas No. 61/UN16.10.D/KEPK-FF/2024, which ensured all participants provided written informed consent and implemented strict confidentiality measures to protect their privacy and data anonymity. This approval ethics updates the previous approval ethics with No. 85/UN.16.2/KEP-FK/2022. These measures aim to uphold the rights, welfare, and confidentiality of everyone involved in researching medication adherence among patients with type 2 diabetes using pillboxes.

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