

THEORETICAL ARTICLE/ESSAY

Therapeutic adherence: contributions to understanding and intervention

Adesão terapêutica: contributos para a compreensão e intervenção

Adherencia terapéutica: contribuciones a la comprensión e intervención

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Abstract

Background: Therapeutic adherence (TA) aims to improve the health of individuals and populations. It is highly complex and influenced by multiple factors. Non-adherence rates are still excessively high, and it is important to know more about them to intervene.

Objectives: To analyze concepts of TA, reflect on factors associated with TA, systematize intervention strategies, and understand assessment methods.

Main topics under analysis: As part of patient behavior, TA is the expected outcome of health professionals' recommendations/prescriptions, following mutual cooperation. Patient motivation is essential to overcome barriers to behavioral change, and patients are considered co-responsible for their treatment. Health professionals adopt TA promotion strategies to benefit and mobilize users. Health services and policies support the minimization of obstacles and encourage the evaluation of TA to improve practices.

Conclusion: TA is multifactorial, which makes the process more difficult. Successful TA requires coordinating all involved stakeholders - users, health professionals, and social and political bodies, by anticipating the appropriate measures.

Keywords: treatment adherence and compliance; patient non-adherence; treatment; intervention; evaluation

Resumo

Enquadramento: A adesão terapêutica (AT) visa a melhor saúde dos indivíduos e populações, reveste-se de grande complexidade e é influenciada por múltiplos fatores. As taxas de não-adesão continuam demasiado elevadas, sendo importante melhor conhecer para intervir.

Objetivos: Analisar conceitos de AT; refletir sobre fatores associados à AT; sistematizar estratégias de intervenção; compreender métodos de avaliação.

Principais tópicos em análise: A AT, enquanto comportamento do utente, é esperada como resposta às recomendações/prescrições dos profissionais de saúde, após cooperação mútua. A motivação do utente para ultrapassar barreiras à mudança de comportamento mostra-se fundamental. O utente é tomado como corresponsável pelo tratamento. Os profissionais de saúde adotam estratégias de promoção da AT em prol dos utentes, mobilizando-os. Serviços e políticas de saúde apoiam a minimização dos obstáculos e incentivam a avaliação da AT para melhorar práticas.

Conclusão: A AT é multifatorial, o que dificulta o processo. Para o êxito da AT é necessária coordenação exemplar de todos os atores envolvidos, utentes, profissionais de saúde e instâncias sociais e políticas, antecipando medidas adequadas.

Palavras-chave: adesão terapêutica; não-adesão terapêutica; tratamento; intervenção; avaliação

Resumen

Marco contextual: La adherencia terapéutica (AT) tiene como objetivo mejorar la salud de los individuos y las poblaciones, es muy compleja y está influida por múltiples factores. Las tasas de no adherencia siguen siendo demasiado elevadas, y es importante comprenderlas mejor para poder intervenir.

Objetivos: Analizar los conceptos de AT; reflexionar sobre los factores asociados a la AT; sistematizar las estrategias de intervención; comprender los métodos de evaluación.

Principales temas en análisis: La AT, como comportamiento del usuario, se espera como respuesta a las recomendaciones/prescripciones de los profesionales de la salud, tras una cooperación mutua. La motivación del usuario para superar las barreras al cambio de comportamiento es esencial. El usuario se considera corresponsable del tratamiento. Los profesionales sanitarios adoptan estrategias de promoción de la AT en favor de los usuarios y los movilizan. Los servicios y las políticas sanitarias apoyan la minimización de los obstáculos y fomentan la evaluación de la AT para mejorar las prácticas.

Conclusión: La AT es multifactorial, lo que complica el proceso. El éxito de la AT requiere una coordinación ejemplar de todas las partes interesadas, los usuarios, los profesionales sanitarios y los organismos sociales y políticos, y anticipar así las medidas adecuadas.

Palabras clave: adherencia terapéutica; incumplimiento terapéutico; tratamiento; intervención; evaluación

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Introduction

Therapeutic adherence (TA) is a multidimensional, multifactorial, and highly complex process with consequences on the health of individuals and populations and social, economic, environmental, and political implications, whose negative effects result from non-adherence to the prescribed therapies (Kini & Ho, 2018; World Health Organization [WHO], 2003).

According to the WHO, TA is the degree or extent to which a person's behavior with regard to taking medication, following a diet, and executing habit or lifestyle changes corresponds with the recommendations provided by health professionals (WHO, 2003). This concept includes prescribed pharmacological or non-pharmacological treatments and all proposed prophylactic and health-promotion measures.

Adhering to the regimen recommended by health professionals is hard. In developed countries, where chronic diseases affect half the population and increase with age, the degree of adherence to treatment for these diseases is about 50%. (Fernandez-Lazaro et al., 2019; Horne et al., 2019; Kini & Ho, 2018). This percentage is lower in developing countries, which seriously harms individual and global health (WHO, 2003).

The global economic impact caused by these diseases is expected to account for 65% of global health care costs, causing strong worldwide public health concerns as this impact is frequent, widespread, and independent of the therapeutic area (Coelho et al., 2017; Kini & Ho, 2018; WHO, 2003).

Since the 1970s, the literature on TA and non-adherence rates has shown great variability, demonstrating difficulties in collecting accurate information. Non-adherence rates range from 4% to 94% (Martins et al., 2017; Meichenbaum & Turk, 2012), with the consensus ranging from 30% to 50% or 60% in long-term, chronic disease-related prescriptions (Coelho et al., 2017; Haynes et al., 1979; Martins et al., 2017; WHO, 2003). In therapeutic regimens, these rates vary between 30% and 40%. In acute, symptom-relieving situations, adherence drops to between 70% and 80% within a short period of 10 days. In more committed patients, treatment adherence tends to decline within 3 to 5 days of starting treatment. Prevention programs have the lowest adherence, as 50% to 70% of patients fail these programs (Meichenbaum & Turk, 2012; Panesar, 2012).

Research is extensive in this area, and some examples can be highlighted. In diabetes, only 7% of patients fully adhere to good disease control. Instead, 80% of patients administer insulin inappropriately (e.g., doses, asepsis, safety, needle and syringe replacements), 73% do not follow their diet, and 50% have poor foot care. (Meichenbaum & Turk, 2012). In arterial hypertension (AH), about 50% of patients do not adhere to the proposed treatment (e.g., adequate diet, exercise, stress management, medication). In HIV (human immunodeficiency virus) infections, adherence rates are higher than 50% (Meichenbaum & Turk, 2012), while, at some point, 44% of transplant patients do not take immunosuppressive therapy (Coelho

et al., 2017). In psychiatry, 51% to 85% of patients with schizophrenia do not adhere to treatment (Gorczyński et al., 2017), as well as 9% to 57% of those with bipolar disorder (Meichenbaum & Turk, 2012). In Portugal, 50.8% of psychiatric patients discontinuously adhere to the therapeutic regimen (Monterroso et al., 2012). In cases of hyperactivity, 20% of parents provide discontinuous treatment to their children by the 4th month, and by the 10th month, this figure rises to 50%. (Meichenbaum & Turk, 2012).

Evidence shows that the first year is the most critical period for deciding whether or not to continue treatment (Coelho et al., 2017). More than 50% of patients discontinue treatment during this period, most of whom do so within the first 3 months. Even with a high adherence rate of 74.1%, more than 80% of patients take an interval without medication longer than 30 days. Non-adherence causes patients problems and places a great burden on health care professionals (Horne et al., 2019).

Multiple internal and external factors influence TA, making it highly complex. One of the necessary conditions for patients to comply with the prescribed treatment seems to be their commitment, which implies understanding the disease and the treatment benefits and making positive behavioral changes. Nevertheless, current studies emphasize the greater importance of intrinsic motivation and the ability to carry out the treatment (Horne et al., 2019). The concept of TA will have to be further rethought based on the clinician's (the prescribing health professional) involvement with the patient. This theoretical article aims to analyze TA concepts, reflect on the factors associated with TA, systematize intervention strategies, and understand the methods for assessing TA.

Development

Concept evolution

The first empirical study on patient adherence to treatment appeared in 1968 (Meichenbaum & Turk, 2012). During the following decade, Haynes, based on a literature review involving 500 studies, and after concluding that 20% to 60% of users of health care services did not *comply* with the treatment prescribed or indicated by the physician, defined *compliance* as the situation in which the patient's behavior corresponds to the clinical instructions provided (Haynes et al., 1979). This first concept is inscribed in the biomedical model, foreseeing the hierarchical subordination of the patient to the physician, denying the person's psychological and social dimensions. However, in a first revision, it was redefined as the extent to which the patient's behavior coincides with medical or health advice (Haynes et al., 1979), allowing for not only therapeutic measures but also the preventive and health-promoting measures proposed by the physician, or other health professionals. This revision aligns with behavioral medicine and health, whose development began in the mid-20th century (Ogden, 2004). Later on, the so-called *compliance*, used in Anglo-Saxon countries, was replaced by *adherence*, abandoning the idea of obedience and supporting the

cooperation and alliance between clinician and patient to achieve treatment effectiveness (Camarneiro, 2002; Meichenbaum & Turk, 2012; Panesar, 2012).

The concept centered on the patient's best interest defines TA as the active attitude, with voluntary and mutual involvement of the patient and the health professional in a collaborative process to change the patient's behavior (Meichenbaum & Turk, 2012). It is a concept inscribed in the biopsychosocial model, which has laid bridges for new practices and research (Camarneiro, 2002).

In the Anglo-Saxon literature, the word *compliance* is still used today, but WHO recommends *adherence* (WHO, 2003) because its meaning corresponds to the current view. Compliance has also been used to characterize the agreement reached regarding medication therapy, after the discussion between the health professional and the patient, to respect the patient's feelings and beliefs regarding if, when, and how the medications should be taken (Panesar, 2012). In Portugal, adherence is the terminology used regardless of the revisions of the concept.

Manifestations and forms of therapeutic adherence and non-adherence

TA is expressed through a set of behavioral changes that coincide with following the prescribed therapeutic regimen, such as taking and purchasing medication, healthy living habits, proper diet, physical exercise, avoiding risky behaviors, and keeping follow-up appointments.

Adherence to therapy generally increases with the severity of the illness and information about it and decreases or disappears during complex or demanding treatments. These include treatments that require lifestyle changes, those with prolonged duration, and those with many side effects.

Non-adherence to therapy is responsible for many deaths and hospitalizations (Kini & Ho, 2018). Non-adherence translates into the patient's negative attitude, involving an evaluative component that is the patient's responsibility, and that can occur at three levels: medication, treatment, and behavior (Meichenbaum & Turk, 2012). In the first case, there is total non-compliance with the medication prescription, failure to follow the instructions given for doses and/or frequency of prescription, and taking non-prescribed medication. In the second case, non-adherence to treatment is observed when the person postpones seeking care, does not start the proposed treatment, deliberately does not follow instructions, or decides to end the prescribed treatment prematurely. Lastly, at the behavioral level, non-adherence is characterized by the rejection of recommended preventive measures, the partial implementation of instructions, the sabotaging of the treatment regimen, the non-participation in prescribed health programs, and the creation of an own treatment regimen and substitution of the recommended treatment. Some of the non-adherence indicators mentioned above refer to the concept of partial, intentional, or unintentional TA. Partial adherence to therapy refers to possible errors or lapses related to complying with the therapy without abandoning it. When intentionality exists, the person chooses to change the prescription unilaterally, without

sharing the decision with the prescriber. This usually occurs when the person feels much better or worse, experiences side effects, is unaware of the real need for treatment or wishes to drink alcohol. In situations where there is no intentionality, the most common causes are forgetfulness, for example, of the prescribed dose, confusion with treatment regimens, difficulties in understanding an imprecise label, and/or the inability to open medication containers. This type of partial adherence is more frequent during the acute phase of the disease (Horne et al., 2019; WHO, 2003).

The consequences of total or partial non-adherence to therapy are very serious, including increased likelihood of treatment failure, avoidable complications and suffering, increased health care costs, increased mortality and morbidity, relapse and extension of the treatment period (WHO, 2003).

Although the focus of following the prescribed therapy is on individual action, several factors involved in the process and (co)responsible for adherence or non-adherence to treatment are presented next.

Factors related to therapeutic adherence

Ever since concerns about TA emerged, there has been an attempt to understand the related factors. Given its complexity, and although none of the factors can explain it sufficiently on its own (Meichenbaum & Turk, 2012), they interact and reinforce each other (Fernandez-Lazaro et al., 2019). WHO has organized into five major groups the factors that are associated with TA, namely: social, economic, and cultural factors; factors related to health professionals and services; factors related to the underlying disease and comorbidities; factors related to the prescribed treatment; and individual patient-related factors (Cabral & Silva, 2010; WHO, 2003). Although WHO uses the terminology *patient*, the word *user* refers to the person using health services. The term patient is reserved for very specific situations of people with a particular disease. Based on the categorization presented, we now discuss and reflect on the key aspects of the factors associated with TA behavior.

- a) Social, economic, and cultural factors. All these factors are interconnected. The most relevant social factors are health services organization, proximity to users, health promotion and disease prevention policies, support networks, access to information, training/education, and health literacy. The economic factors include the financial resources, access to services, costs, and time needed for treatment. The cultural factors involve health beliefs, health practices, disease stigma, context, and environment.
- b) Factors related to the underlying disease and comorbidities. The type of disease, chronic or acute, symptomatic or asymptomatic, the severity and duration, the number of associated diseases, and the risk of contracting other diseases are all key aspects in adherence to treatment. Silent diseases mislead patients into thinking that there is no disease because of the lack of symptoms. This is

largely due to the invisibility of the immediate deterioration caused by non-adherence to medication (Horne et al., 2019).

- c) Factors related to health care professionals and services. Communication between clinicians and patients is crucial. Managing communication is the health professionals' responsibility as it must be essentially therapeutic, user-centered, and context-appropriate. Health professionals favor oral communication when providing information to their users, but unfortunately, communication problems are the main reasons people do not adhere to therapy. Examples of these problems include people's fear of asking questions and asking for clarification, lack of attention to explanations given about treatment, poor understanding of the benefits of treatment, and lack of confidence (Cabral & Silva, 2010). Ley's Cognitive Hypothesis Model of Communication (Ogden, 2004) places the focus of TA on the user's satisfaction with the appointment. This includes the user's perception of the clinician's behavioral aspects (attitude, assessment of vital parameters, prescription filling, or handing out information documents such as leaflets), affective aspects (e.g., mutual gaze, empathy, active listening), and professional competence (at the time, or previously following the advice of others). User satisfaction is mediated by understanding the disease and the affected organ and by mnemonic capacity (the ability to remember the information provided during the consultation). Information memorization tends to decrease when high levels of anxiety are present. Health professionals who can establish adequate communication and trust relationships can capture the patient's attention for the success of the therapy.
- d) Factors related to the prescribed therapy. These assume greater relevance when they concern pharmacological therapies. Their intake and organic effect refer to the type of medication, adverse reactions, side effects, length of action, treatment complexity and demand, and perception of the need for the medication. Many people hold a negative view of medications because they are chemicals, not natural products, perceiving them as harmful if taken for long periods or in high doses, accumulating in the body and creating dependencies (Horne et al., 2019). Overall, patients report feeling well with the medications they take. However, some patients indicate side effects, deterioration of their condition, poor treatment effect, doubts about efficacy, overly long prescriptions and/or too many medications, difficulty complying with prescriptions, and discontinuing medication because they feel well (Cabral & Silva, 2010; Fernandez-Lazaro et al., 2019; Monterroso et al., 2012). A small number of patients also abandon treatment to avoid mixing medication with alcohol or other substances that they cannot do without (Cabral & Silva, 2010). Furthermore,
- regarding the factors under analysis and from an instrumental point of view, the management required by the therapy, the possible financial issues, the medication distribution system, the number of medications, and the type of packaging/containers available, plus the belief that brand-name medications work better than generic ones, form important barriers to adherence. Adherence to the pharmacological treatment regimen is associated with responsibility, knowledge about the medications, and understanding the therapeutic scheme and proactive strategies.
- e) Individual person-related factors. These relate to personal and psychological characteristics associated with TA behavior. Age is the most relevant of the personal demographic characteristics. WHO recommends that age be considered in a particular and independent way from other factors. Research suggests that adolescents adhere less to treatment than younger children, which seems related to parental understanding and supervision of compliance with treatment instructions. Adolescents, unlike children, perceive this supervision as a form of control, and the consequence is non-compliance with the proposed therapeutic regimen (Horne et al., 2019; Eindhoven et al., 2018). Among older adults, a polymedicated group that requires special attention, the lack of memory may condition TA, but the fact that they have more time available or perceive more effectively that disease severity can anticipate death may promote greater adherence to the proposed treatment. Other relevant personal characteristics contribute to lower TA, such as gender, in which women adhere less than men to treatment after myocardial infarction (Eindhoven et al., 2018), low intellectual level, and poor knowledge about the medication regimen (Fernandez-Lazaro et al., 2019). With regard to psychological aspects, understanding the seriousness of the disease, experiencing it as threatening, and perceiving the high risk involved increase adherence rates. The belief that treatment will be effective, the self-perception of having a good quality of life (Fernandez-Lazaro et al., 2019), and being married (Adams et al., 2020) are also favorable. Current literature has found that motivation for treatment, associated with the ability to follow through with it, is the most relevant internal attribute for successful TA (Horne et al., 2019). In the 1990s, Leventhal explained the motivation to resume health status in the face of symptoms or signs in the Self-Regulation Model of Illness. The model is based on the representations of health threats and emotional states, as well as triggered avoidance or approach coping strategies, and reflection on the action (Ogden, 2004). Forgetfulness and mnemonic capacity have also been strongly related to low levels of adherence, and it is highly important to continue to consider their relevance (Cabral & Silva, 2010; Fernandez-Lazaro et al.,

2019; Monterroso et al., 2012). Other psychological variables compromise TA, such as attitudes and beliefs, namely beliefs about pharmacological treatments or a particular medication, which are more predictive than beliefs about diseases (Horne et al., 2019), reduced awareness of triggers, external locus of control, poor self-efficacy, low level of acceptance, lack of motivation, maladaptive coping styles (Matsuzawa et al., 2019), personality characteristics, expressed by oppositional behavior (the unwillingness or dislike of taking medication), and carelessness and/or falling asleep before the time to take medication (Cabral & Silva, 2010). And also psychopathological disorders, such as anxiety and depression, or other altered mental states (Matsuzawa et al., 2019).

The complexity of all these variables makes interventions difficult. The proposed changes will have to consider the context, the health system, and individual factors.

Intervention

Treatment adherence is the ultimate outcome of health intervention programs. Promoting behavior modification is the most challenging task of those interested in changing populations' lifestyle habits, promoting health, preventing disease, and providing well-being to people with chronic diseases. Some predictive models of behavior help plan interventions. For example, the classic Health Belief Model, including self-efficacy (the people's belief in their abilities, particularly those to face challenges and achieve goals) and cues to action, as well as later models and theories with the same principles (Ogden, 2004), have contributed to interventions, greatly improving the intended outcomes (Panesar, 2012). All these models clearly show that successful interventions largely rely on making individuals co-responsible for their health. Together with health professionals, they become active participants in promoting preventive or therapeutic care (Martins et al., 2017). Nevertheless, these interventions should aim at improving the motivation for treatment, which may include, as much as possible, the elimination of barriers to adherence (Horne et al., 2019; Kini & Ho, 2018; Matsuzawa et al., 2019; Panesar, 2012). The most effective interventions combine cognitive, behavioral, and affective components and can be educational, behavioral, and digital.

Educational interventions promote knowledge. These interventions highlight the benefits and need for treatment, as well as explaining beliefs about diseases. The programs can be individual and/or group-based and offer the advantage of improving people's knowledge of the disease and treatment and understanding the need to comply with the proposed regimen. Personalized telephone counseling or sessions with health educators can be used.

Behavioral interventions incorporate adaptation and facilitation mechanisms into the daily routine to achieve compliance with the proposed treatment.

Digital interventions, in the form of programs or applications (APPs), are becoming increasingly important in health and have the advantage of integrating educational

and behavioral aspects. They can be accessed through mobile phone APPs, automated phone messages, computer-generated messages, and video consultations providing recommendations and increasing health literacy. They alert, for example, to adherence to appointments, medical examinations, therapy, prescription purchase for maintenance of the proposed regimen, and vaccination. A study on mobile APP use showed that it increases TA by 10% to 33% (Kini & Ho, 2018), reduces missed doses and medication errors, and becomes an appropriate method of medication management at home. Nonetheless, after 12 to 18 months, this effect may reverse, perhaps due to an accommodation effect (Pérez-Jover et al., 2019). Patients' internet use should be monitored due to some difficulties noted in the short term. In particular, patients who used the internet after the consultation, compared to those who did not, reported lower adherence after 3 weeks. The ones who already used the internet before the consultation, compared to those who did not, reported having more concerns about their medication. Those who used the internet throughout treatment valued their concerns higher after 6 months (Linn et al., 2019).

Health professionals are responsible for applying and proposing a set of educational, behavioral, and digital actions for patients to adopt that ensure better TA. Their responsibility is further increased in the following aspects.

- 1) Communication. During consultations or direct follow-up telephone calls, communication and direct counseling help improve and develop the relationship established with the patient. It is necessary to minimize the disadvantages of oral communication, the primary method of relationship, to ensure users' easy access to clinicians by placing the patient at the center of care, the improvement of teaching skills, the recognition of patients' spiritual and psychological dimensions, and the accurate recognition of the problem (Panesar, 2012). Furthermore, it is essential to take into account some principles, such as the primacy effect, the clarification of the importance of TA, the simplification of information, the use of repetition, the clarity of the language used, and following the consultation with additional interviews (Ogden, 2004). Digital, written, or audiovisual information has great advantages when used in association with oral information because it increases knowledge and adherence and improves outcomes (Meichenbaum & Turk, 2012).
- 2) Therapeutic regimen. To maximize the simplification of therapeutic regimens or facilitate the management of the therapeutic regimen by reducing the number of doses and medications.
- 3) Treatment value. To highlight the value of the treatment and indicate the benchmarks for assessing treatment success, including a description of treatment complexity, benefits, and associated side effects. To include the treatment in the client's daily routine.
- 4) Access to treatment. To make the best choices to facilitate access. To provide medication supply at

- the workplace (occupational health).
- 5) Minimizing forgetfulness and errors. To ensure that the action is carried out, creating reminders that prevent forgetfulness, such as digital or manual organizers and reminders, including blister packs, calendars, dose counters, medication counter and dispenser boxes, controlled-delivery devices, calibrated forms of dosage, special containers (e.g., organizing medication in individual packs/containers with the information of the day of the week and time), and/or using visual instructions for taking medication.
 - 6) Reinforcement and/or reward. To reward users for their efforts to improve therapeutic outcomes by reducing visit frequency, providing financial incentives, or facilitating the acquisition of goods (e.g., sphygmomanometer in patients with AH; installation of an APP).
 - 7) Involvement. To involve users in their treatment by promoting and improving the self-monitoring of the disease (e.g., blood glucose, blood pressure, respiratory function) and self-administration of treatment increases the likelihood of users being receptive to change because they believe they are acting independently with regard to that change. Family involvement should be considered according to the users' wishes and needs.
 - 8) Counseling and cognitive therapies. In cases where it is necessary to increase or maintain adherence behavior through additional measures, counseling or brief therapies have shown good results. Motivational interviewing is one of the most widely used techniques, as it has proven more favorable than traditional counseling approaches. It focuses on the user's intrinsic motivation and explores the reasons behind the barriers to taking medications or other therapies. Nevertheless, it is a decision to be made by the therapist.

In the process of adjusting to chronic illness, mediated by beliefs, self-efficacy, and motivation, the key is to educate, empower, and persuade, as well as changing relationships, concepts, beliefs, attitudes, and environment.

Evaluation

The assessment of TA is done using direct and indirect methods. The direct measurement methods include several tests with biological and biochemical screening markers to detect medication levels in body fluids. Although these methods are more accurate than indirect methods, they are expensive, require close monitoring, and their execution is not always possible. They are most common in hospitals or other inpatient settings. Moreover, some issues regarding the variability of pharmacokinetics cannot be controlled (Panesar, 2012).

Indirect methods of measuring adherence (self-report) are subject to greater bias and are not as accurate as direct methods. User reports and family interviews are highly subjective and tend to overestimate adherence. Nevertheless, they can provide useful data, among others, to personalize the patient's medication/treatment. The main

problem is the possibility that patients will lie out of a desire to please.

Besides interviews, indirect methods include diaries, pill counts, prescription filling dates, prescription renewal rates, and electronic medication monitors. However, these methods also present disadvantages. Pill counts are useful for evaluation but encourage waste. Dates are only accurate if the user purchases the medication at the same pharmacy and the database is accurate. Filling a prescription on time does not necessarily mean that the user is taking the medication correctly. Medication event monitoring systems (MEMS) are newer electronic forms that note the time and date a medication bottle is opened. However, this does not necessarily mean that the user took the medication when the bottle was opened. Furthermore, the user's condition may change due to factors other than the medication, and the resulting therapeutic outcome may be altered (Panesar, 2012).

The clinical criterion, which corresponds to "best adherence, best clinical outcome," is not a valid criterion for evaluation because the patient may adhere and not manifest the desired outcome or may not adhere and improve for unknown reasons. In addition, both the so-called *toothbrush* effect, where the patient adheres to treatment immediately before the visit to the health professional, and the *white coat* AH alter the results. Lastly, based on professional experience, as pointed out by some health professionals, the so-called *clinical eye* criterion is useless and worthy of criticism. Most published literature is based on this type of measurements.

Every method has methodological limitations and advantages and disadvantages, differing in validity, reliability, and sensitivity (Coelho et al., 2017). Thus, combined methods are the most effective.

Conclusion

TA is a behavior with multifactorial and multimodal influences. Health professionals' actions and the user's active participation are important parts of the solution. TA is promoted through educational, behavioral, and digital technology measures taking into account cognitive, affective, and behavioral dimensions. During the intervention, interpersonal relationships and communication are highlighted, taking into account the explanation of the belief model, the understanding of the person's concerns and expectations about the disease and treatment, as well as the follow-up with interviews, home visits, and/or follow-up consultations. The involvement of a close family member can be considered helpful. Facilitating the therapeutic scheme, assessing its difficulties, and using an APP/digital medium help develop strategies to avoid forgetfulness. However, strengthening motivation through, for example, motivational interviewing or another appropriate cognitive strategy is essential.

The evaluation of TA should be ongoing, using combined methods, and carried out with all involved in the process. Health professionals never give up on their patients, and small improvements produce great effects.

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