Physician–patient partnership — can it help increase adherence to the therapeutic recommendations in cardiovascular disease?

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Abstract

Efforts to increase adherence to the therapeutic recommendations in primary and secondary prevention of cardiovascular disease include focuses on the improvement of communication between patients and physicians. Physicians need to promote patients' education and combat disinformation available on the Internet. Use of the electronic methods (e.g., SMS reminders/prompts), elimination of economic barriers, and monitoring of adherence may be also of help. With relation to pharmacotherapy, simplification of drug regimens with wide use single-pill combinations (SPCs) may provide effective measure to substantially improve adherence. Only comprehensive efforts to improve adherence by building a partner patient-physician relationship, may contribute to an increase in persistence and lead to reduction of cardiovascular morbidity and mortality in the general population.

Key words: drug adherence; pharmacotherapy; partnership; integrated care; mobile technologies; telemedicine; patient-centered care; single-pill combinations (SPC)

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Introduction

Nonadherence in regard to both lifestyle modifications and drug therapy is an increasingly recognized reason why therapeutic targets are not achieved, leading to increased cardiovascular morbidity and mortality, along with increased healthcare spending, e.g., due to avoidable cardiovascular hospitalizations. For example, the annual cost of treatment nonadherence in Germany has been estimated at 10 billion euro [1]. It has also been estimated that in Europe, an improvement in adherence might save nearly 200,000 persons' lives annually and result in the overall savings of 125 billion euro [2].

Multiple studies indicate that nonadherence in regard to cardiovascular risk-reducing therapies translates directly into an increased cardiovascular event risk. For example, Seaman et al. evaluated all-cause mortality and mortality due to ischemic heart disease/stroke during a 2-year follow-up in patients who discontinued, reduced or continued statin therapy [3]. In a model adjusted for other risk factors, an increase in all-cause mortality by 39% to 61% was shown in patients who reduced or stopped statin therapy compared to those who continued therapy. In addition, this study showed that patients who stopped statin therapy did not continue treatment with at least two other drugs compared to those who continued statin therapy.

The issue of treatment adherence is particularly pertinent in two groups of patients: 1) young and middle-aged patients, as multiple studies showed that persistence is lowest in these age groups; 2) patients initiating therapy with cardiovascular risk-reducing drugs, as it was shown that early discontinuation of cardiovascular risk-reducing drugs (e.g., antihypertensive medications and statins) following treatment initiation is associated with not only a higher risk of cardiovascular morbidity but also a higher risk of death [4–6].

In the present article, we examined the complex and dynamic issue of the lack of therapeutic adherence/persistence and the importance of building a proper, partner physician-patient relationship for increasing treatment adherence and reducing cardiovascular morbidity and mortality.

Methods to evaluate adherence

Multiple observations regarding drug treatment of hypertension indicate clearly that nonadherence is the major factor responsible for antihypertensive treatment failure at the population level [7]. The degree of adherence must always be taken into account when making clinical decisions, and the problem must be addressed in patients who do not reach therapeutic targets. Nonadherence may involve irregular drug taking, inappropriate dosing, making "therapeutic holidays", or complete drug withdrawal. Therapeutic nonadherence may also relate to the institution of lifestyle modifications. Both on the individual and population level, several approaches are available to assess adherence regarding drug treatment in patients with chronic diseases. In the literature, several terms are frequently used, including compliance, adherence, persistence, concordance, and shared decision making. These English terms often lack appropriate translations to other languages, which unfortunately contributes to misunderstandings regarding the nature of the problem [8]. Of note, this terminology issue is also present in the English language where compliance, adherence, and concordance are often inappropriately used as synonymous terms [9].

The oldest term, which appeared in the literature already in the 1970s, is *compliance*, describing the degree to which the patient's behavior is in accordance with the physician's recommendations. This term, currently becoming obsolete, implies the historical approach to the patient-physician relationship, in which the terms of cooperation are dictated only by the physician. This problem was noted and after about 20 years, the term compliance became to be superseded in the literature by *adherence*, a wider term that by definition includes a dialogue with the patient. Adherence is the measure of patient engagement in the therapeutic plan beyond simple drug taking. According to the World Health Organization, adherence is the degree to which the patient's behaviors, i.e., drug taking, adherence to diet, and exercising, are consistent with the plan determined together with the physician [10]. In turn, the least questionable term is *persistence* which is the measure of patient's perseverance in the long-term continuation of the set treatment plan, where the beginning and the definitive end of the therapy may be easily defined. Until recently, the term *concordance* also appeared in the topical discussions, describing the degree of a widely understood consent for cooperation between various healthcare professionals (physician, nurse, and pharmacist) and the patient to agree on the treatment plan, therapeutic goals, and drugs used [8, 11]. Currently, this term is more and more frequently replaced by the term *shared decision making*, interpreted as "cooperation in de-

Table 1. Terms used to describe the degree, extent and nature of cooperation with the patient [10, 113, 8, 11, 12, 9]

English term	Polish term	Definition
Compliance	Zgodność	Degree to which the patient's behavior is in accordance with the physician's recommendations
Adherence	Przestrzeganie	Degree to which the patient's behaviors, i.e., drug taking, adherence to diet, and exercising, are consistent with the plan determined together with the physician
Persistence	Wytrwałość	Measure of patient's perseverance in the long-term continuation of the set treatment plan
Concordance	Zgoda na współpracę	Consent for cooperation between various healthcare professionals (physician, nurse, and pharmacist) and the patient to agree on the treatment plan, therapeutic goals, and drugs used
Shared decision making	Współdziałanie w podejmowaniu decyzji; współdecydowanie	Shared decision making indicates (1) empowerment, (2) engagement, and (3) agreement between all parties in setting the therapeutic plan (patient + physician/nurse/pharmacist)

cision making" (joint decision making), in which concordance, or acceptance of the solutions arrived at, is one of the important elements [9, 12]. The goal of this cooperation is to develop patient motivation to adhere to the therapeutic plan he has jointly decided on (Tab. 1).

Assessment at the individual level

Studies using objective methods to monitor antihypertensive drug therapy ruthlessly verify physicians' perceptions regarding the degree of patient adherence. Based on one-year follow-up of more than 1000 veterans, Meddings et al. concluded that the physician's ability to identify nonadherent patients may be estimated at about 50%, and thus is comparable to a toss of a coin [13]. Clearly, competencies of individual physicians differ but in general we should acknowledge that we cannot precisely diagnose the problem of inadequate adherence. For this reason, we should seek alternative approaches that would allow an objective assessment of the scope of this problem, feasible enough as to offer the potential of their wide implementation in the shortest time possible.

In 2019, the Polish National Health Fund (NFZ) published a report on hypertension which included data on adherence. In this report, it was estimated that in 2013–2018, as many as 24.3% of patients with a first-time diagnosis of hypertension did not fill any prescription for the drugs reimbursed in the treatment of hypertension [14]. For this reason, among others, an integrated electronic medical data system ("e-zdrowie", P1) that will allow tracking the management history, including all drug prescriptions within the system, is currently being developed in Poland [14].

Estimating adherence in clinical trials

Interpreting the results of clinical trials of drug therapy may be significantly hampered if patient adherence is not assessed simultaneously. For example, in the recently reported ALL-HEART trial (2022), it was shown that half of patients randomized to active therapy did not take the recommended medications [15]. Obviously, this does not preclude evaluation of the clinical effect of the intervention studied but the quality of the collected evidence becomes significantly lower in such circumstances.

Patient adherence regarding medications can be estimated in several ways. It seems that the only fully objective (though not perfect) approach to the monitoring of drug treatment adherence is measuring drug or its metabolite level in the body. Unfortunately, the major limitation of this approach is its invasive or cumbersome nature which, together with significantly higher costs, marginalizes the use of this method to strictly selected medical experiments. However, objective drug/metabolite level monitoring confirms nonadherence in 19% to 86.1% of patients with apparently resistant hypertension [16]. Of note, evaluation of nonadherence in the clinical trial setting underestimates the true scope of this problem [17].

In population studies (mostly registries), the common approach to the evaluation of medication adherence involves calculating two indices derived from the defined daily dose (DDD) of the drug, i.e., the medication possession ratio (MPR) and the proportion of days covered (PDC). These simple tools show the proportion of therapy days during which the patient has an access to the given drug or drugs in the defined period. Calculation of MPR usually overestimates true adherence due to previous drug supply to the patient, while the more rigorous PDC algorithm which accounts for the way of patient's drug stock replacement is a more precise measure of drug adherence. Obviously, drug possession does not equate with actual drug taking, which is an inherent limitation when estimating drug adherence based on MPR or PDC.

In several medical experiments, the method of electronic monitoring of drug package opening by

the patient/study participant (Medication Event Monitoring System, MEMS) was used. This method is not only a modernized version of manual tablet counting during follow-up visits, e.g., in clinical trials, but with log recording, it also shows patient's habits and regularity regarding drug taking and reduces the possibility of bias that might affect the result of monitoring [18, 19]. As shown by Burnier et al. during several weeks of follow-up, electronic monitoring of antihypertensive drug taking has a beneficial effect on the quality of blood pressure control in patients who were previously unable to attain the therapeutic goals [19].

In clinical trials where a certain level of adherence is a key prerequisite for patient selection for a specific procedure (e.g., renal artery denervation, clinical evaluation of patients with suspected resistant hypertension), a short-term alternative to the monitoring of drug taking is directly observed therapy, i.e., drug taking in the presence of healthcare personnel [20]. Visual monitoring of drug taking is nearly 100% effective in assuring that the patient actually swallows the medication but the utility of this method is very limited. Clinical experience indicates that it is the most effective method of identifying patients with truly resistant hypertension in controlled conditions (e.g., during hospitalization) [21].

Why do patients not continue cardiovascular disease therapies?

As shown in Figure 1, multiple patient-, physician-, and healthcare system-related factors have been identified which lead to the ultimate success in adherence, i.e., closure of the therapeutic persistence cycle that includes medication prescription, filling the prescription, regular drug taking as recommended, follow-up visit attendance, and prescription renewal.

Basic prerequisites for patient adherence include acceptance and knowledge about the disease, trust in the treating physician, and patient's belief that the recommended therapy will be effective [1]. Other important patient-related factors include age, sex, level of education, and social support (Fig. 1) [22]. Neurologic and psychiatric disorders are also of importance, including cognitive dysfunction, depression, and anxiety. Another factor is therapy availability and ease of use — mostly the cost, but also the dosing regimen, the number of tablets, and the number of medications. Adverse effects of the therapy, both true and nocebo effect-related, are also factors that affect therapy persistence [1, 22].

Physician-related causes of nonpersistence should not be forgotten. These include therapeutic inertia and physician unawareness of patient nonadherence [23]. Therapeutic inertia may negatively affect the attainment of therapeutic goals and thus discourage the patient from continuing the therapy. On the other hand, the lack of time and awareness on the part of the doctor of the importance of building a partnership with the patient in the therapeutic process may additionally contribute significantly to reducing the effectiveness of treatment. The partnership relationship should be based, inter alia, on providing the patient with relevant information on the background of the disease, the risks associated with not taking the treatment and the benefits of the medicines used, while also presenting the risks of adverse effects and taking into account the patient's concerns and preferences [23].

Studies indicate the existence of a "healthy adherer" effect. Adherent patients are not only more systematic and persistent in taking the recommended medications but also pay more attention to their health in terms of lifestyle modifications, more frequent physician visits, and performance of preventive diagnostic tests [24]. A metaanalysis of clinical trials showed that in placebo groups, strict adherence to the recommendations was associated with a lower mortality risk compared to nonadherence [24]. Thus, the "healthy adherer" effect may be a marker of patients' healthy behaviors in general [22].

Opportunities for increasing therapeutic persistence

Systematic adherence to the therapeutic advice, including taking the recommended medications and adhering to lifestyle modifications, is challenging for many patients [26, 27]. Thus, actions to increase therapeutic persistence become a key element of contemporary cardiovascular disease prevention and treatment. Increasing adherence requires a comprehensive approach that includes both individual interventions and systems-oriented efforts [25, 28]. Below, we review the most important approaches that may increase adherence, highlighting the practical aspects of their use and underscoring the special importance of methods supporting the patient-physician relationship.

Patient education and engagement in the therapeutic process

Engaging the patients in the decision-making process, empowering them to actively participate in

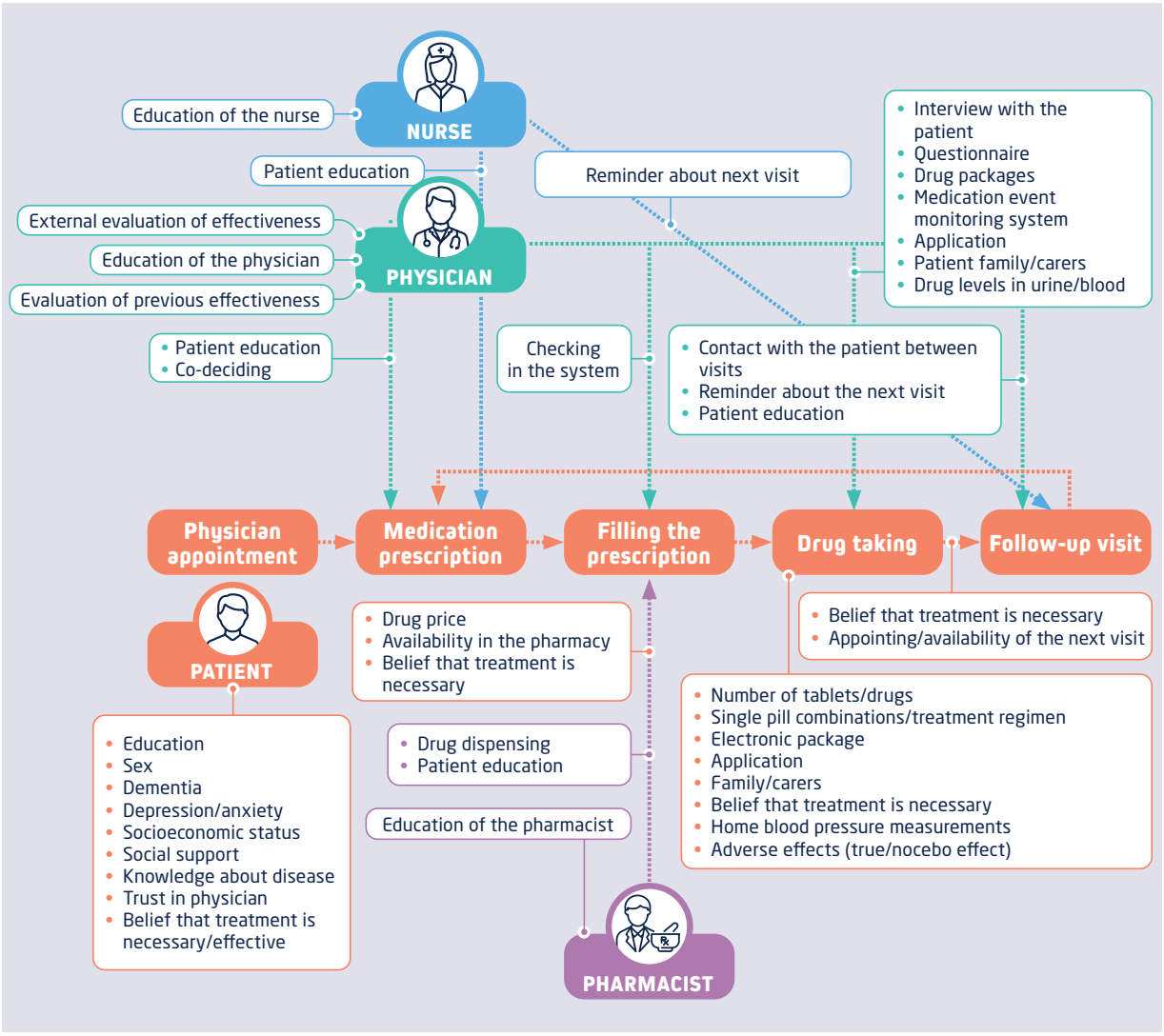

Figure 1. Therapeutic persistence cycle — medication prescription, filling the prescription, regular drug taking as recommended, follow-up visit attendance, and prescription renewal. The authors' original idea based on [1, 22, 23, 25]

the treatment planning, and providing them with easily comprehensible information may significantly increase therapeutic persistence [7]. If the patients understand the disease, treatment goals, and benefits from the therapy, it may significantly increase their motivation to adhere to the therapeutic recommendations. In addition, the patients should be informed about the importance of blood pressure self-management which may help them understand their disease and motivate them to take their medications regularly [29]. An important element of education is teaching the patients when to seek medical help and how to manage potential side effects of the medications. Education should be tailored to the individual patient needs and provided on an ongoing basis to maintain patient engagement. Using visual materials, mobile phone applications, and e-learning platforms in the educational process may increase the effectiveness of the educational message.

Patient-physician cooperation and communication

Maintaining patient motivation to adhere to the therapeutic recommendations is a challenge that requires cooperation and open communication. For this reason, the importance of creating a successful physician-patient relationship, based on empathy, openness to the needs and problems of the patients, and building mutual trust, cannot be overestimated [30]. Physicians should actively listen to patients' concerns, tailor therapeutic plans to the individual needs, and motivate patients to participate actively in the treatment process. Physi-

cian support may help overcome barriers in adherence, such as concerns for medication side effects or weariness due to chronic therapy [31]. Regular meetings and communication with the physician help monitor progress and tailor the therapy as needed. This in turn builds trust and the sense of safety in patients who feel that their health is under control.

Tailoring the treatment regimen — therapy personalization

Personalization, or tailoring the treatment to individual patient characteristics such as sex, age, lifestyle and concomitant conditions, allows optimization of the therapeutic effects and minimization of adverse effects. Adjusting the therapeutic regimen to individual patient needs, expectations, and preference may largely increase therapeutic persistence.

Simplifying the treatment regimen by using long-acting drugs or extended-release medications that can be dosed once daily may significantly improve adherence. In addition, using single-pill combinations (SPC) reduces the number of tablets that need to be taken by the patient, and thus also simplifies the treatment regimen, which may also increase therapeutic persistence [32].

The scientific literature from the recent years has provided increasing evidence of benefits from therapy personalization in the management of cardiovascular disease. Clinical trials and metaanalyses indicate the personalized approach and use of SPC may not only significantly increase adherence but also reduce the risk of hospitalizations due to cardiovascular causes and as a result reduce the total mortality [5, 33].

Psychological support

Psychological support may help patients cope with stress, increase their motivation to change health behaviors, improve adherence, and help overcome psychological barriers that limit the effectiveness of the therapy.

Stress-reducing techniques such as relaxation training, mindfulness, and cognitive-behavioral therapy, may help reduce blood pressure and increase adherence. Educating the patients how to cope with emotions and stress may reduce the adverse effects of psychological factors on the cardiovascular system [34].

Support groups and social intervention may be additional sources of motivation and incentives. Support from the family, friends, and other patients may increase the sense of responsibility and improve adherence.

Integrated care

Increasing cooperation between various professionals involved in patient care, including primary care physicians, specialists, nurses, and pharmacists, may improve the management of care and increase therapeutic persistence [35]. Integrated care in which all patient carers are well informed about the treatment plan helps coordinate efforts and allows consistent communication with the patient.

Mobile technologies and telemedicine

Mobile technologies and telemedicine offer new possibilities in the monitoring and support of patients with cardiovascular disease [36].

Smartphone applications may help patients adhere to the therapeutic recommendations by providing educational information, reminding them to take medications, and tracking the treatment progress. In this way, the patients become more engaged in the treatment process which translates to better outcomes.

Wearable monitoring devices, such as smartwatches, allow constant monitoring of important parameters such as heart rate, sleep quality, and physical activity. Such data may already be used by the physicians when tailoring the treatment plan. In the future years, we may expect these devices to allow reliable blood pressure measurements which will be used to monitor the effects of antihypertensive therapy in the routine clinical practice.

Telemedicine allows regular monitoring of the patient health status without the need for physical attendance at healthcare facilities, which helps maintain the continuity of care and may contribute to better adherence. This is particularly important for patients living in remote or poorly accessible areas. These options are specially preferred by younger patients. Telemedicine visits proved to be a key element in patient support during the COVID-19 pandemic.

Big data and artificial intelligence tools may also be useful in the management of cardiovascular disease by analyzing large data sets to identify patterns and predict treatment outcomes, which may lead to more personalized and more effective therapeutic strategies.

Systems-oriented efforts at the national and international level

The above discussed methods require systems-oriented efforts. Healthcare systems must promote the patient-oriented approach, with tailoring of

the treatment plans to the individual patient needs, preferences, and abilities. Monitoring therapeutic persistence must become an indicator of healthcare quality. Further studies and analyses in this area are of key importance for further improvement of the effectiveness of cardiovascular disease treatment and prevention.

Teacher, parent, preacher, or partner?

In the 1940s, with the shift in viewing health from a purely biological absence of disease to a wider, interdisciplinary paradigm of physical, mental, and social wellbeing, the World Health Organization paid attention to the importance of not only the factual knowledge of healthcare professionals but also their social competences. As a result, the shape of the patient-physician relation in the physician's office has gained a major importance in the process of attaining health. Effective communication, ability to listen, empathy, openness, patience, and the ability to motivate effectively are often the primary criteria by which the patients judge their physicians, affecting the patients' willingness to cooperate, and ultimately the therapeutic success.

In the physician offices, conversations regarding the introduction of various changes in the patients' life take place daily. In some cases, these conversations lead to the modification of habits, initiation of a systematic treatment, or achievement of the set therapeutic goals. In other cases, despite high professional quality, nothing changes, and the meeting leaves both the patient and the physician with a feeling of a lost chance and a lack of understanding. Initiation and continuation of the therapy, modification of dietary habits, and regular checking of some parameters (blood pressure, blood glucose level, body weight) disrupt the previous routine and require patients to be adequately engaged in the implementation of the proposed changes.

Factors determining the effectiveness of physician's advice

To understand these factors, we need to think about the reasons why people change, and where they get motivation for their actions from.

Motivation, by definition, is a process which initiates, directs and sustains specific human behaviors to reach specific goals.

The source of this process may be external, e.g. willingness to receive a reward or avoid a punishment, or internal, resulting from beliefs, values or priorities. It is important to recognize this distinction when trying to persuade the patients that some changes in their previous habits are reasonable.

In the traditional way of conversing with the patient, which is disease-oriented, the aspect of internal motivation has been neglected. The premise of the traditional approach is the need to correct an existing objective pathology, disease or disorder, achieve measurable results, regardless of the nuisance of the management and complaints, previous experiences, or patient's beliefs. In this model, physician's advice is created for an average patient, without taking individual needs into account. The physician is a person who knows and recommends a specific management approach, mostly uniform for the whole group of patients with a given disorder or disease, and the patient should comply with these recommendations. The source of motivation is considered to be the need to correct an abnormality or initiate treatment. However, this approach has not been particularly effective until now — on average, only about 50% of patients adhere to the physician recommendations [22, 37], 40–80% of information conveyed by the physicians during appointments is immediately forgotten, and half of the memorized information is recalled erroneously [38]. A question thus arises how to increase the likelihood of actual patient engagement in changing previous habits, increase adherence regarding medications, and motivate the patients to long-term, regular adherence to the recommendations.

Patient-centered care

One suggested approach is to shift the focus of the conversation with patients on their needs, i.e., transferring the source of motivation to the internal one. Patient-centered care (PCC) is based on several important premises and differs significantly from the traditional model of care (Tab. 2).

To define PCC, it is important to stress the need for a partnership between physicians and patients and their families that allows health-related decision-making with a respect for patient priorities, preferences and needs, provided that the patient has necessary knowledge and support to be able to make health-related decisions, and strives to improve the quality of cooperation [39].

The key factors in this approach to patient care include the physician's ability to communicate effectively [40] (Fig. 2), knowledge of behavioral techniques facilitating the search for the internal mo-

Table 2. Differences between disease-centered care and patient-centered care (based on [47])

Disease-centered/traditional model	Patient-centered model
The basis is physician authority along with benefits from the proposed management approach	The basis is patient autonomy (the patient has the right to refuse or accept the management)
Focused on medically important outcomes, objective parameters	Focused on outcomes important for the patient
Patient preferences and perspective are usually disregarded when planning the management	Patient preferences, concerns, and values are taken into account when making the decisions regarding the management
Adherence to recommendations formulated by the physician	Joint decision-making by the patient and the physician
Improved outcomes in an average patient in the study group	Improved outcomes in the individual patient

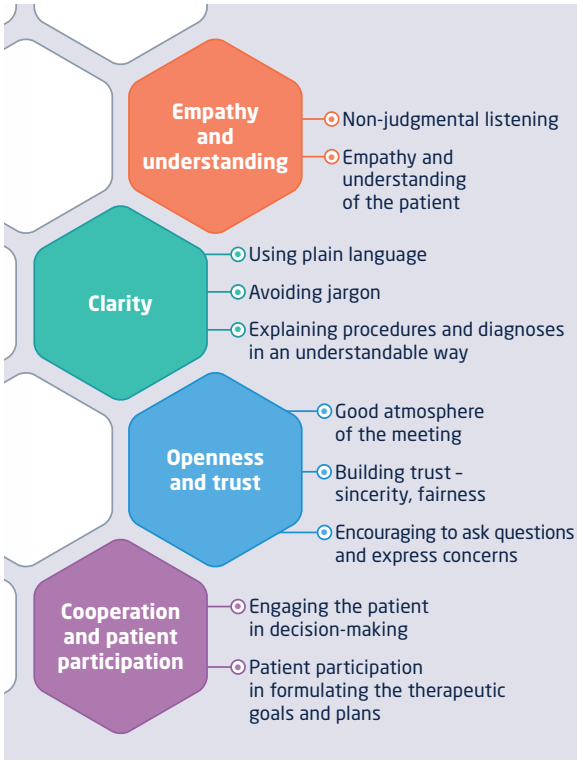

Figure 2. Principles of effective communication

tivation of the patient, and proper education of the patient and other individuals providing support to the patient, without which PCC cannot be fully implemented.

There are many models developed for the education of patients and their families. Studies evaluated their effectiveness in increasing the level of knowledge and improving objective parameters, such as blood pressure values or cardiovascular event incidence rate [41, 42]. However, no model has been identified that would universally fit to every situation. Therefore, it is important to be able to adjust the educational approach to the conditions of care and the abilities and needs of individual patients and their relatives. Educating patients and their families, as well as healthcare professionals in regard to the occurrence of nonadherence [43], evaluation of this phenomenon, and methods of motivational interventions may have an effect on the improvement of adherence [44].

An element of effective communication is the ability to identify patient complaints or concerns using open questions with a non-judgmental attitude, particularly at the beginning of the patient-physician interaction. At this stage, it is very important to allow the patient speak freely, without interruptions. Studies indicate that physicians tend to interrupt patients after on average 30 seconds, this limiting the ability to collect information on issues that are important for the patient [45]. Even in the settings of time constraints, it should be reminded that patients rarely need more than 120 seconds to finish their storyline. In the open questions technique, we avoid questions starting with "Do you…?". Instead, phrases like "What do you think on that?", "Please tell me about…", "How would you react to…", or "What else would like to talk about?" may be used.

Based on the collected information, it becomes possible to determine priorities of individual patient complaints or concerns, also in relation to the previous treatment. Using medical knowledge, the physician may then indicate which patient problems require most urgent intervention and discuss possible approaches to their management.

It is extremely important to recognize the patient's attitude to the proposed solutions, along with previous experiences, doubts and expectations of the patient. The empathic attitude of the physician, in contrast to the judgmental one, allows accepting the patient's perspective regarding disease-related experiences and associated emotions. Communicating a new diagnosis or the need to initiate a new therapy or modify the existing therapy should be preceded by the recognition of the current knowledge and experiences of the patient in regard to the possible therapeutic options, and identification of the need to expand that knowledge. In this situation, the "ask-tell-ask" technique may be used. This

Table 3. Examples of the „ask-tell-ask" technique when providing information to the patient

Step	Examples
Ask: for permission to convey information or about the existing patient knowledge on a given issue	**Permission:** "As your physician, I am very worried about your high blood pressure values and I would like to know what you think about it". "Can we talk about regular medication taking?". "I would like to know more on how you take your medications". **Existing knowledge:** "What do you know about the effect of regular medication taking on health?". "Is there anything more you would like to know about high blood pressure values?" "There are some things we should talk about. What would you like to start with?"*
Tell: Objective information Several facts Using an understandable language	**Information tailored to the patient, referring to the current situation:** "You have mentioned that you are worried about your high blood pressure values …" **Facts, without the intention to persuade the patient:** "High blood pressure may result from…, … or …". "Based on available data, high blood pressure may result in …, … and …". **Several (2–3) key facts:** "In this situation, two issues seem to be the most important …" (use plain, understandable language, use leaflets or other educational material). Highlight the possibility of choice — avoid phrases like "you cannot", "you need", "you have to" "In this situation, the following options are possible…"
Ask: for feedback information regarding the conveyed information or make sure the patient has understood the information by asking him/her to summarize it	**Feedback information:** "And what do you think about it?". "And what importance does it have for you?". "What do you think we should do?". or "I would like to make sure that I have explained everything well — may I ask you to summarize it?". "Can you tell me what you will now pass to your wife on this issue?". "Can you tell me how you will take your medications now?".

*If the patient asks for advice, remember to highlight the possibility of deciding whether to accept the proposed option/to suggest various possible options, e.g., I cannot tell you to do anything but would you like to hear about possible options? Maybe one of these would be effective in your case — give possible solutions and ask the patient about them – Do you think that any of these solutions might be helpful in your case?

technique involves identifying the need for additional information on a given issue and only after such need is ascertained, providing the patient some new information, and finally confirming the information has been understood, or obtaining feedback information about the conveyed information. Several examples of this technique are provided in Table 3.

In addition to the emphatic education in the physician's office, an element of the improvement of the physician-patients cooperation is a skillful help in discovering patient's values and priorities to support the internal motivation to continue therapy. One effective method, based on the principles of effective communication and respect for patient autonomy, is motivational interviewing [46].

Motivational interviewing

The method of motivational interviewing is based on a partner, goal-oriented approach to communication [46]. It is based on the willingness to discover what is important for the interlocutor, acceptance of the right to change or not to change, partnership in working together with the interlocutor, and discovery of solutions, strengths and experiences of the interlocutor, all aiming to uncover the "language of change". The "language of change" is a narration stating that the more reasons, methods, consequences, and benefits from a change will be discussed, the more likely the change becomes. The method of motivational interviewing aims to strengthen the internal motivation of the patient and oblige him to achieve a specific goal by identifying and enhancing the patient's reasons for change. During such an intervention, it is important to create conditions for the development of the action plan by the patients themselves, ultimately aiming to achieve the set goals. The basic assumptions of this approach to the conversation with the patient include acknowledging the patients' autonomy (the right to accept or refuse a given solution) and considering them the experts on self. During the conversation held in accordance with the assumptions of motivational interviewing, the physician and the patient cooperate to identify the current resources and abilities of the patient, focusing on strengths and positive patient characteristics and skills.

Table 4. Examples of motivational interviewing questions aimed at improving adherence

Identifying goals/motivation that would help adhere to the recommendations
What is most important for you at the present stage of life? At the present stage of the disease?
What do you value the most in your life? How does the change we are talking about relates to what is important for you?
Why do you contemplate the need to take medications regularly?
What benefits from this behavior do you see?
Are there any additional benefits from this behavior you have not thought about yet?
If you start taking medications regularly now, how would that, in your opinion, affect your health in several years?
Indicating benefits acquired by the patients from regular adherence to the recommendations:
How did you feel in those days when you took the medications regularly?
When you managed to take medications regularly in the past, how did that affect you?
What was the effect of regular drug taking on your mood? Well-being? Fitness?

Table 4 shows several questions or statements that might be useful in the physician's office settings, formulated in accordance with the ideas of PCC and motivational interviewing.

Another important element is a joint search for solutions of the identified problems — and here, the motivational interviewing methods, patient-centered and acknowledging the patient autonomy, are also helpful. Behavioral methods, for example the SMART goal-setting method (Fig. 3), may help develop a precise plan regarding the change the patient would like to make.

Obviously, a question arises why the physician should be interested in patients' motivation and seek new solutions when they are already known and have been effective for many years. This is the difference between problem-oriented medicine where the solutions have been developed for an average patient, and patient-centered medicine where each solution should be individually tailored to a given patient.

Of note, changes will occur when they are individually important and when the patient believes the change is feasible. Thus, when discussing adherence with the patients, it is so important to build on those values which are most important for the patient and elucidate, together with the patient, how systematic adherence to the therapeutic recommendations aligns with these values, encouraging the patients to find their own unique solutions to implement the desired changes.

Figure 3. SMART goal-setting method

Facts and myths regarding cardiovascular drugs

Elevated blood pressure, cholesterol, and glucose values are major risk factors for the development of atherosclerotic cardiovascular disease. Due to common occurrence of these risk factors, antihypertensive, lipid-lowering, and blood glucose-lowering drugs are frequently used. In addition, primarily in case of antihypertensive and lipid-lowering treatment, these drugs are used in apparently healthy persons, and thus the way these medications are perceived in the society is extremely important in the context of adherence.

Numerous myths have arisen in regard to the association between elevated cholesterol levels and cardiovascular disease, lipid-lowering treatment, and particularly statin use. Mass media play a major role in promulgation of those myths. A strong association was shown between the mass media message and the effect on treatment continuation. For example, it was estimated that in Denmark, the annual number of articles on statin in lay press increased from 30 in 1995 to 400 in 2010, and most articles were neutral or negative towards statins [6]. The authors of this study evaluated whether negative information on statins translates into early discontinuation of the treatment with these drugs (within 6 months after the treatment initiation) and affect the mortality risk in patients with established atherosclerotic cardiovascular disease [6]. A 9% increase in the risk of early statin treatment discontinuation

related to negative articles on statins was shown. In addition, negative information on statin was also associated with a higher (by 15%) risk of antihypertensive treatment discontinuation but did not translate into discontinuation of insulin treatment in diabetes. Of note, articles presenting positive information reduced the risk of early statin treatment discontinuation by 8%. The authors of the study noted that the effect of negative information regarding drugs is particularly important in patients with newly diagnosed disease and at the treatment initiation. In patients who discontinued statin therapy within 6 months, a 26% increase in the incidence of myocardial infarction and an 18% increase in cardiovascular deaths was shown compared to those patients who continued the therapy.

The above study dealt with information on statin in lay press articles before the era of universal internet access and development of social media. The development of electronic mass media only aggravated this problem. In addition, "nothing ever gets deleted from the internet", and all articles, posts and commentaries are easily retrievable and may have an effect on patients' beliefs regarding treatment utility even many years after their publication on the internet [48]. In an interesting study, artificial intelligence was used to analyze more than 10,000 of discussions with remarks on statins, authored by more than 5,000 people. Six thematic groups were identified in these discussions: (1) ketogenic diets, diabetes, dietary supplements, and statins; (2) adverse effects of statins; (3) hesitancy regarding statin treatment; (4) evaluation of clinical studies; (5) pharma industry bias regarding statins; and (6) red yeast rice preparations and statins. An analysis of attitudes showed that these discussions were mostly neutral or negative. The results of this study allow defining the major issues or myths regarding statin use and show that analyses based on the use of artificial intelligence may help dispel the myths regarding treatment with statins and other cardiovascular risk-reducing drugs [48].

Important information is also provided by the studies showing that nonadherence regarding statin treatment correlates with nonadherence regarding other therapies benefiting subjects with established atherosclerotic cardiovascular disease, in particular vaccinations against influenza [49, 50]. The level of vaccinations against influenza and use of lipid-lowering therapy in patients at high cardiovascular risk is low, partly due to disinformation regarding statins. In this regard, very interesting data were provided by a 2024 paper on the association between vaccinations against influenza and the frequency of statin use [51]. This study included more than 66,000 patients with established atherosclerotic cardiovascular disease. The study showed that not vaccinating against influenza was independently associated with a 34% lower likelihood of the use of statin-based lipid-lowering therapy among adult Americans, after adjusting for traditional factors associated with underuse of preventive therapies.

This study indicates that among patients with cardiovascular disease, there is a group of patients in whom adherence might be affected by eliminating disinformation regarding therapy which makes the patients inclined to not use or discontinue the therapy. Currently, this problem mainly affects statin use and vaccination but in the future, it may increasingly affect antihypertensive therapy, blood glucose-lowering therapy, or drug treatment or obesity. Thus, in contrast to the above described "healthy adherer" effect, an effect of "unhealthy interest in information" also exists.

A negative attitude towards treatment, resulting mostly from an imbalance between reliable information provided by physicians and other healthcare professionals and myths and disinformation arising from the internet sources, may lead to a nocebo effect. Muscle symptoms related to statin use are the scientifically best described example of a nocebo effect. In one analysis, any muscle weakness or pain occurred in 166 persons per 1000 patient-years of statin therapy, compared to 155 persons per 1000 patient-years of placebo use. Thus, more than 90% of muscle symptoms attributed to statin therapy are not related to statin use [52]. This was confirmed in n-of-1 trials which showed a comparable severity of muscle symptoms in patients receiving blinded sequential placebo and statin treatment [53].

In summary, widely available false and negative information on cardiovascular risk-reducing therapies lead to therapy non-use or early discontinuation, translating to a risk of cardiovascular morbidity and mortality. Providing access to reliable information may have a significant effect on the degree of adherence.

Adherence in relation to age and sex

The problem of nonadherence in regard to the drug treatment of hypertension is common in the general population of hypertensives and affects patients in all age groups but the published studies clearly indicate that age is one of the major factors determining the level of adherence. However, the relationship between the degree of adherence and age

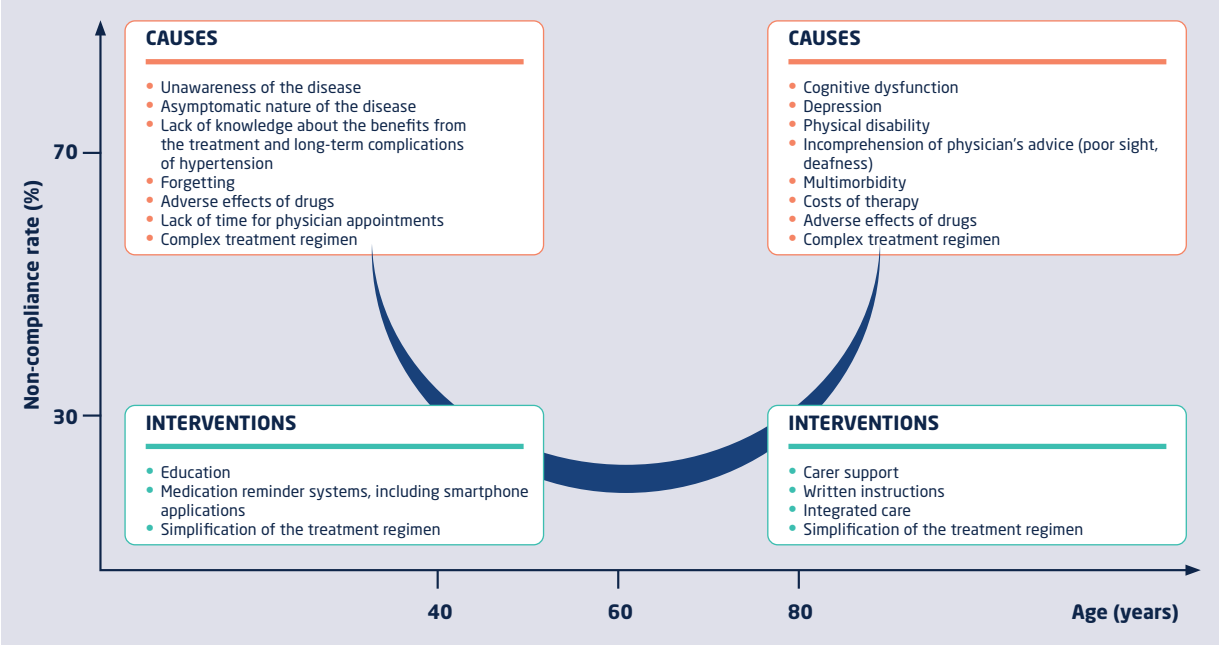

Figure 4. The relationship between adherence and patient age is U-shaped. Orange boxes show causes of nonadherence in younger and older age groups. Green boxes show interventions to improve adherence in both age groups

is not linear but U-shaped (Fig. 4). Adherence is lower in both young and very elderly patients compared to middle-aged subjects.

The degree of nonadherence in regard to antihypertensive therapy in young adults with newly diagnosed hypertension in whom the treatment is initiated is alarmingly high, and the association between nonadherence and long-term risk has been well documented. In a retrospective analysis that included 123,000 persons aged 20–44 years with newly diagnosed hypertension, including 75% of men, only 37% of patients were adherent and took their medications regularly (defined as PDC >80% based on prescription filling reports) [5]. Nonadherence was associated with a higher risk of future cardiovascular events. Over 10 years of follow-up, a 57% higher risk of myocardial infarction, stroke, and cardiovascular death was noted in the nonadherent group [hazard ratio 1.57, 95% confidence interval (CI): 1.45–1.71].

Among young patients with newly diagnosed hypertension, the major factor limiting adherence is unawareness of the treatment goals and the nature of cardiovascular risk. In this group, hypertension is frequently the first chronic, asymptomatic disease that requires drugs to be taken regularly on a daily basis. Unawareness of the benefits from achieving target blood pressure values and the risk associated with hypertensive disease, concerns related to the need for drug therapy and possible drug adverse effects, stigmatization due to being diagnosed with a chronic disease, lack of time for physician appointments, and lack of interest in long-term health preservation are among the factors underlying low level of adherence among young patients with hypertension.

Among middle-aged patients, a higher degree of adherence regarding antihypertensive therapy is observed. In a British study that included 37,643 patients above 40 years of age in whom antihypertensive therapy was initiated within 6 months from the diagnosis, 40–50% patients continued the therapy [54]. Much higher persistence in antihypertensive therapy is seen among subjects above 60 years of age. As indicated by a Swedish study in a cohort of 5225 patients followed-up in 48 primary care centers, 70% of patients continued the therapy at 2 years since their first prescription of antihypertensive medications, and this proportion was significantly higher compared to patients aged 30–49 years, half of whom did not continue the treatment during the follow-up [55].

In patients above 75 years of age, adherence regarding drug therapy tends to decrease. This may be due to several causes, including both medical and psychosocial issues. One reason is cognitive dysfunction. Regardless of its etiology, dementia impairs the ability to plan, organize, and implement tasks related to adherence to therapeutic recommendations [56–58]. In addition, adequate cognitive function is necessary to attend scheduled physician

appointments, obtain and fill prescriptions, adjust doses if needed, and cope with missed doses.

In a recently published systematic review, a clear association was shown between cognitive dysfunction and the level of adherence. Of note, differences in the level of adherence between patients with cognitive dysfunction and the control group disappeared when drug taking was managed by the carer of a patient with hypertension and dementia [58].

Concomitant depression is another neuropsychological problem affecting adherence. Depression is associated with a 2- to 3-fold increase in the likelihood of functional disability or cognitive dysfunction [59]. Importantly, the relative risk of therapeutic inertia, defined as no treatment intensification, referral to a hypertension specialist, or referral for investigations to identify the cause of uncontrolled blood pressure, was significantly higher in hypertensive patients with depressive symptoms (adjusted relative risk 1.49, 95% CI: 1.06–2.10, p = 0.02) [60].

In older patients, problems with drug taking may also be related to a physical disability. Impaired hearing or sight may result in problems when communicating with the physician, reading written physician instructions, or reading drug names on their packages.

Limitations related to musculoskeletal system disorders may impair attendance at physician appointments, and hand joint disease may result in difficulties with opening of drug bottles or getting tablets out of blister packs.

Problems related to treatment cost may arise in all age groups but may be most pronounced in the oldest patients. In a large study performed in the United States, cost issues were a major reason for decisions not to fill a prescription, omit doses, or take lower doses to increase the duration of drug possession [61]. In that study, most patients were above 65 years of age, and the estimated negative effect on poor adherence was 7.5% to 11%.

Multimorbidity, complex treatment regimens, being cared for by various specialists, concerns for drug adverse effects, or perceived lack of treatment benefits are also challenges in the management of the elderly patients. In this context, one possible solution may be to involve care and support by other healthcare providers (nursing care, pharmacist care) that may adjust the treatment and increase the quality of cooperation with patients in the oldest age groups. In a randomized Italian study, it was shown that integrated care involving community nurses contributed to an improved blood pressure control [62].

Multiple other studies, both in Europe and in the United States, provided consistent results indicating that the patient age is the strongest determinant of adherence [63–68].

The much more controversial issue is the effect of sex on the level of adherence. Women are frequently perceived as more orderly and responsible than men, and thus they may be expected to be more adherent regarding both non-drug therapy and the use of antihypertensive medications. However, the published studies yielded inconsistent results. Several observational studies indeed showed higher adherence in women [69–71] but multiple analyses indicated otherwise. In a recently published Italian population study that included 232,507 patients with hypertension, it was shown that adherence was lower in women but the latter were more frequently prescribed antihypertensive drugs [72]. Similarly, in a study that evaluated continuation of antihypertensive therapy in patients with newly diagnosed hypertension, it was shown that persistence was higher in men (53%, compared to 42% in women), with a 10% lower risk of treatment discontinuation regardless of patient age and the type of drug [73].

Similarly, a large Dutch population study yielded similar results, as female sex was associated with lower adherence to antihypertensive therapy at one year after its prescription [74]. In a study that evaluated the degree of adherence based on the analysis of drug levels in patients with resistant hypertension (174 patients, 48% of women), a high rate of nonadherence (40%) was found in general but women were three times more likely to be nonadherent compared to men [75].

A recently reported metaanalysis of 82 studies that evaluated adherence to antihypertensive drug therapy did not show significant differences between women and men [76].

These discrepant results may be related to differences in study methodology or inherent limitations of the analyses of adherence, including the declarative nature of the questionnaires used.

Clearly, women more frequently report adverse effects of antihypertensive drugs and more frequently show drug intolerance, particularly with multidrug therapy [77].

Women are more frequently treated for hypertension but less frequently achieve target blood pressure values [78, 79]. However, it is not known whether and to what extent this might be related to nonadherence.

Single-pill combinations

Use of SPC is currently the standard approach to the treatment of hypertension (using two-

and three-drug combinations), it is frequently used in the treatment of hypercholesterolemia (using statin and ezetimibe combinations), and recently it has also been preferred in the guidelines on the management of diabetes [7, 80–82]. SPC of two antiplatelet drugs are also available on the market. In addition to two- and three-drug combinations used in the treatment of a given single disease, polypill formulations have also been developed, combining medications used in the treatment of multiple diseases. The most commonly used polypill formulations are combinations of a statin with one or two antihypertensive drugs. Other polypill formulations include a combination of acetylsalicylic acid (ASA) and an antihypertensive drug (ASA plus a beta-blocker combination available in Poland) or an antihypertensive drug and a statin [a combination of ASA, an angiotensin-converting enzyme (ACE) inhibitor, and a statin].

Single-pill combinations are used to increase adherence. Low adherence and low persistence are among major challenges in the contemporary drug therapy. Among patients after myocardial infarction (secondary prevention), 34% to 50% do not take the recommended cardiovascular drugs [83–85]. In the primary prevention of myocardial infarction, as many as half of patients do not adhere to the therapeutic recommendations [83]. It was shown that better adherence regarding the use of statins and antihypertensive drugs (particularly ACE inhibitors/angiotensin receptor blockers and — in patients after myocardial infarction — beta-blockers) is associated with lower total mortality [84, 86, 87].

Use of SPC increases adherence and persistence [85]. Most data are available for antihypertensive therapy. In an analysis of an Australian registry, use of perindopril-amlodipine SPC was associated with significantly higher adherence (66% *vs.* 43% at 12 months) and persistence (median duration of treatment continuation 42 months *vs.* 7 months) compared to the use of the same drugs as separate formulations [87]. In a multivariate analysis, the risk of treatment discontinuation was nearly twice higher with the use of perindopril and amlodipine as separate formulations compared to the use of SPC. At 4 years of follow-up, total mortality in the SPC group was 8%, compared to as much as 18% in the group treated with separate formulations of perindopril and amlodipine. In a multivariate analysis, mortality risk was more than 80% higher in the separate formulations group compared to the SPC group [87].

Improved outcomes with SPC result from improved adherence, which in turn leads to an increased therapeutic effect of a given intervention

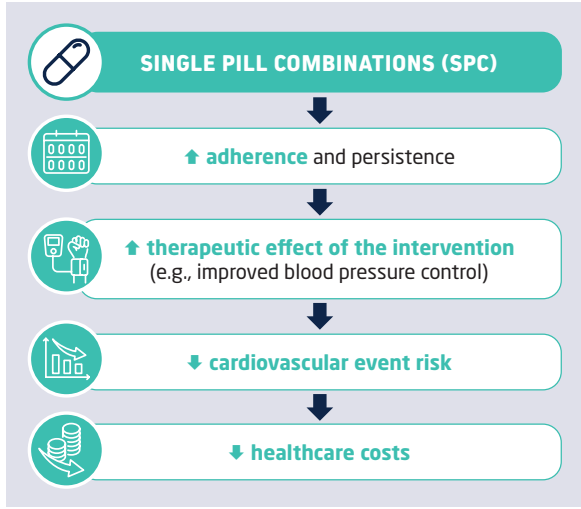

Figure 5. The effect of using single pill combination on adherence, cardiovascular event risk, and healthcare costs

(e.g., better blood pressure control) — Figure 5. An improvement of blood pressure control with SPC (including the combination of perindopril, indapamide, and amlodipine) was shown compared to the use of the same drugs as separate formulations [88]. In a metaanalysis of 11 studies that included more than 170,000 patients receiving combined antihypertensive and/or lipid-lowering therapy as SPC *vs.* separate formulations, significantly higher adherence and persistence were found in the SPC group [89]. Use of SPC was associated with significantly better blood pressure control and a higher proportion of patients achieving therapeutic targets. Use of SPC was also associated with a lower rate of hospitalizations and emergency room visits [89].

Ultimately, the evidence of better outcomes with the use of SPC was provided by the Secondary Prevention of Cardiovascular Disease in the Elderly (SECURE) study, published in the New England Journal of Medicine in 2022 [90]. This was a randomized, controlled trial in which nearly 2,500 patients aged 65 or above, with a history of myocardial infarction within 6 months, were randomly assigned to the polypill group (ASA, ACE inhibitor, and statin) or the standard care group. At 3 years of follow-up, better adherence and a 24% reduction in the risk of the primary endpoint (cardiovascular death, nonfatal myocardial infarction or stroke, or urgent revascularization), along with a 33% reduction in cardiovascular mortality and a 29% reduction in the risk of myocardial infarction, were noted in the polypill group compared to the standard care group [90].

Table 5. Components of patient-centered intervention to increase long-term adherence regarding the use of cardiovascular drugs

- **Patient-physician relationship based on trust** (listening to the patient, answering the questions asked, attempting to solve the problems reported).
- **Patient education** (discussion of the goals and importance of the therapy; discussion of the effect, e.g., of elevated blood pressure values on cardiovascular disease; discussing the benefits of treatment, e.g., that it leads to a reduction in the incidence of myocardial infarction and stroke; frank discussion regarding adverse effects; dispelling myths on treatment, e.g., that statin use leads to dementia).
- **Reminding/persuading** (asking about adherence at each visit, medication reminder systems, e.g. SMS-based).
- **Financial aspect** (tailoring the therapy to the financial status of the patient).
- **Formulation of advice** (clear and simple message to the patient when formulating advice).

Benefits in regard to cardiovascular events resulting from the use of SPC translate into lower healthcare costs [91, 92]. In an analysis of Italian administrative data from more than 18,000 patients, treatment with perindopril, indapamide, and amlodipine SPC was associated with a significant improvement of adherence compared to the group treated with the same drugs but in two or three separate formulations (60% *vs*. 27%). At one year of follow-up, a significantly lower total mortality (30 *vs*. 34/1000 patient–years, $p < 0.05$) and a lower overall incidence of deaths and cardiovascular events (106 *vs*. 139/1000 patient–years, $p < 0.001$) were noted in the SPC group compared to the group treated with the same drugs in two or three separate formulations. Annual direct costs for the healthcare system were lower by nearly one fifth for SPC compared to the use of two or three separate formulations, which was related to both lower cost of SPC formulations and lower rate of hospital admissions in the SPC group [91].

In summary, the use of SPC, both targeted at the treatment of a single disease and polypill formulations, is associated with improved adherence due to simplification of the treatment regimen. In turn, improved adherence leads to better therapeutic effects which translate into a cardiovascular event risk reduction and lower costs for the healthcare system. In case of SPC targeting a single disease (e.g., hypertension), an additional advantage are complementary mechanisms of action of the individual components of the combination, which 1) increases the overall effect of the combination and allows more rapid achievement of the therapeutic target; and 2) is associated with a lower risk of adverse effects. Both these effects (lower rate of adverse effects and more rapid achievement of the therapeutic target) may improve the patient-physician cooperation. In addition, use of SPC, by reducing the number of tablets that need to be taken, is more convenient for patients and, as indicated by the studies on polypharmacy, may lead to an improvement in the quality of life [92]. This effect may clearly help in building a partner relationship between the patient and the physician who cares not only about the patients' outcomes but also about their quality of life.

The recent introduction of drug cost reimbursement for most SPC of antihypertensive drugs in Poland, also when initiating the therapy, has removed an administrative barrier in initiating the treatment with SPC in hypertension, and resulted in the cost of this treatment being similar and frequently even lower compared to the cost of treatment with separate formulations. The proven benefits of the use of SPC, including SPC of three antihypertensive drugs, in terms of both improved outcomes and lower costs for the healthcare system, should serve as a rationale for the introduction of drug cost reimbursement for further SPC categories in Poland.

Telemedicine

Contemporary technologies offer many modern methods for the diagnosis, monitoring, education, and treatment of patients with chronic diseases. Telemedicine offers significant benefits, particularly in the context of remote monitoring of the patient health status. A classical approach to telemonitoring, rooted already in the analog era, is tele-ECG, or remote evaluation of the ECG tracing. Contemporary telemonitoring systems are much more advanced. Currently, telemedical systems and various applications may be used to monitor physical activity, dietary choices, amount of calories consumed, body mass, blood pressure, blood glucose levels, body hydration status, blood oxygen saturation, heart rhythm and many other parameters, which allows monitoring of the health status and the treatment effectiveness in many diseases. Some applications may transfer biometric data to the treating physician. Regular monitoring allows early detection of abnormalities and rapid reaction to changes in the patient health status. Systems monitoring various parameters of the health status may prevent serious complications also by early detection of health problems. By allowing physicians to monitor the health status of their patients more easily, which leads to more rapid responses to changes in the health status, these approaches may decrease the risk of various complications, prolong patients' life, and improve their quality of life. An additional but no less

important advantage is an increased patient sense of safety. The awareness of continuous monitoring of the health status, creating an opportunity for an easy response by the system and the healthcare personnel involved in the monitoring, reduces anxiety in many patients which in turn affects, among others, their quality of life. An important advantage of systems that monitor various parameters is their educational value, and an effect on patients' everyday decisions. For example, use of pedometers increases the average daily number of steps by more than one thousand and reduces the duration of time spent in a sitting or reclining position [93, 94]. It was also shown that the use of continuous glucose monitoring systems not only allows more rapid and precise adjustments of blood glucose-lowering drug doses but also promotes beneficial modifications of patients' dietary habits.

Modern monitoring systems also allow evaluation of prescription filling in pharmacies. Such systems may send messages to patients, reminding them about the need to fill a prescription. Smartphone applications and SMS systems may send reminders to patients about the need to take medications at a specified time, and may also send reports to the treating physician. Such reminders help maintain regularity and adhere to the treatment plan, increasing the proportion of patients with well controlled disease, for example hypertension or hypercholesterolemia. Higher persistence in the use of recommended therapies may also translate into a lower risk of complications resulting from untreated or poorly treated disease, such as myocardial infarction or stroke.

A recently published metaanalysis of several trials showed that blood pressure telemonitoring was associated with a significant blood pressure reduction by 6/2 mm Hg [95]. Similarly, a beneficial effect was shown of telemedicine intervention on, among others, diabetes control. Use of diagnostic, support, and educational telemedicine methods was associated with a reduction in fasting blood glucose level by on average 0.6 mmol/L, postprandial blood glucose level by 1.6 mmol/L, and HbA_{1c} level by 0.5% [96]. Telemedicine monitoring and treatment systems are also effective in individuals witch ischemic heart disease. A metaanalysis of 24 studies showed that compared to standard care, use of telemedicine methods was associated with a significant reduction in waist circumference, low-density lipoprotein (LDL) cholesterol and triglyceride levels, blood pressure and smoking rate, and with an increase in physical activity [97]. Use of telemonitoring in patients with heart failure was associated with a 20% lower risk of all-cause death and a 29% lower risk of hospitalization due to heart failure [98]. Use of modern technologies in post-hospitalization care is associated with a lower rate of emergency room admission, shorter re-hospitalizations, and in patients with heart failure with a lower mortality risk [99]. A metaanalysis of 5 studies also showed that use of telemedicine methods was associated with better quality of life of the patients [100].

In a recently published systematic review of studies that evaluated the effect of interventions using modern technologies on adherence in patients with hypertension, diabetes and/or dyslipidemia, a significant effect of such interventions was shown in 8 of 13 analyzed studies [101]. In a similar systematic review that focused on patients with hypertension, interventions were shown to be effective in 7 of 9 studies [102]. As highlighted by the authors of these reviews, the most effective interventions are those which engage patients, remind them about the recommended timing of drug taking or the need to resupply drugs, and use educational tools to help patients understand the importance of medications and their regular taking [103].

One method of reminding about the need to take drug doses as scheduled is sending short text messages (SMS). Compared to other e-health strategies, advantages of using text messages include wide availability of mobile phones capable to receive SMS, low cost, easy use and integration with the existing medical systems, and independence from the internet communication [103]. A metaanalysis of 6 randomized studies showed higher regularity of drug taking in the intervention groups which translated to lower blood pressure values [104]. Current technologies, including instant messaging applications, allow sending multimedia messages. In a recently published randomized study that evaluated the effect of a 16-week intervention using text, voice and video messages sent by the WhatsApp service, a 15% difference in the regularity of drug taking was noted between the study groups. This effect did not reach statistical significance ($p = 0.08$), likely due to the limited size of the study sample [105]. In an interesting novel pilot study, Roca et al. showed potential effectiveness of virtual assistants that supported patients in adhering to the physician recommendations [106].

Another form of intervention are mobile phone applications which may remind about the need to take drugs or fill the prescription, and promote healthy lifestyle by sending multimedia educational and motivational messages [103]. In addition, tracking and analysis of the biometric data allow

personalization of such messages, sending alarms in case significant abnormalities are found, and may facilitate interactions with healthcare professionals. Personalization of the touchscreen, adjustable font size, and possibility to adjust audiovisual materials may be liked by users with lower self-health competencies. Three metaanalyses of randomized studies showed the effectiveness of these applications [107–109]. It was also shown that telemonitoring of blood glucose levels and blood pressure values improves the regularity of drug taking and increases patients' persistence in treatment [110, 111].

Although the acceptance of telemedicine approaches by the patients is relatively high, ranging from 76% to 97% [93], whenever use of any telemonitoring system is recommended, the patients should be assured about the safety of the data being transmitted. Some patients may perceive continuous monitoring as a form of control, or intrusion into their privacy and autonomy. Open communication between the physician and the patient is necessary to allow a positive perception of telemonitoring. The patient should be made aware of the benefits from telemonitoring and should feel empowered as an equal partner in the treatment process. Telemedicine, including telemonitoring, has a great potential for improving the quality of healthcare but requires careful implementation and monitoring. It is important that these systems be user-friendly for both patients and physicians, and both parties should be aware of the benefits and limitations of this form of health monitoring. Complying with these conditions allows maximization of benefits from the use of telemedicine systems.

Summary

As summarized in the present article, multiple and varied factors affect adherence to the therapeutic recommendations. Previous studies on this issue have had many limitations that hinder translating their results to clinical practice. These were mostly observational studies which only identified factors associated with nonadherence. The number of prospective interventional studies has been small. In addition, an increase in adherence is a net result of many even minor actions which increase the chance of success when applied together. This also explains the failure of some studies that evaluated isolated interventions. Varying methods to evaluate effectiveness and inability to extrapolate the results of some studies to local conditions are also limitations of previous studies.

Efforts to increase adherence to the therapeutic recommendations in primary and secondary prevention of cardiovascular disease must focus on the improvement of communication between patients and physicians, building a partner relationship between them, patient education and combatting disinformation on the internet, use of electronic methods (e.g., SMS reminders/prompts), elimination of economic barriers, and monitoring of adherence. An important aspect is therapy simplification by using simple treatment regimens and SPC. Only comprehensive efforts to improve adherence, e.g., by building a partner patient-physician relationship, may contribute to an increase in persistence and lead to reduction of cardiovascular morbidity and mortality in the general population.

Conflict of interest

All authors are frequent speakers and receive fees for lectures on hypertension.

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