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Impact of Poor Therapeutic Adherence in Diabetes and Strategies for Improvement

Definition of Therapeutic Adherence and Measurement Methods: According to the World Health Organization (WHO), therapeutic adherence is defined as the extent to which a patient follows the guidelines established by health care professionals, including both the prescribed pharmacological treatment and the recommended lifestyle changes (1).

To measure adherence, we can use different methods, which can be classified as direct and indirect. Each of them has advantages and limitations, and the choice will depend on the type of treatment, the patient’s condition, and the available resources (2).

1. Direct Methods:

- **Biological Analysis:** These are the most precise but are costly and not always accessible. They include measuring drug or metabolite levels in blood or urine samples.

- **Direct Observation:** This refers to the direct supervision of administration in certain contexts, such as in hospitals or when treatments are dispensed at home by health care teams.

2. Indirect Methods: These are the most common in clinical practice.

- **Interviews or Questionnaires:** These ask the patient how they are following the treatment. One of the most well-known is the Morisky-Green questionnaire (*Table 1*), although there are many other validated tools.

- **Prescription Review:** This involves counting the withdrawal of pharmacy prescriptions.

- **Electronic Devices:** Some medication packaging records each time the bottle is opened, providing data on the frequency of use.

- **Patient Diaries:** The patient records when and how they take their drugs.

- **Clinical Evaluation:** This involves observing changes in the patient’s health status that

may be indicative of whether they are adhering to treatment (e.g., monitoring blood glucose levels in people with diabetes).

Despite having multiple options to assess therapeutic adherence, its measurement is still scarcely reported in the scientific literature and rarely addressed in consultations, which remains a pending issue in our clinical practice.

HOW IS THERAPEUTIC ADHERENCE IN DIABETES?

In chronic diseases that require lifelong treatment, achieving high therapeutic adherence is a difficult challenge and can have serious health repercussions.

If we focus specifically on treatment adherence in diabetes, the published data clearly reflect these difficulties (3).

Type 1 Diabetes Mellitus (T1DM):

In Spain, studies on adherence in T1DM are limited. An analysis conducted in Galician pharmacies showed that approximately 50% of patients did not adequately follow therapeutic guidelines. Another study in Andalusian hospitals in children and adolescents with T1DM observed that adolescents had lower adherence than children. Internationally, studies show that between 20% and 45% of people do not use insulin correctly, leading to worse blood sugar control and more hypoglycemic episodes. Factors such as adolescence, weekends, or holidays can affect compliance. Additionally, in developing countries, up to 14% of patients voluntarily abandon insulin within the first month of treatment. »

INTERNATIONAL STUDIES SHOW THAT BETWEEN 20% AND 45% OF PEOPLE WITH TYPE 1 DIABETES MELLITUS DO NOT USE INSULIN CORRECTLY, WHICH WORSENS THEIR CONTROL AND INCREASES THE RISK OF HYPOGLYCEMIA

TABLA 1: Test de morisky green

1.- Do you ever forget to take your drugs for your condition?	YES	NO
2.- Do you take your drugs at the prescribed times?	YES	NO
3.- When you feel well, do you stop taking your medication?	YES	NO
4.- If medication makes you feel unwell, do you stop taking it?	YES	NO

A person answering “Yes” to all the questions would be indicative of good adherence.



» Regarding adherence to treatments to prevent complications, such as statins, it is also insufficient in this population. For example, in a cohort of T1DM patients who started statin treatment, 27% abandoned therapy within the first 18 months. In adolescents with T1DM, the use of drugs to reduce cardiovascular risk decreased significantly over time, from over 90% at the start of treatment

to < 80% after 2-4 years. These data highlight the challenges of maintaining adherence in T1DM, especially in youth and with long-term prevention therapies.

Type 2 Diabetes Mellitus (T2DM):

In Spain, it is estimated that between 35% and 50% of T2DM patients have

difficulties in adequately following treatment, with better adherence in newly diagnosed patients that decreases over time. Factors such as primary care follow-up and education in healthy lifestyle habits seem to positively influence adherence. Even with new antidiabetic drugs, adherence remains a challenge. A study in Catalonia showed that more than 30% of patients on treatments like SGLT-2 »

» inhibitors had insufficient adherence at 24 months (5), and another study with GLP-1 receptor agonists found that while initial adherence was 74%, it dropped down to 50% after 2 years (6).

Internationally, just over half of people with T2DM have good adherence, although there are variations between countries with available studies. A recent review including nearly 70,000 patients from representative studies across all continents concluded that global adherence to oral antidiabetic treatments was 52%, with the main reasons for low adherence including forgetfulness, concerns about drug side effects, the complexity of therapeutic guidelines, and dissatisfaction with treatment (e.g., due to pill size or taste) (4).

Regarding therapies not focused on glucose control, such as statins, initial adherence is high, but up to 25% abandon treatment within the first 6 months. This pattern of progressive decline in adherence, especially with cardiovascular prevention therapies, reflects global challenges in managing T2DM.

IMPACT OF LACK OF THERAPEUTIC ADHERENCE ON THE HEALTH OF PEOPLE WITH DIABETES

Type 1 Diabetes Mellitus (T1DM):

Adequate adherence to nutritional treatment and insulin is essential to control blood glucose and prevent serious complications in T1DM. Studies such as the DCCT (Diabetes Control and Complications Trial) have shown that patients on intensive therapy significantly reduced the occurrence of microvascular complications and major cardiovascular events in the long term, and for this, treatment adherence is essential (7). Conversely, lack of adherence, especially in adolescents, has been linked to complications such as ketoacidosis, frequent hypoglycemia, and psychiatric disorders. Additionally, poor compliance with other treatments that reduce cardiovascular risk, such as statins, can accelerate the onset of cardiovascular events.

Type 2 Diabetes Mellitus (T2DM):

Adherence to treatment is also crucial to maintain good blood glucose control and re-»

LACK OF ADHERENCE IN PEOPLE WITH TYPE 2 DIABETES MELLITUS IS ASSOCIATED WITH A HIGHER RISK OF POOR GLUCOSE CONTROL, AS WELL AS SEVERE HYPOGLYCEMIA, HEART ATTACKS, STROKES, AND HEART FAILURE



TABLA 2: causas de insuficiente adherencia en diabetes

CAUSE	DESCRIPTION
<i>Systemor health care professional-related factors</i>	
Lack of communication with health care professionals	A lack of educational resources, poor communication, and limited knowledge of the disease can lead patients to believe that treatment is inadequate, making adherence more difficult.
Lack of trust in health care professionals	Limited consultation time and frequent doctor turnover can hinder the development of a trusting relationship between doctor and patient, negatively affecting adherence.
Therapeutic inertia or outdated medical knowledge	Failure to stay updated and poor adherence to clinical guidelines among health care professionals can negatively impact patient adherence to recommended treatments.
Economic cost of medication	The high cost of medications in non-subsidized health care systems may discourage patients from following treatment, especially those who are most vulnerable.
Complex insulin regimens	Complicated treatment plans, including multiple doses, increase the risk of errors and make adherence more difficult, particularly for elderly patients.
Polypharmacy	Taking multiple medications simultaneously increases the risk of forgetfulness or confusion, which can negatively impact adherence.
<i>Patient-related factors</i>	
Lack of support from close contacts	The absence of a trained caregiver or knowledgeable individuals in the patient's environment may lead to a lack of motivation in following treatment.
Socioeconomic status and personal circumstances	Low health literacy in certain populations makes it difficult for patients to understand their disease and the importance of adhering to treatment.
Low satisfaction with prescribed treatment	Side effects, such as weight gain, or negative perceptions of treatment (e.g., fear of insulin therapy) can reduce adherence.

» duce the risk of serious complications, such as cardiovascular diseases or kidney failure. Lack of adherence is associated with a higher risk of poor glucose control, but also of severe hypoglycemia, as well as the risk of heart attacks, strokes, and heart failure. Non-compliance with other treatments for blood pressure or cholesterol can also accelerate the onset of serious complications. Additionally, maintaining a healthy lifestyle, including a balanced diet, regular exercise, and avoiding tobacco and alcohol, is essential to prevent complications and improve the quality of life of people with T2DM. Finally, there are indications that good adherence to antidiabetic drug may reduce the risk of overall mortality and hospitalization in T2DM, although few studies investigate these aspects (8).

Beyond the impact on health, diabetes management represents a high economic cost for health care systems, closely linked to therapeutic adherence and prevention of complications. In the United States, approximately 1 in 7 dollars of health care spending is allocated to diabetes and its complications, and studies show that good therapeutic adherence can significantly reduce long-term costs, despite higher initial spending on drugs and devices (9). However, practices such as insufficient monitoring of renal function prevent the detection of chronic kidney disease (CKD) in early stages, which considerably increases health care costs. For example, patients with T2DM and advanced albuminuria generate significantly higher annual costs due to more hospitalizations and prolonged stays. In Europe, costs associated with hospitalization for complications represent between 40% and 60% of the total, highlighting that early treatment intensification is cost-effective by reducing the frequency and severity of these complications.

STRATEGIES TO IMPROVE THERAPEUTIC ADHERENCE IN DIABETES

Some of the main causes of insufficient adherence in diabetes are summarized in Table 2. Of note, not all depend on the patient, but also on the professional or even the health care system. Therefore, the strategies we must apply to improve therapeutic compliance should also be designed to address problems from different areas (Figure 1A and 1B). **D**

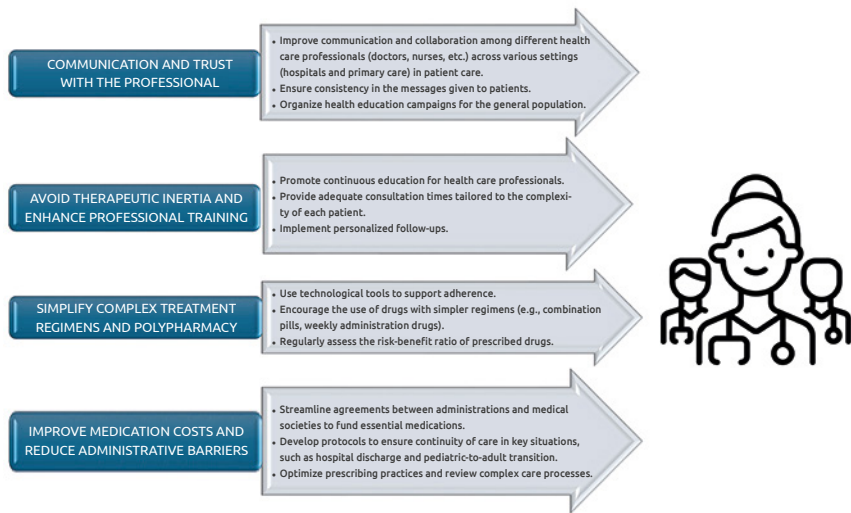


FIGURE 1A: Strategies to improve adherence focused on the health care system and professionals

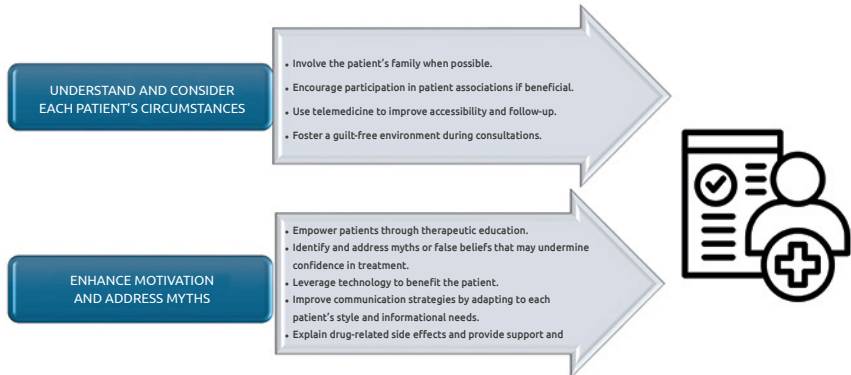


FIGURE 1B: Strategies to improve adherence focused on the patient

CONCLUSION

In conclusion, adherence is a key factor in diabetes management, and lack of therapeutic compliance has a huge impact on patient health, increasing their risk of complications and associating higher health care costs. Although we have various methods to measure adherence, it remains a significant challenge, especially in young populations and in the context of long-term therapies, such as those aimed at preventing cardiovascular complications. It is essential to address the multiple causes influencing treatment non-compliance, not only from the patient's perspective but also considering factors related to health care professionals and the health care system. Implementing effective strategies that address these causes could significantly improve clinical outcomes, reduce long-term costs, and ultimately improve the quality of life of people with diabetes.

REFERENCES

1. Adherence to long-term therapies: evidence for action. Geneva, World Health Organization, 2003, accesible en <https://www.paho.org/en/documents/who-adherence-long-term-therapies-evidence-action-2003>. [página visitada el 26 de diciembre de 2024]
2. Jimmy B, Jose J. Patient medication adherence: measures in daily practice. *Oman Med J*. 2011;26(3):155-9.
3. Cebrián-Cuenca AM, Villar-Taibo R, Bellido V, Pinés-Corrales PJ. Consecuencias de la inadecuada adherencia terapéutica en diabetes mellitus y propuestas de mejora. *Aten Primaria Pract*. 2024;6. doi: 10.1016/j.appr.2024.100207.
4. Boonpattharatthiti K, et al. Prevalence of adherence to oral antidiabetic drugs in patients with type 2 diabetes: A systematic review and meta-analysis. *J Diabetes Investig*. 2024;15(11):1614-25.
5. Vlachó B, Mata-Cases M, Mundet-Tudurí X, et al. Analysis of the adherence and safety of second oral glucose-lowering therapy in routine practice from the Mediterranean area: A retrospective cohort study. *Front Endocrinol (Lausanne)*. 2021;12:708372.
6. Palanca A, van Nes F, Pardo F, Ampudia Blasco FJ, Mathieu C. Real-world evidence of efficacy and safety of SGLT2 inhibitors as adjunctive therapy in adults with type 1 diabetes: A European two-center experience. *Diabetes Care*. 2022;45:650-8.
7. The Diabetes Control and Complications Trial Research Group. The effect of intensive diabetes therapy on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329(14):977-86.
8. Khunti K, Seidu S, Kunutsor S, Davies M. Association between adherence to pharmacotherapy and outcomes in type 2 diabetes: A meta-analysis. *Diabetes Care*. 2017;40(11):1588-96.
9. Mehta RR, Edwards AM, Rajpathak S, Sharma A, Snow KJ, Iglay K. Effects of conformance to type 2 diabetes guidelines on health care resource utilization, clinical outcomes, and cost: A retrospective claims analysis. *J Clin Transl Endocrinol*. 2020;19:100215.