

The topic was officially incorporated into medical terminology in 1976 when Sackett and Haynes introduced the term 'compliance' (40). Then, in 1993, the discourse shifted from 'compliance' to 'adherence', signifying a more nuanced understanding of patient engagement with their medication regimens (41). The term 'persistence' was introduced in 2001, further expanding the scope of this field. In a significant development in 2003, the World Health Organization (WHO) released a comprehensive report on medication adherence, contributing greatly to the body of knowledge (42). Between 2008 and 2009, the term 'medication adherence' was recognized as a MeSH term, marking its significance in medical research. In 2010, the International Society for Medication Adherence (ESPACOMP) introduced the ABC taxonomy, a framework for categorizing adherence (Fig. 1) (41, 43).

## Definition and significance of adherence

In order to properly understand the concept of medication adherence, it is essential to grasp the distinction between adherence and compliance. While these terms are often used interchangeably, they carry nuanced yet significant differences in their meaning. Medication adherence, as defined by the WHO, refers to "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." Compliance, on the other hand, indicates a more passive and authoritarian approach where patients simply follow prescribed directives without active involvement in decision-making. Recognizing this difference is fundamental in promoting effective healthcare outcomes and patient-centered care (42). According to the 2003 WHO report, adherence is a multidimensional phenomenon influenced by five key dimensions: health system/healthcare team, social/economic, condition-related, therapy-related, and patient-related factors. This challenges the traditional misconception that adherence is solely the patient's responsibility (42, 44). Viewing medication non-adherence as the patient's "fault" is a misinformed and detrimental perspective. As

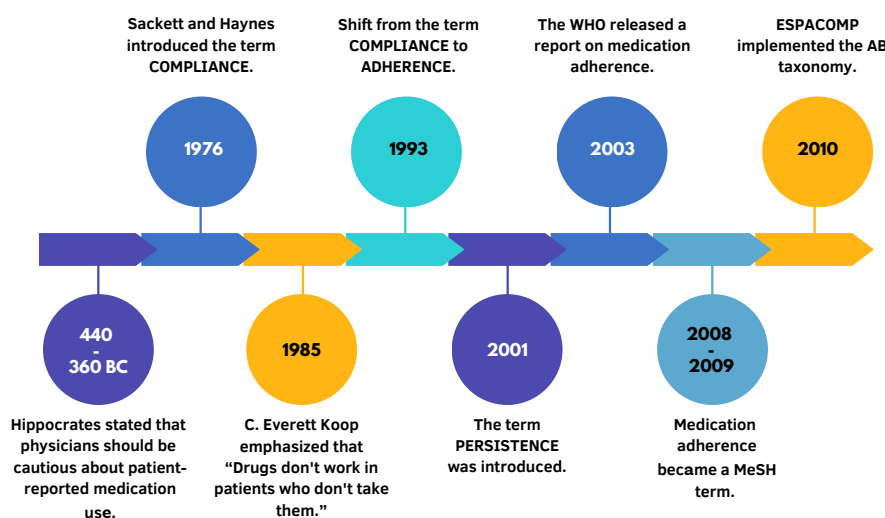
Everett Koop emphasized, "Drugs don't work in patients who don't take them." Therefore, it is crucial for health professionals to acknowledge that inadequate medication adherence leads to suboptimal clinical outcomes. This is supported by the WHO's statement that improving adherence may have a greater impact on health than enhancing specific medical treatments. A continuous, collaborative approach is required to achieve optimal medication adherence and fully utilize the benefits of current therapies (45). The Medication Adherence Reporting Guideline (EMERGE), adopted by the ESPACOMP, employs a three-phase classification known as the ABC taxonomy to categorize medication adherence. The phases include (a) initiation, (b) implementation, and (c) persistence. Persistence is defined as the duration from initiation to the final dose before discontinuation. In each phase, there are

distinct methodological challenges related to defining, measuring, and analyzing medication use (43). Non-adherence comes in eight forms, adapted from Arnet et al.'s classification, including primary non-adherence, drug holidays, the toothbrush effect, perfect adherence with the wrong medication, dosage errors (overdose, underdose, erratic dosing), incorrect dosing frequency, early therapy discontinuation, and polypharmacy (Table 2) (46).

## Understanding the underlying mechanism of non-adherence

Our comprehension of non-adherence remains partial, with some factors and treatments not fully addressing the underlying causes of this behavior. Therefore, selecting the appropriate treatment should be guided by the reasons behind non-adherent behavior and the patient's level of commitment (47).

**Fig. 1.** Illustration of the history of medication adherence with significant events modified according to Vrijens et al. (41)



**Tab. 2.** Eight forms of non-adherence, modified and adapted from Arnet et al.'s classification (46)

Abbreviation	Form	Description
<b>NON</b>	Primary non-adherence	Medication is not obtained or picked up from the pharmacy.
<b>A</b>	Drug holidays	Patients temporarily stop taking their prescribed medication.
<b>D</b>	Toothbrush effect	Patients start following doctor's recommendations shortly before an appointment but may otherwise ignore them.
<b>H</b>	Perfect adherence but with the wrong medication	Patients take medication as prescribed, but it is the incorrect medication.
<b>E</b>	Dosage errors, overdose	Patients take more medication than prescribed.
<b>R</b>	Dosage errors, underdose	Patients take less medication than prescribed.
<b>E</b>	Dosage errors, erratic dosing	Patients inconsistently follow the prescribed dosing schedule.
<b>N</b>	Incorrect dosing frequency	Patients take medication at the wrong frequency (e.g., twice a day instead of the prescribed three times).
<b>C</b>	Early therapy discontinuation	Patients discontinue therapy prematurely.
<b>E</b>	Medication cocktail, polypharmacy pattern	Patients engage in a pattern of taking multiple medications simultaneously.