# Original Research Article

# Use of Therapy Diary as a Method for Monitoring and Improving Adherence to Metformin Therapyin Diabetic Patients


## ABSTRACT

**Aims:**To determine the effectiveness of using a therapy diary in improving adherence and blood glucose levels.
**Study design:** A randomized multicenter study.
**Place and Duration of Study:**The research was conducted in the primary Health Centers of Tuzla Canton from March to August 2024.
**Methodology:**This study involved 44 participants, age 35-65, who had previously been diagnosed with type 2 diabetes mellitus.Includedparticipants used metformin irregularly for at least 6 months andhad not been diagnosedwith a malignant disease or a severe mental disorder. Every participantgave written consent to participate in the research. A therapy diary was used as a method for monitoring adherence to metformin over a period of 3 months. Participants were trained to independently measure and record blood glucose level with a glucometer every morning for 3 months.
**Results:**32 (72.73%) participants had adherence greater than 80% after 3 months, while 12 (27.27%) had adherence less than 80%, which is considered insufficient. Themean value of blood glucose level for all participants at the beginning of the study was 8.9 mmol/L. The mean value of morning blood glucose level for all participants after 3 months was 0.6 mmol/l lower. The mean value of morning blood glucose level in adherent patients after 3 months was 8.2 mmol/L, which shows that morning glucose level decreased by 0.7 mmol/L on average. The mean value of morning blood glucose level in non-adherent patients was 9.1 mmol/L, which is on average 0.2 mmol/L higher than the mean value of measured blood glucose level at the beginning of the study.
**Conclusion:**These results indicate that using a therapy diary can help with identification of trends in patient's blood glucose levels and medication adherence, but further research is needed to establish more successful methods for improving adherencein diabetic patients.



*Keywords: adherence; metformin; diary; therapy; diabetes.*


## 1. INTRODUCTION

One of the most common forms of medication error is patient's non-adherence. Adherence has been defined as the extent to which a person's behavior, taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider. The definition was presented by the World Health Organization (WHO) in 2006, emphasizing the importance of adherence in the success of therapy and highlighting non-adherence as a significant global health and economic problem [1].
Patients were considered adherent if the percentage, defined as the number of doses missing in a certain time period divided by the number of doses prescribed by the doctor in the same time period, was greater than 80% [2]. The number of missing doses means doses used by the patient, which does not show whether the patient took that dose correctly and whether he took the missing dose at all.
The need for the development of numerous types of methods for assessing adherence is increasing every day, however, there is still no method that will unequivocally prove whether a patient is adherent or not, and that this method is at the

same time available to every individual, reliable, authoritative and economically acceptable.Over the past few decades, researchers have become increasingly interested in methods to measure patient adherence to medical recommendations. The literature offers a plethora of both subjective and objective methods. However, despite the many measurement tools available, it is impossible to conclusively determine the criterion standard for measuring patient adherence[3].
The methods that have been developed and applied so far can be divided into two groups: direct and indirect [4]. Direct methods include the determination of the amount of the drug or its metabolites in tissues or body fluids, most often in blood, urine or saliva. Indirect methods include procedures such as various questionnaires and surveys for patients, pill counters, patient notes, monitoring the frequency of taking medications, and various electronic programs for monitoring therapy intake. Although these methods are more available and cost-effective, their disadvantage is susceptibility to data manipulation and lack of objectivity [4,5].
It is important to note that none of the methods applied so far are ideal and there is currently no standardized procedure for assessing adherence that could cover all aspects and determine all causes of non-adherence [4]. In addition, there are numerous variations of certain methods for examining adherence, and over the years of research they are used inconsistently, the data are not systematized according to common guidelines, and the defined thresholds of the level of adherence may differ from study to study, which makes it difficult to interpret the data obtained and use them in clinical practice [6].
Important factor that determines medication adherence is forgetfulness. The odds of being adherent in patients responded forgetfulness is lower than the other reasons provided by the patients, like drug unavailability, financial shortage and drug adverse effects. That means, being forgetfulness was associated with 90.6% decreased medication adherence level as compared to the other reasons provided[7].
The World Health Organization, informed by the trials conducted so far, concluded that an increase in the degree of adherence can affect the patient's health more than any change in medication [8]. In the USA, as many as two-thirds of patients are hospitalized precisely because of the consequences of non-adherence, which indicates the importance of implementing already available interventions to improve adherence, as well as the development of new techniques and interventions [2].Although deaths caused by nonadherence are hard to measure, the estimate of 125,000 deaths per year is widely cited in the literature. Disease-specific meta-analyses validate a significantly increased risk of death in nonadherent patients[9].One of the first steps in improving medication nonadherence would be to increase public awareness of the magnitude of the problem. Articles are beginning to appear in popular media on this topic [10].

## 2. MATERIAL AND METHODS

This study involved 44participants, age 35-65, who had previously been diagnosed with type 2 diabetes mellitus within the primary healthcare centers of Tuzla Canton. Includedrespondentsusedmetforminirregularly, and had notbeendiagnosedwithmalignantdiseaseorseverementaldisorder.The research was conducted from March, 2024, to August, 2024, on a voluntary basis, withwrittenconsentoftheparticipantsto participateintheresearch, ensuring that each participant's privacy was protected, and the data were used solely for research purposes. A therapy diary was used to monitor metformin intake, as an indirect method for monitoring adherence over a period of 3 months. Participants were trained to independently measure and record blood glucose levels every morning for 3 months.Allrespondents had their blood glucose levels measured at the beginning of the research and after three months ofwriting a therapydiary.Following the completion of the study, collected datawere processed statistically.

## 3. RESULTS AND DISCUSSION

Adherence to therapy and the number of missed daily doses are shown in Table 1. The maximum number of days in which some of the participants did not take the prescribed daily dose of metformin for a period of 3 months was 90 days, which represents 100% of the sample and speaks of an extremely high degree of non-adherence in some participants. The minimum number of days in which prescribed daily doses of metformin were missed was 0 days. As a definition of good adherence to chronic therapy, the research used a level of 80% of the daily doses of the drug taken by the doctor's recommendation. 32 (72.73%) participants had adherence higher than 80% after 3 months, while 12 (27.27%) participants had adherence lower than 80% (more than 17 prescribed daily doses were not taken during 3 months), which is considered insufficient adherence to therapy. From the obtained results, it is evident that even with daily measurement of morning blood glucose and writing a therapy diary, almost a third of the participants after 3 months had insufficient adherence to the therapy. It was found that the majority of participants (45.45%) had from 0 to 5 missed daily doses in a period of 3 months, while 9 participants (20.45%) had from 6 to 17 missed doses in the same period.

Table 2 shows the influence of the participant's adherence on blood glucose values. Allparticipants who missed therapy for more than 17 days within three months for any reason are characterized as non-adherent, and conversely all those who have less than 17 such days are characterized as adherent. The maximum blood glucose level of the participants at

the beginning of the study was 16.5 mmol/L, while the lowest value was 2.6 mmol/L. The average value of blood glucose level for all participants at the beginning of the study was 8.9 mmol/L. The range of morning blood glucose values at the beginning of the study was 13.9 mmol/L. After 3 months of monitoring, the maximum blood glucose level was 14.7 mmol/L, the minimum value was 5.0 mmol/L, while the mean value for all participants was 8.3 mmol/l. The range of morning blood glucose values after 3 months was 9.7 mmol/L. The mean value of morning blood glucose for all participants after 3 months is lower by 0.6 mmol/L compared to the mean value calculated at the beginning of the study. The mean value of morning blood glucose in adherent participants (n=32) after 3 months was 8.2 mmol/L, which shows that morning glucose decreased by 0.7 mmol/L on average in adherent patients for three months. The mean value of morning blood glucose in non-adherent participants (n=12) was 9.1 mmol/L, which is on average 0.2 mmol/L higher than the mean value of measured morning blood glucose at the beginning of the study.

**Table 1. Adherence and number of missed daily doses for metformin after 3 months**

| Respondents n (%) | Adherence (%) | Missed daily doses |
|---|---|---|
| Adherent 32 (72.73%) | >80% | 0-17 |
| Non-adherent 12 (27.27%) | <80% | >17 |

**Table 2. Influence of the respondent's adherence on blood glucose values**

| | Average value of blood glucose before research | Average value of blood glucose after 3 months | Range |
|---|---|---|---|
| All respondents | 8.9 mmol/L | 8.3 mmol/L | -0.6 mmol/L |
| Adherent | -8.2 mmol/L | | -0,7 mmol/L |
| Non-adherent | | -9.1 mmol/L | +0.2 mmol/L |

This study indicated that the use of a therapy diary does not lead to an improvement in adherence in a large number of participants, which confirmed the results of other similar studies.According to the study by Webber et al. [11] there were no significant differences in the change in blood pressure as a result of the reminder diary and the telephone call. However, the small drop in blood pressure, combined with the improved blood profile, waist–hip ratios and distances walked, provide encouraging findings for the use of a reminder diary plus telephone calls to improve adherence to lifestyle modifications in order to reduce blood pressure. However, research conducted by Santoleri et al. [12] indicated that treatment adherence with the diary calculated using received daily dose/prescribed daily dose method was 93.6% (imatinib 94.9%, nilotinib 91.1%, and dasatinib 95.8%). Adherence during the period without a diary was 86.5% (84.9, 87.4, and 90%). Adherence was significantly greater with than without a diary ($p < 0.0001$).It is important to emphasize that in the aforementioned study, the degree of adherence to therapy before using the therapy diary was already above 80%, which is considered an acceptable degree of adherence. On the other hand, our study followed the improvement of adherence in highly non-adherent patients.

## 4. CONCLUSION

The obtained results of this study indicate that the use of a therapy diary does not lead to an improvement in adherence in a large number of diabetic patients. The results also indicate the satisfactory effectiveness of the prescribed therapy when it is taken in accordance with the prescribed regimen and a clear correlation between non-adherence, lower effectiveness of the therapy and the increase in morning blood glucose levels.These findings suggest that writing a therapy diary should not be the only method used to monitor and improve adherence to therapy. It should also be emphasized that the actual degree of adherence of the respondents considered as adherent after 3 months may be lower than the obtained one, because the participants independently wrote the therapy diaries.Considering that, there is a possibility that the results recorded in the therapy diaries may be manipulated by the respondents. Consequently, further research is needed to establish more successful methods for improving adherencein diabetic patients.

## DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

## CONSENT

The research was conducted after obtaining the informed consent of the respondents.

## ETHICAL APPROVAL

Ethical approval was obtained from the Ethical Committee of the Public Health Institution “Health Center” Srebrenik (number: 212-2/24, date: 08.03.2024.) andPublic Health Institution “Health Center” Živinice (number: 03-1087/24, date: 13.02.2024.).

## REFERENCES


1. Roebuck MC, Liberman JN, Gemmill-Toyama M, Brennan TA. Medication adherence leads to lower health care use and costs despite increased drug spending. Health Aff (Millwood). 2011 Jan;30(1):91-9.
2. Brown MT, Bussell JK. Medication Adherence: WHO Cares? Mayo Clin Proc. 2011 Apr; 86(4): 304–314.
3. Gackowski M, Jasińska-Stroschein M, Osmałek T, Waszyk-Nowaczyk M. Innovative Approaches to Enhance and Measure Medication Adherence in Chronic Disease Management: A Review. Med Sci Monit. 2024 Jul 16;30:e944605. doi: 10.12659/MSM.944605. PMID: 39012851; PMCID: PMC11302205.
4. Frommer M, Aslani P, Chen T, Tiller D. Use of medicines by the elderly: The role of pharmacy in promoting adherence. Sydney: International Pharmaceutical Federation (FIP); 2018. Accessed 19 August 2024.
Available at:
https://www.fip.org/files/fip/publications/Use_of_medicines_by_the_elderly_The_role_of_pharmacy_in_promoting_adherence.pdf.
5. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med. 2005 Aug 4;353(5):487-97.
6. AlHewiti A. Adherence to Long-Term Therapies and Beliefs about Medications. Int J Family Med. 2014 Feb 13; 479596.
7. Derejie MN, Dereje EN, Alemu DM, Tesfay YG, Hunduma F, Temie NM. Medication non-adherence and its associated factors among kidney transplant patients in a large teaching hospital in Ethiopia. BMC Nephrol. 2024 Jun 1;25(1):187. doi: 10.1186/s12882-024-03620-z. PMID: 38824513; PMCID: PMC11144307.
8.Burkhart PV, Sabaté E. Adherence to Long-Term Therapies: Evidence for Action. Geneva, Switzerland: World Health Organization; 2003. Accessed 19 August 2024.
Available at: https://iris.who.int/bitstream/handle/10665/42682/9241545992.pdf?sequence=1&isAllowed=y.
9. Wu JR, Moser DK. Medication adherence mediates the relationship between heart failure symptoms and cardiac event-free survival in patients with heart failure. J Cardiovasc Nurs. 2018 Jan-Feb; 33(1):40-6.
10. Brody JE. The cost of not taking your medication [Internet]. New York, NY: The New York Times; 2017 4 17 [cited 2024 Aug31]. Available at: www.nytimes.com/2017/04/17/well/the-cost-of-not-taking-your-medicine.html.
11. Webber, J., Stewart, A.V., & Becker, P.J. (2013). The effect of a reminder diary on risk factors in patients with chronic hypertension attending a clinic at a hospital in Johannesburg, South Africa. African Journal of Primary Health Care & Family Medicine, 5.
12. Santoleri F, Lasala R, Logreco A, Ranucci E, Costantini A. Using a treatment diary to improve the medication adherence in patients with chronic myeloid leukaemia. J Oncol Pharm Pract. 2019 Jul;25(5):1035-1041. doi:10.1177/1078155218759184. Epub 2018 Feb 20. PMID: 29460706.