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Pillbox Interventions Enhance Medication Adherence and Postprandial Blood Glucose in Patients with Type 2 Diabetes: A Two-Year Follow-Up Study

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ABSTRACT

This follow-up investigation examined the sustained effects of pillbox utilization on medication adherence among individuals with type 2 diabetes mellitus (T2DM) across a two-year period. A cross-sectional analysis involving 52 participants was separated into two cohorts: the pillbox (intervention) group and the non-pillbox (control) group. Adherence was evaluated via the pill count technique, while clinical parameters including blood glucose concentrations were documented. The findings indicated that the pillbox group maintained markedly superior adherence rates throughout the duration, rising from 94.01% at baseline to 96.67% at the two-year mark. By comparison, adherence in the non-pillbox group decreased from 88.62% to 88.26%. Postprandial blood glucose management showed significant improvement in the pillbox group (141.38 mg/dl to 129.88 mg/dl), whereas the non-pillbox group exhibited a rise (137.96 mg/dl to 145.69 mg/dl). No statistically significant alterations were observed in fasting or random blood glucose values. The analysis highlighted education and occupation as key determinants of adherence, while variables such as age, gender, comorbidities, and adjustments to medication demonstrated limited or insignificant influence. The results imply that pillbox-based interventions can successfully enhance prolonged medication adherence and postprandial blood glucose regulation in patients with T2DM, especially when accounting for sociodemographic variables like education and occupation. Additional studies are recommended to investigate the wider applications of these outcomes for diabetes care and possible approaches to boost adherence across varied patient groups.

Keywords: Long-term adherence, Pillbox, Predictors, Type 2 diabetes

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Introduction

Compliance with prescribed medications represents a vital element of successful disease control, particularly in chronic illnesses like type 2 diabetes mellitus (T2DM) [1]. Medication adherence denotes the degree to which individuals follow their treatment regimens as directed by healthcare professionals [2]. Elevated adherence is linked to superior clinical results, encompassing better glycemic management, lowered likelihood of diabetes-associated complications, and improved overall quality of life [3-5]. In contrast, inadequate adherence may result in poorer clinical performance, elevated healthcare expenditures, and increased rates of morbidity and mortality [6-9].

Type 2 diabetes mellitus is a persistent metabolic condition marked by insulin resistance and relative insulin insufficiency, resulting in heightened blood glucose concentrations [10]. Long-term consequences of inadequately controlled diabetes encompass cardiovascular disorders, nephropathy, retinopathy, and neuropathy [10]. As reported by the International Diabetes Federation, diabetes prevalence is increasing worldwide, with Indonesia placed among the nations with the greatest number of cases [11]. This escalating prevalence emphasises the

importance of implementing robust measures to enhance medication adherence and, consequently, optimise diabetes management.

In research carried out at the Public Health Center (PHC) Lubuk Kilangan in Padang City, the pill count approach was applied to measure medication adherence in T2DM patients. The investigation contrasted adherence between two patient groups: those utilising pillboxes and those who did not. The outcomes demonstrated a notable disparity in adherence, with the pillbox group exhibiting greater compliance. In particular, 96.15% of pillbox users followed their medication schedule, versus 76.92% in the non-pillbox group [5, 12].

The pillbox, alternatively termed a pill organiser, is a straightforward but efficient device intended to assist patients in organising their medication consumption [13]. It offers a visual and functional means of arranging daily doses, thus minimising the chances of omitted or erroneous intake. The original study's results indicate that pillbox usage can substantially improve medication adherence in T2DM patients [5]. Nevertheless, although encouraging, these observations reflect only a single point in time.

Building upon these observations, the present follow-up study seeks to investigate the enduring influence of pillboxes on medication adherence within the identical patient cohort. This subsequent research is critical to ascertain whether the early gains in adherence persist over a longer timeframe and to identify the elements affecting sustained adherence.

The main goal of this follow-up study is to determine the ongoing effect of pillbox use on medication adherence in patients with type 2 diabetes mellitus over a prolonged duration. More precisely, the study intends to measure long-term adherence in pillbox users and to compare adherence rates from the original study phase with those of the follow-up phase in order to detect any shifts or patterns. Through these aims, the study endeavours to deliver thorough understanding of the efficacy of pillboxes as a sustained adherence tool for individuals with T2DM. Such knowledge can guide healthcare practitioners and policymakers regarding the advantages of integrating pillboxes into diabetes management initiatives and support the creation of focused interventions to elevate medication adherence in this patient group.

Materials and Methods

Research design

This study adopted a longitudinal follow-up design spanning 2 years to assess the sustained effects of pillbox usage on medication adherence among patients with type 2 diabetes mellitus (T2DM). The research targeted patients with T2DM registered at PHC Lubuk Kilangan in Padang City. The sample consisted of T2DM patients who had taken part in the original study, thereby maintaining continuity and allowing evaluation of adherence changes over time. The design has certain limitations, such as failing to examine behavioural elements including motivation and forgetfulness, which restricts deeper understanding of adherence issues. It also does not thoroughly investigate predictive factors like education and occupation, and offers only limited discussion of outliers, resulting in unexplored anomalies. Furthermore, the single-site approach limits generalizability, thereby reducing the broader applicability of the results to diverse populations or healthcare contexts.

Population and sample

When determining sample size for a small population, particularly one totaling only 52 individuals, the initial sample size is calculated using the formula: , where Z2 is the Z-score for the chosen confidence level (1.96 for 95% confidence) [14]. The variable p denotes the anticipated population proportion with the characteristic of interest (0.5 if unknown). The term e2 represents the acceptable margin of error (0.05 for 5% error). Subsequently, the sample size is adjusted for finite population using the correction formula (FPC): . With a population of 52, applying a 95% confidence interval and 5% error margin yields 46 participants. This total was then allocated equally to the intervention and control groups, resulting in a minimum of 23 participants per group.

Inclusion and exclusion criteria

Participants included individuals with type 2 diabetes mellitus (T2DM) aged 18 years or older who had been involved in the initial study and consented to continue for the second year. Exclusion criteria encompassed patients with severe complications or comorbid conditions that might affect medication adherence, as well as those unable to communicate effectively or provide reliable information regarding their medication intake.

Type of pillbox

The pillbox was developed to facilitate safe and orderly medication storage. It features 21 compartments, each fitted with rubber seals to ensure airtight conditions, and is made from lightproof materials to shield contents from light and humidity, thereby maintaining medication integrity. Its ergonomic design permits easy opening of individual compartments without affecting others, improving user convenience.

Patient training

Patients received instruction on filling the compartments according to their prescribed medication schedules, with the goal of promoting adherence and reducing errors. This approach is especially advantageous for chronic disease management, as it helps preserve drug effectiveness and encourages organized, practical medication routines.

Variables

Multiple variables were examined in this study. The dependent variables comprised medication adherence, assessed via the pill count method, and random blood glucose levels. The independent variable was pillbox utilization (yes/no). Confounding variables encompassed age, gender, duration of diabetes, education level, social support, number and type of medications prescribed, and comorbid diseases.

Procedures

Data collection commenced with a baseline evaluation that gathered demographic information, medical history, and initial adherence levels. At this stage, pillboxes were distributed to the intervention group. Follow-up evaluations tracked medication adherence over 2 years using the pill count method for reliable and consistent measurement. Data were collected only at two time points. Adherence percentage was subsequently computed by dividing the number of remaining pills by the number of days of medication consumption [5].

Statistical analysis

The statistical methods employed in this study encompassed both descriptive and inferential techniques. Descriptively, participant demographic and clinical characteristics were summarized for the intervention and control groups, alongside calculation of medication adherence rates at baseline (1 month) and at the 2-year mark (24 months). For inferential analysis, the Mann-Whitney test was applied to compare adherence between groups at each time point, while logistic regression was used to determine factors significantly associated with long-term adherence [15]. Together, these methods seek to offer a thorough evaluation of the efficacy and influencing factors of pillbox use on medication adherence in patients managing type 2 diabetes mellitus.

Results and Discussion

This study initiated by detailing the initial sociodemographic profiles of the control group (without pillbox) and the intervention group (with pillbox) in patients diagnosed with type 2 diabetes mellitus (T2DM) at PHC Lubuk Kilangan. Variations in medication adherence were evaluated by comparing levels from the first month to the conclusion of the two-year follow-up, aiming to identify sustained adherence trends. Comparisons of clinical results across the pillbox and non-pillbox groups were conducted to gauge the intervention's efficacy, alongside an examination of elements affecting adherence among T2DM patients, covering demographic, clinical, and therapy-associated factors.

Table 1 displays the initial sociodemographic profiles for the control (non-pillbox) and intervention (pillbox) groups, summarizing critical aspects including age, gender, educational background, occupational status, and comorbid conditions before the intervention began. Such profiles are vital for assessing the initial equivalence between the groups.

Table 1. Baseline Sociodemographic Characteristics of the Control (Non-Pillbox) and Intervention (Pillbox) Groups

Demographic or Clinical Feature	Non-Pillbox Group (N=26)		Pillbox Group (N=26)		p-value	Overall (N=52)	
	N	%	N	%		N	%
Age in years (Mean ± SD)	63.04 ± 5.723		56.54 ± 9.05		0.006[a]	52 (100%)	

30-39	0	0	1	3.8		1	1.9
					0.006[b]		
40-49	1	3.8	4	15.4		5	9.6
50-59	7	26.9	13	50.0		20	38.5
60-69	14	53.8	5	19.2		19	36.5
≥70	4	15.4	3	11.5		7	13.5
Sex							
Male	5	19.2	6	23.1	0.736[c]	11	21.2
Female	21	80.8	20	76.9		41	78.8
Level of Education							
Never attended school	3	11.5	1	3.8		4	7.7
					0.431[c]		
Elementary school	14	53.8	15	57.7		29	55.8
Junior high school	3	11.5	5	19.2		8	15.4
Senior high school	5	19.2	2	7.7		7	13.5
University/College	1	3.8	3	11.5		4	7.7
Occupation							
Homemaker/Housewife	28	63.64	16	69.6		44	65.67
					0.431[b]		
Driver	1	3.8	0	0		1	1.9
Trader/Merchant	1	3.8	1	3.8		2	3.8
Private sector employee	1	3.8	0	0		1	1.9
Civil servant/Government employee	1	3.8	0	0		1	1.9
Unemployed	3	11.5	4	15.4		7	13.5
Comorbid Conditions							
Hypertension alone	10	38.5	13	50.0		23	44.2
					0.107[b]		
Hypertension + heart disease	2	7.7	0	0		2	3.8
Hypertension + gout	2	7.7	1	3.8		3	5.8
Hypertension + hyperlipidemia	2	7.7	1	3.8		3	5.8
Hyperlipidemia alone	0	0	1	3.8		1	1.9
Hyperlipidemia + gout	1	3.8	5	19.2		6	11.5
Osteoarthritis	2	7.7	0	0		2	3.8
Tuberculosis	0	0	1	3.8		1	1.9
No underlying diseases	7	26.9	4	15.4		11	21.2

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

A notable difference emerged in age, where the non-pillbox group had a higher average age. Distributions of gender, educational attainment, employment, and comorbid illnesses revealed no meaningful differences. The pillbox group's average age stood at 56.54 ± 9.05 years, versus 63.04 ± 5.72 years for the non-pillbox group, marking a significant statistical distinction (p=0.006) and confirming the greater age in the non-pillbox cohort. Regarding age categories, the non-pillbox group included more individuals in the higher brackets (60-69 and ≥70 years), contrasted with a greater share in the 50-59 bracket for the pillbox group. Gender breakdown indicated no significant variation, with females dominating both cohorts (76.9% in the pillbox group and 80.8% in the non-pillbox group, p=0.736).

Hypertension ranked as the primary comorbid condition across both cohorts, impacting 50% of the pillbox group and 38.5% of the non-pillbox group. Multiple comorbidities (for instance, hypertension combined with cardiac issues or gout) appeared more frequently in the non-pillbox group, yet without reaching statistical significance (p=0.107). Interestingly, 21.2% of the non-pillbox participants reported no comorbid conditions, against 15.4% in the pillbox group.

Variations in medication adherence from the baseline first month to the close of the second-year follow-up are depicted in **Table 2**, revealing temporal shifts in adherence for the control and intervention cohorts. These findings offer valuable perspectives on the enduring influence of the pillbox approach on adherence behavior.

Table 2. Changes in Medication Adherence from the First Month to the End of the Two-Year Follow-Up

Adherence Level	Group	Mean ± SD	95% CI (min-max)	SE	p-value
Initial	Pillbox	94.01 ± 8.43	57.5 - 100	1.65	0.067a
	Non-Pillbox	88.62 ± 15.83	28.33 - 100	3.1	
2-year Follow-up	Pillbox	96.67 ± 2.59	90 - 100	0.51	0.000a*
	Non-Pillbox	88.26 ± 8.51	62.5 - 99.17	1.67	

a = Mann Whitney
* = Significant level <0.05

Over the study duration, adherence patterns diverged noticeably between the pillbox and non-pillbox cohorts. At the outset, the pillbox cohort recorded a superior mean adherence rate (94.01 ± 8.43) relative to the non-pillbox cohort (88.62 ± 15.83), though this gap lacked statistical significance (p=0.067). This suggests marginally better regimen consistency among pillbox users early on, accompanied by wider fluctuations in the non-pillbox cohort. At the two-year endpoint, the pillbox cohort's adherence rose to 96.67 ± 2.59, whereas the non-pillbox cohort's fell modestly to 88.26 ± 8.51. The resulting difference proved highly significant (p=0.000), indicating that the pillbox strategy effectively preserved or boosted adherence long-term, in contrast to a slight deterioration without it. Despite the non-significant early difference, the substantial superiority in the pillbox cohort by the follow-up endpoint emphasizes the intervention's favorable lasting benefits.
Additionally, a box plot visualization of the data helps to illustrate the variations in adherence rates between the groups at the 2-year follow-up **(Figure 1)**.

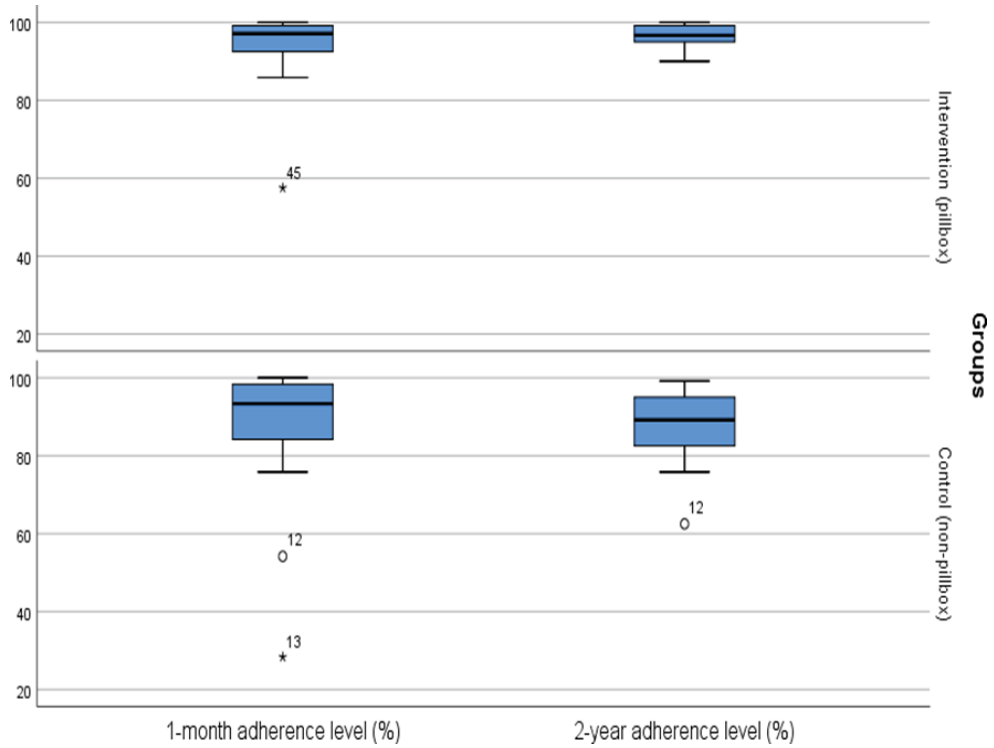

Figure 1. Adherence rate variations between the baseline (first month) and the conclusion of the two-year follow-up, displayed in a boxplot format.

Figure 1's boxplot provides a visual comparison of adherence percentages across the intervention and control groups at baseline and endpoint assessments. For the intervention group, adherence stayed reliably high, with the median nearing 100% and most values concentrated in the 80%-100% bracket, except for one outlier at 45%. Post-intervention, the pattern held steady without notable shifts, maintaining a median close to 100%. In comparison, the control group revealed broader dispersion in adherence scores, featuring a lower median than the

intervention group—yet largely within 80%-100%—along with two distinct outliers at 12% and 13%. By the endpoint evaluation, the control group registered a small drop in adherence from baseline, with the median hovering near 80% and a single outlier at 12%. Taken together, the intervention group achieved greater consistency and higher overall adherence at both stages, accompanied by minimal outliers. The control group, however, revealed increased fluctuation and occasional substantially reduced adherence. Consequently, the intervention successfully supported sustained high adherence, unlike the control group which underwent a modest reduction.

Consistent medication-taking strongly correlates with better health status. **Table 3** details variations in clinical parameters between the pillbox and non-pillbox groups, emphasizing major metrics like blood glucose readings.

Table 3. Comparison of clinical outcomes between participants using a pillbox and those not using one.

Clinical Outcome	Group	2-Year Follow-Up (mean ± SD) (mg/dl)	Baseline (mean ± SD) (mg/dl)	p-value
Fasting Blood Glucose	Pillbox	113.81 ± 17.55	112.50 ± 9.98	0.527[a]
	Non-Pillbox	111.04 ± 14.96	122.62 ± 25.30	
2-Hour Postprandial Blood Glucose	Pillbox	129.88 ± 9.56	141.38 ± 11.42	0.000[a]*
	Non-Pillbox	145.69 ± 8.28	137.96 ± 20.17	
Random Blood Glucose	Pillbox	132.31 ± 7.54	133.73 ± 6.63	0.107[a]
	Non-Pillbox	136.23 ± 9.46	149.65 ± 22.11	

a = Mann Whitney

* = Significant level <0.05

Across the 2-year observation, comparisons were made for fasting blood glucose, 2-hour postprandial blood glucose, and random blood glucose between the pillbox and non-pillbox groups. Fasting blood glucose in the pillbox group rose marginally from 112.50 mg/dl to 113.81 mg/dl. The non-pillbox group, meanwhile, fell from 122.62 mg/dl to 111.04 mg/dl, without reaching statistical significance (p=0.527). Regarding 2-hour postprandial blood glucose, the pillbox group recorded a marked decline from 141.38 mg/dl to 129.88 mg/dl, in opposition to an elevation in the non-pillbox group from 137.96 mg/dl to 145.69 mg/dl. This contrast proved highly significant (p=0.000), signaling superior postprandial control among pillbox users. Random blood glucose in the pillbox group dipped slightly from 133.73 mg/dl to 132.31 mg/dl, against a steeper reduction in the non-pillbox group from 149.65 mg/dl to 136.23 mg/dl, though not statistically meaningful (p=0.107). Collectively, the pillbox cohort achieved meaningful gains in postprandial glucose regulation, whereas group differences in fasting and random glucose lacked significance.

Adherence trajectories were grouped into decrease, stable, and increase categories—taking the increase category as reference—to pinpoint contributing factors, as displayed in **Table 4**.

Table 4. Determinants of medication adherence among T2DM patients at PHC Lubuk Kilangan.

Effect	-2 Log Likelihood of Reduced Model	df	Chi-Square	p-value
Intercept	30.738[a]	0	0	-
Age	34.704	2	3.965	0.138[d]
Gender	30.738	2	0	1.000[d]
Age Groups	40.972	8	10.234	0.249[d]
Education	49.240	8	18.501	0.018[b]
Occupation	52.232	12	21.494	0.044[b]
Underlying Disease	55.499	16	24.761	0.074[c]
Change in Drug Name	30.738[a]	0	0	-
Change in Number of Drug Consumption	36.442	2	5.704	0.058[c]
Change in Regimen / Drug Dose	31.927	4	1.188	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

Within this framework, education ($p = 0.018$) and occupation ($p = 0.044$) stood out as the primary drivers of adherence, underscoring the substantial role of educational level and job status in shaping compliance. Comorbid conditions ($p = 0.074$) and alterations in medication quantity ($p = 0.058$) displayed borderline significance, hinting at potential contributions needing more study. Variables such as age, gender, age category, switches in drug names, and modifications to dosage or scheduling showed no meaningful links to adherence. In essence, education and occupation dominate as influential elements, with remaining factors demonstrating limited effects.

To grasp the full meaning of these results, several pivotal topics deserve exploration, encompassing group age discrepancies, sociodemographic profiles, clinical findings, and adherence influencers. The pronounced age gap between pillbox and non-pillbox cohorts ($p=0.006$) calls for scrutiny of how age could shape adherence and health results. While age and medication count might affect pillbox acceptance, they do not necessarily create adherence disparities across groups [16]. Numerous investigations align with this, especially those on treatment compliance among seniors with heart-related issues [17]. Employing pillboxes can further cut healthcare expenses; pairing them with customized reminders yielded enhanced self-assessed mental wellness and fewer expensive medical interactions after 12 months, sans extra routine appointments [18]. Greater age representation in the non-pillbox cohort may arise from multiple causes: seniors commonly encounter thinking declines and several ongoing illnesses, hindering handling of complicated drug schedules that involve pillboxes [19]; mobility restrictions and device inexperience contribute as well [16]. Yet, research shows seniors gain substantially from adapted pillboxes [17, 20]. Those in midlife also handle pillboxes adeptly for demanding regimens [16]. Youth tend to avoid pillboxes, and usage yields smaller adherence gains when adopted [21]. Broadly, pillboxes represent a practical resource for boosting medication compliance, most notably in senior groups.

Despite no statistically significant differences in gender, education, occupation, or comorbidities between the groups, prior research offers useful context. Findings on gender and medication adherence are mixed: some studies report that women have lower adherence for conditions such as hypercholesterolemia and type 2 diabetes, whereas other studies find no significant gender-based differences5, [22-24]. Education generally correlates with better adherence, though results are sometimes inconsistent [22, 23, 25]. Employment presents a complex picture: working individuals may struggle with adherence due to time limitations, yet some studies suggest employment can improve adherence through better access to healthcare resources [23, 26].

Over the two-year follow-up, the groups showed divergent patterns in clinical outcomes. Fasting blood glucose increased slightly in the pillbox group (112.50 mg/dl → 113.81 mg/dl) but decreased in the non-pillbox group (122.62 mg/dl → 111.04 mg/dl), with no statistical significance ($p=0.527$). Significant changes were noted in 2-hour postprandial glucose: the pillbox group experienced a reduction (141.38 mg/dl → 129.88 mg/dl), whereas the non-pillbox group saw an increase (137.96 mg/dl → 145.69 mg/dl, $p=0.000$). Random glucose decreased in the non-pillbox group, although this difference was not statistically significant ($p=0.107$). Overall, pillbox users achieved better postprandial control, reflecting improved long-term glycemic management. Medication adherence increased significantly in the pillbox group ($p=0.000$) but declined in the non-pillbox group. Contributing factors for reduced adherence in the control group included forgetfulness, low responsibility, extended sleep, and caring for a disabled or young child [27]. Additionally, challenges with refilling prescriptions and intentional nonadherence affected compliance in the non-pillbox group [28].

The improvements in postprandial glucose in the pillbox group are clinically meaningful. These findings support prior research suggesting that pillbox interventions can enhance adherence and quality of life in diabetes patients, although some studies report no impact on clinical outcomes. In type 2 diabetes, pillbox use is associated with significant reductions in blood sugar12. Combining pillboxes with pharmacist-led educational interventions further enhances adherence [28, 29] and improves quality of life in older adults with type 2 diabetes [6, 30, 31]. The influence on broader clinical outcomes, however, remains less consistent; some studies note no significant change despite improved adherence [32].

Education and occupation were identified as significant predictors of adherence ($p=0.018$ and $p=0.044$), while age and gender were not. Educational interventions can improve knowledge, adherence, and quality of life, though higher knowledge alone does not guarantee better adherence [29, 33]. Education also promotes health literacy, which is closely linked to effective disease management and medication compliance [34].

Strengths and limitations

The study presented adherence data with clarity, using statistical analyses to highlight the impact of the pillbox intervention. It thoroughly examined adherence patterns and clinical outcomes while connecting them to the

intervention. Boxplots and other visual aids improved comprehension, and the logical organization enhanced readability. Limitations include limited exploration of predictive factors like education and occupation, minimal discussion of outliers, and a lack of focus on practical applications. Behavioral factors such as motivation and forgetfulness were not addressed, yet these can have a substantial impact on adherence and outcomes.

Conclusion

The pillbox intervention significantly enhanced postprandial glucose control and medication adherence over two years, while fasting and random glucose remained largely unchanged. Adherence increased in the pillbox group and decreased in the non-pillbox group, demonstrating the intervention's effectiveness. Education and occupation were key adherence predictors, emphasizing the role of sociodemographic factors. Although comorbidities and medication changes had some influence, further investigation is warranted.
The study offered limited insight into unexplained clinical outcomes and adherence outliers. Future research should explore behavioral determinants and practical strategies to improve adherence, particularly in patients with low health literacy or complex medication regimens.

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