

Aldona Kubica<sup>1</sup>, Marcin Gruchała<sup>2</sup>, Miłosz Jaguszewski<sup>2</sup>, Piotr Jankowski<sup>3</sup>, Damian Świeczkowski<sup>2</sup>, Piotr Merks<sup>1</sup>, Izabella Uchmanowicz<sup>4</sup>

<sup>1</sup> Nicolaus Copernicus University, Collegium Medicum, Bydgoszcz, Poland

<sup>2</sup> First Department of Cardiology, Medical University of Gdansk, Poland

<sup>3</sup> Jagiellonian University, Collegium Medicum, Kraków, Poland

<sup>4</sup> Wrocław Medical University, Wrocław, Poland

# Adherence to treatment — a pivotal issue in long-term treatment of patients with cardiovascular diseases. An expert standpoint

## Corresponding author:

Aldona Kubica, MD, PhD  
Department of Health Promotion,  
Collegium Medicum, Nicolaus  
Copernicus University  
ul. Łukasiewicza 1  
85-821 Bydgoszcz, Poland  
e-mail: aldona.kubica@gmail.com

## ABSTRACT

The adherence to treatment is defined as the extent to which a person's behaviour, including taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider. Non-adherence to medication may lead to increased morbidity, mortality, and costs to the healthcare system. Therefore, it is pivotal to know the patient's true adherence to medication, understand the causes of low adherence, and take actions to improve adherence.

The authors assumed that individual, complex health education started during hospitalisation and continued after discharge, explaining the pathophysiology and symptoms of the disease, elucidating goals and potential benefits of treatment, and highlighting the risk of premature termination of therapy, with use of additional methods helping patients to remember treatment schedule will enhance adherence to treatment. There is an urgent need to develop and test a dedicated procedure covering all these activities.

**Introduction.** A substantial proportion of patients with cardiovascular diseases do not respond to the treatment sufficiently [1–3]. Several factors of poor response to medication should be taken into account, including inadequate drug intake [4–6]. To systematise the phenomenon of following medical recommendations, the term “adherence” was proposed. The World Health Organisation (WHO) defines “adherence” as “the extent to which a person's behaviour, including taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider” [7]. Adherence has been also defined as the “active, voluntary, and collaborative involvement of the patient in a mutually acceptable course of behaviour to produce a therapeutic result” [8]. Previously the term ‘compliance’ was widely used, particularly in negative concord as ‘non-compliance’. Nowadays ‘compliance’ is associated with a more pejorative connotation than ‘adherence’ because ‘non-compliance issues’ are mostly patient-oriented without a deeper view into the different set of factors, e.g. obstacles identified in the healthcare system. Thus, currently in scientific deliberations we usually prefer usage of the term ‘adherence’ [9].

**Keywords:** Adherence, cardiovascular diseases, self-reported questionnaires

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## The prevalence and consequences of non-adherence

According to the Food and Drug Administration data, from 30 to 50% of patients do not exactly adhere to recommendations received from their healthcare providers, which significantly increases the risk of death.

These data were confirmed in several studies [6,10–16]. Non-adherence to medication may lead to increased morbidity, mortality, and costs to the healthcare system [8,16–19]. Therefore, it is pivotal to know the true patient's adherence to medication, understand the causes of low adherence, and take actions to improve adherence [20].

Results of the Prospective Registry Evaluating Myocardial Infarction: Event and Recovery (PREMIER) trial showed that failure of treatment plan implementation is associated with poor clinical outcome [21]. In 1521 myocardial infarction survivors at one month after discharge from the hospital with the recommendation of combination therapy with three drugs (aspirin, a beta-blocker, and a statin), 12% of patients discontinued treatment with all three drugs, 4% — with two drugs, and 18% — with one drug. One-year survival rate of patients who completely stopped their medication was significantly lower compared with those who continued their therapy (88.5% vs. 97.7%). Discontinuation of treatment was an independent risk factor for death (hazard ratio 3.81). Multivariate analysis showed that the probability of discontinuation of all three drugs was higher among those with higher education (hazard ratio 1.76). The impact of older age on treatment discontinuation was higher among women (hazard ratio 1.77) than among men (hazard ratio 1.23) [21]. The Prospective Urban Rural Epidemiology (PURE) study showed that adherence to secondary prevention therapy was more influenced by general socioeconomic factors at the national level than to individual factors, such as age, gender, education level, smoking, body mass index (BMI), hypertension, and diabetes [22]. It is worth mentioning, however, that studies based solely on a quantitative approach may underestimate the true nature of the non-adherence phenomenon, and qualitative studies are highly anticipated to detect nuances that can deteriorate adherence [9].

## Determinants of non-adherence

In several studies the age of patients was indicated as one of the factors affecting adherence to medication [8,14,18–19,23–24]. Comorbidity burden increasing with age is associated with the necessity of polypharmacy. Elderly patients often do not understand the reasons for the complexity of the treatment, and have problems with remembering and adapting to the treatment schedule [25]. Holt et al. conducted a qualitative study based on a focus group, which revealed that memory-related problems and forgetfulness were factors mostly reported by the elderly in the context of the non-adherence phenomenon. Patients emphasised that knowledge about the nature and seriousness of the primary disease, i.e. hypertension, can improve adherence to recommended therapy. These findings may suggest the potential target of new interventions [26]. The Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PACE) study showed that in elderly patients with hypertension, adherence to the treatment plan was worse in the coexistence of asthma or chronic obstructive pulmonary disease (odds ratio

[OR] = 0.43), depression (OR = 0.5), gastrointestinal disorders (OR = 0.59), or musculoskeletal diseases (OR = 0.63) compared with hypertensive patients without concomitant diseases (OR = 1.0) [27]. Moreover, it was revealed that polypharmacy has a negative impact on the implementation of the treatment plan [18]. In another study, the co-existence of diabetes was found to be an independent factor reducing adherence to treatment [14]. Low adherence occurs in all age groups; however, older patients are particularly exposed to multiple challenges regarding this issue, including difficulty hearing, comprehending, and remembering instructions, managing multiple medications, and tolerating side effects of medication and drug-drug interactions [28]. Due to differences of cultural, social, and medical nature, the adherence determinants for distinct patient populations differ [24]. Many studies have tried to identify patients jeopardised with future failure to follow the doctor's recommendations after hospital discharge [28–29]. Several different factors associated with low adherence to medication were identified, including female gender [8,18,25,27,30], low level of education [8,17], adverse effects of therapy [31], insufficient instructions given to patients [31], poor financial status preventing purchasing of medicines [31–33], lack of acceptance of the need for treatment by the patient [31], and poor relationship between the patient and medical staff [31–34].

Failure to follow the treatment plan is a relatively common problem, which is a serious and often underestimated factor limiting the effectiveness of treatment. Unfortunately, non-adherence to treatment often remains both common and difficult to detect [34]. Identifying the key determinants of low adherence and early discontinuation of treatment may aid in the development of interventions aimed at increasing adherence and addressing this high-risk population, in order to improve health outcomes [34–35].

## The adherence assessment

There are some direct and indirect methods of assessing adherence to treatment; however, there is no single “gold standard” or a universal tool for determining the level of adherence [36–39]. Asking patients is the simplest and most frequently used method of adherence assessment. However, it has been shown that the data obtained in this way have limited credibility [14,20]. Objectification of patient-reported information is usually difficult and costly. On the other hand, some experts argue that the positive relationship between subjective data (e.g. questionnaires) and objective data (e.g. obtained from the medical reports) is high, so validated tools should be considered as a reliable instrument aimed at detecting non-adherence problems

[40]. The application of specially developed questionnaires or scales to assess the risk of low adherence may be helpful in allowing extensive screening of patients. Moreover, well-designed questionnaires may also identify obstacles, gaps in patients' knowledge, and the problems in cooperation with patients. Nevertheless, even access to validated questionnaires does not diminish all potential obstacles associated with this social technique. For instance, due to memory-related issues, questionnaires can only measure non-adherence within a period of several weeks, which is not satisfactory from the scientific point of view and provides a limited scope of information for healthcare providers [40].

Recently, Buszko et al. [41] published an article validating the Adherence in Chronic Diseases Scale (ACDS). The ACDS allows assessment of adherence itself, as well as identification of the most important factors influencing adherence, such as: acceptance of a therapy plan, cooperation between a patient and health care professionals, and the economic status of a patient [42–44]. The ACDS scores range from 0 to 28 points. Results below 21 points, between 21–26 points, and above 26 points correspond respectively to low, medium, and high adherence, respectively. The internal consistency of the ACDS final version was assessed using Cronbach's alpha coefficient, and the value of 0.752 confirmed high reliability and homogeneity of the questionnaire [41]. The ACDS was subsequently applied in a single-centre, prospective, observational cohort clinical study with a six-month follow-up [45]. In a population of 221 patients with myocardial infarction treated with PCI, lower scores for ACDS items 2 and 3 were associated with increased risk of acute coronary syndrome during follow-up (for item 2:  $3.11 \pm 0.68$  vs.  $3.45 \pm 0.73$ ;  $p=0.02$ , and for item 3:  $3.28 \pm 0.89$  vs.  $3.64 \pm 0.64$ ;  $p=0.04$ ), indicating the predictive value of these items [45]. The scale is simple to use and may be applied in everyday medical practice and for research purposes [44–45]. It can be successfully used as a tool to support medical staff in identifying patients requiring personalised educational activities [41].

## Summary

Medication adherence is an issue of growing concern for those working to improve health system performance, and promoting adherence to medications offers a rare opportunity to simultaneously improve health outcomes while reducing costs. Jankowski et al. [46] pointed out different healthcare-related factors and patient-related factors affecting proper treatment of patients with cardiovascular diseases. According to Jankowska-Polanska et al. [47], the knowledge deficits

contribute to a lack of adherence and worse clinical outcome. Therefore, education of patients regarding the risks and benefits of treatment is pivotal to avoid premature discontinuation of medication [48]. Nevertheless, no standard approach has been developed. Pharmaceutical care including educational interventions and reminding methods in patients with chronic diseases is also beneficial, both to the patients and to the entire healthcare system [49]. To sum up, we should admit that inter-professional collaboration is needed to improve adherence and outcomes. Thus, we should reveal the concept of 'concordance' as the deep agreement between patients and health-care providers, where the patients' needs are the matter of paramount importance [50].

## Conclusions

The authors assumed that individual, complex health education started during hospitalisation and continued after discharge, explaining the pathophysiology and symptoms of the disease, elucidating goals and potential benefits of treatment, and highlighting the risk of premature termination of therapy, with use of additional methods helping patients to remember the treatment schedule will enhance adherence to treatment. There is an urgent need to develop and test a dedicated procedure covering all these activities.

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