How to optimize the adherence to a guideline-directed medical therapy in the secondary prevention of cardiovascular diseases: a clinical consensus statement from the European Association of Preventive Cardiology (EAPC)

*__Roberto F.E. Pedretti__, MD: Cardiovascular Department, IRCCS MultiMedica, Sesto San Giovanni, Milano, Italy

*__Dominique Hansen__, PhD: REVAL/BIOMED, Hasselt University, Belgium, Heart Centre Hasselt, Jessa Hospital, Hasselt, Belgium

__Marco Ambrosetti__ , MD: Cardiovascular Rehabilitation Unit, ASST Crema, Santa Marta Hospital, Rivolta D´ Adda, Italy.

__Maria Back__, PhD: Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg and Department of Health, Medicine and Caring Sciences, Linköping University, Sweden.

__Thomas Berger__, MD: Cardiomed Linz, St.John of God Hospital Linz, Austria

__Mariana Cordeiro Ferreira,__ Psychologist, Centro de Reabilitação Cardiovascular do Centro Universitário Hospitalar Lisboa Norte, Portugal

__Véronique Cornelissen__, PhD: Department of Rehabilitation Sciences, KU Leuven, Leuven, Belgium

__Constantinos H Davos,__ MD, PhD: Cardiovascular Research Laboratory, Biomedical Research Foundation, Academy of Athens, Athens, Greece

__Wolfram Doehner__, MD, PhD: BIH Center for Regenerative Therapies (BCRT), Berlin Institute of Health at Charité - Universitätsmedizin Berlin, Berlin, Germany, Department of Cardiology (Virchow Klinikum), Charité Universitätsmedizin Berlin, and German Centre for Cardiovascular Research (DZHK), partner site Berlin, Berlin, Germany, Center for Stroke Research Berlin, Charité-Universitätsmedizin Berlin, Berlin, Germany.

__Carmen de Pablo y Zarzosa__, MD, PhD: Department of Cardiology. University Hospital Ramón y Cajal, Madrid, Spain

__Ines Frederix__, MD, PhD: Heart Centre Hasselt, Jessa Hospital Hasselt Belgium, Hasselt University, Faculty of Medicine and Life Sciences Diepenbeek Belgium, University of Antwerp, Faculty of Medicine and Health Sciences Antwerp Belgium, Antwerp University Hospital Edegem Belgium.

__Andrea Greco__, PhD: Department of Human and Social Sciences, University of Bergamo, Bergamo, Italy

__Donata Kurpas__, MD, PhD: Department of Family Medicine, Wroclaw Medical University, Poland

Matthias Michal, MD: Department of Psychosomatic Medicine and Psychotherapy, University Medical Center Mainz, Mainz, Germany; German Center for Cardiovascular Research (DZHK), Partner Site Rhine-Main, Mainz, Germany

Elena Osto , MD, PhD: Institute of Clinical Chemistry & Department of Cardiology, Heart Center, University & University Hospital Zurich, Zurich, Switzerland

Susanne Pedersen, PhD: Department of Psychology, University of Southern Denmark, Odense Denmark, and Department of Cardiology, Odense University Hospital, Odense, Denmark

Rita Esmeralda Salvador, MD, PhD: Vienna, Austria

Maria Simonenko, MD, PhD: Heart Transplantation Outpatient Department, Cardiopulmonary Exercise Test Research Department, Almazov National Medical Research Centre, St. Petersburg, Russia

Patrizia Steca , PhD: Department of Psychology, University of Milan-Bicocca, Italy

David R. **Thompson**, PhD: School of Nursing and Midwifery, Queen's University Belfast, Belfast, UK

Matthias Wilhelm, MD: Department of Cardiology, Bern University Hospital, University of Bern, Bern, Switzerland

** **Ana Abreu**, MD, PhD: Department of Cardiology of Hospital Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Institute of Preventive Medicine and Institute of Environmental Health of the Faculty of Medicine of University of Lisbon, Centre of Cardiovascular Investigation of University of Lisbon (CCUL) and Academic Centre of Medicine of University of Lisbon (CAML), Portugal

*Shared first autorship

**Shared last autorship

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Address correspondence:

Roberto F.E. Pedretti, MD, FESC

Cardiovascular Department, IRCCS MultiMedica

Via Milanese, 30, I-20099, Sesto San Giovanni, Milano, Italy

E-mail: robertofrancoenrico.pedretti@multimedica.it

Abstract

A key factor to successful secondary prevention of cardiovascular disease (CVD) is optimal patient adherence to treatment. However, unsatisfactory rates of adherence to treatment for CVD risk factors and CVD have been observed consistently over the last few decades. Hence, achieving optimal adherence to lifestyle measures and guideline-directed medical therapy in secondary prevention and rehabilitation is a great challenge to many healthcare professionals. Therefore, in this European Association of Preventive Cardiology (EAPC) clinical consensus document a modern reappraisal of the adherence to optimal treatment is provided, together with simple, practical, and feasible suggestions to achieve this goal in the clinical setting, focusing on evidence-based concepts.

Keywords: cardiovascular disease, cardiovascular risk, secondary prevention, adherence

Introduction

In secondary prevention of cardiovascular disease (CVD), significant room for improvement is present as many lifestyle measures and/or guideline-directed medical therapy remain too poor.[1,2] Medication adherence ranges from 50% for primary CVD prevention to 66% for secondary prevention; of all medication-related hospital admissions in the United States, 33 to 69 % and approximately 9% of CVD cases in Europe can be attributed to poor medication adherence.[3–5]

In this regard, sufficient treatment adherence is a key element for (i) improving prognosis in CVD and/or high-risk patients, (ii) reducing the burden of morbidity and mortality associated with CVD, and (iii) decreasing costs due to rehospitalizations.[6] The promotion of treatment adherence should embrace all pharmacological and non-pharmacological interventions in secondary CVD prevention, including lifestyle and behavioural changes. In this perspective, multidisciplinary CVD prevention and rehabilitation programs are the most appropriate and cost-effective settings for delivering structured and multi-component interventions on patients' adherence.

Despite the realization that treatment adherence is a key aspect of successful secondary CVD prevention, optimisation of treatment adherence remains a great challenge to many healthcare professionals. In coronary artery disease (CAD) patients, ≥6 months after hospital discharge, 42% still had a blood pressure ≥140/90 mmHg, 71% still had low-density lipoprotein cholesterol ≥1.8 mmol/L (≥70 mg/dL) and 29% had insufficiently controlled diabetes.[1]. In the EUROASPIRE IV and V surveys, 16259 coronary artery disease (CAD) patients were examined and interviewed during a study visit ≥6 months after hospital discharge.[2] Data gathering was fully standardized and the Brief Illness Perception questionnaire was completed by a subsample of 2379 patients.[2] Half of those who were smoking prior to hospital admission were still smoking; 37% of current smokers had not attempted to quit and 51% were not considering to do so.[2] The prevalence of obesity was 38%, in relation to physical activity, 40% was on target with half of the patients trying to do more everyday activities.[2] Less than half had the intention to engage in planned exercise and only 29% of all patients were on target for all three lifestyle factors[2]. The number of adverse lifestyles was strongly related to the way patients perceive their illness as threatening.[2] Although a lack of adherence to guidelines by healthcare professionals cannot be ruled out, there is a very high likelihood that also patient adherence to treatment or advices is still too poor.

Aim

The preventive cardiology community needs a formal clinical consensus document detailing how to optimize patient adherence to treatment for the secondary prevention of CVD. Aims of this clinical consensus document are to provide a modern reappraisal of the concept of adherence together with simple, practical, and feasible

suggestions to achieve optimal adherence in the clinical setting, focusing on evidence-based concepts. Although aspects of adherence have been discussed fragmentally in previous guidelines and position statements, the novelty of this paper is thus that all clinically relevant and state-of-the-art knowledge on adherence on all aspects of guideline-directed medical therapy is brought together.

Methods

The accumulation of the current evidence was based on a search strategy of English language published research, consensus documents and policy documents, by using electronic databases (MEDLINE, EMBASE, CINAHL), as selected, evaluated and reviewed by experts from the EAPC, and authors of the original documents. In the development process of this position paper, individuals from relevant healthcare professional groups (e.g. cardiologists, general practitioners, psychologists, psychosomaticists, nutritionists, physiotherapists, nurses) were included. From the collected evidence, consensus statements have been formulated (see Table 1), as well as an agreed approach with respect to adherence optimisation strategies (see Figures 1, 3). Finally, all position statements were carefully aligned with current EAPC/ESC position papers or guidelines.[7–13]

Definition and measurement of adherence

Adherence is defined as the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes - corresponds with agreed recommendations from a healthcare provider.[14] The term "adherence," is preferred to "compliance," and strong emphasis is placed on the need to differentiate adherence from compliance. The main difference is that adherence requires the patient's agreement ('informed consent') to the recommendations.[14] Patients should be active partners with healthcare professionals in their own care and thus, good communication between patient and healthcare professional is a must for an effective clinical practice.[14] The process starts with the informed consent of the patient and is followed by the initiation of treatment, when the patient takes the first dose of a prescribed medication or initiates lifestyle changes.[15] The process continues with the implementation of the dosage regimen, defined as the extent to which a patient's actual dosing corresponds to the prescribed dosage regimen, from initiation until the last dose is taken.[15] Discontinuation marks the end of therapy, when the next dose to be taken is omitted and no more doses or lifestyle changes are taken thereafter.[15] Persistence is the length of time between initiation and the last dose or lifestyle action.[15] Non-adherence to medication or healthy lifestyle behaviours can occur in the followingcases: late or non-initiation of the prescribed treatment/therapy, sub-optimal implementation of the dosing regimen or early discontinuation of the treatment/therapy.[15] Non-

adherence behaviours include intentional and unintentional components. The former refers to an active and reasoned process that leads the patient to modify the treatment plan, deviating from the agreed prescriptions, while the latter is considered a passive process in which patients are careless, forgetful, or unable to adhere to the treatment plan for other reasons, such as unable to collect their medications or not understanding the information on medications provided.[16] In some cases, i.e. significant cognitive impairment, the patient is not able to agree to the recommendation and in these cases the healthcare provider is responsible for providing the necessary support and/or information. It is also important to note that some behaviours affecting treatment adherence may represent specific mental disorders per se, acknowledged in ICD classification**,** that needs to be diagnosed and treated. In the ICD-11-CM a specific clinical entity, defined as 'psychological and behavioural factors that may adversely affect the manifestation, treatment, or course of a physical condition by affecting treatment adherence or care-seeking' exists and is coded 6E40.[17] In everyday clinical practice, however, the awareness of these diagnoses is extremely poor and healthcare providers are very reluctant to assess, code, and treat these mental disorders although the mental comorbidity mitigates therapeutic efforts.[18]

Measurements of adherence can be direct, including observed administration or measuring the blood concentration of a metabolite, measuring physical activity by step counters/accelerometers, or measuring carbon monoxide (CO) exhalation, or they can be indirect, including patient self-reporting, pill counting, pharmacy refill rates, physical activity or dietary questionnaires, and electronic monitoring systems.[19] Indices such as the medication possession ratio (MPR) or the proportion of days covered (PDC), based on counting the number of days the patient has been in possession of the drug and has actually used it, as derived from the intervals between supplies of the drug. Using PDC for statins and angiotensin-converting enzyme inhibitors, stratification of patients with known CVD as fully adherent (≥80%), partially adherent (≥40% to≤79%), or nonadherent (<40%) was able to identify groups with a significantly different event rate.[20] There are numerous methods for measuring adherence by self-reported questionnaires: at least 43 adherence scales exist.[21] Of these, two instruments are particularly used in CVD medicine to assess the degree of patient adherence, which are based on the patients' answers to specific questions. The Morisky Medication Adherence Scale (MMAS) investigates only the domain of the pharmacological treatment [22], while the Hill-Bone Compliance Scale (HBCS) also investigates behavioural domains.[23].

Why are patients non-adherent to cardiovascular prevention recommendations?

The need to integrate the therapeutic routine into one's daily life and to cope with the onset of potential side effects and undesirable changes in lifestyle, or in established habits, represent challenges that many patients

face, using their own inner resources in the search for a balance among the need to take care of oneself, preventing relapses, and the need to maintain an acceptable quality of life.[24] The distinction between the intentional and unintentional components of non-adherent behaviours is very important.[16,25,26] Understanding the nature of the non-adherence processes, which can be highly variable (see Table 2), is important not only for the purpose of defining useful strategies to manage their detrimental effects, but also for decreasing these phenomena. Therefore, it is fundamental to understand the emotional and cognitive aspects underlying patients' choices and behaviours regarding treatment. Although the risk factors for CVD are often acknowledged by patients as predisposing them to CVD, their risk perception can still be inadequate, thus affecting preventive behaviours. Moreover, a lower health literacy could also be highly prevalent among patients with CVD risk. As a result, there is a tendency to underestimate the causal link between CVD risk factors and disease manifestations among many patients.[27–31] Indeed, a patient's lower perceived necessity for secondary prevention is related to non-adherence.[28,32] Concerns and irrational beliefs about preventive measures are identified as powerful predictors of (un)intentional non-adherence to treatment.[29] On the other hand, coping skills and the perception of (personal) control over the management of care are important elements capable of increasing the adherence to treatment.[33–35] Patients tend to modify their use of medications in an improper way when they feel they are no longer able to integrate the therapeutic routine into their daily life, due to consequences on their quality of life, which results in their health condition worsening.[34] This highlights the significant role of a high level of self-efficacy in the processes of adherence to treatment.[35] Also the quality of patients' social support, understood as family relationships and available healthcare networks, can affect individual coping and the development of self-care skills:[33] weaker practical/social support is associated with non-participation in rehabilitation programs and non-adherence to medication.[36,37] Also mental disorders (especially mood disorders, depression, anxiety disorder and personality disorders) are associated with poorer adherence to treatment,[34,35,38][39][40] and favor development of irrational beliefs about pharmacotherapy or lifestyle measures. Therefore, it is useful to conduct a careful assessment of the above-mentioned psychosocial variables at entry of prevention and rehabilitation programs, to detect potential contributors to a lower treatment adherence and, by appropriate actions, maximize the patients' adherence to treatment (see Figure 2).

Poor adherence to treatment in patients with specific CVD risk factors and diseases

Next to medication intake, the implementation of lifestyle changes such as a healthy diet, physical activity/exercise training and smoking cessation is recommended by ESC Guidelines in secondary prevention of CVD.[11,13] Poor adherence to long-term therapies, including lifestyle changes, has important public health

implications, as it leads to increased morbidity and mortality, as well as significant economic costs (e.g. number of visits, diagnostic procedures, prescribed drugs), and should thus be prevented.[14] Additionally, in specific CVD's and risk factors, some factors seem highly predictive of low adherence to therapy (see Figure 2).

Overweight and obesity

The adherence to treatment is generally lower in persons with overweight or obesity.[41] Barriers to lifestyle change include poor motivation, environmental, societal and social pressures, lack of time, health and physical limitations, negative thoughts and moods, socioeconomic constraints, gaps in knowledge or awareness, and lack of enjoyment of exercise.[41] Therefore, a good preparticipation screening is of utmost importance to detect such factors or contributors. On the other hand, the most prominent predictors of greater adherence to lifestyle treatment in obese patients include: early weight loss success, a lower baseline body mass index (BMI), having existing cardiometabolic comorbidities, better baseline mood, being male and older age.[41,42] As the overweight/obesity and unhealthy lifestyle cluster are overrepresented in economically disadvantaged and other more vulnerable populations (including people with psychological issues), they are also important contributors to health disparities. In line with this notion, all lifestyle modifications must be personalized according to the availability of foods, geographic localizations, health status and psychosocial factors of the patient to fully exert their health-promoting effects.[41,42]

Hypertension

Despite large evidence confirming the importance of blood pressure (BP) lowering and the availability of many effective and well-tolerated antihypertensive drugs, BP control rates are still unsatisfactory.[1] This is, at least in part, related to poor adherence to lifelong anti-hypertensive therapy. The most common predictors/determinants for a lower adherence to the intake of BP-lowering medications are: lower diastolic blood pressure, higher cost or insurance type/coverage, non-white race/ethnicity, fewer healthcare contacts within six months after the prescription, and ≥4 comorbidities.[43] Distrust, (concern for) side effects, and lack of perceived need for the medication (becausehypertension is often a symptomless condition it will further lower the adherence to treatment).[43] Crucially, also a lack of patient involvement in the treatment decision-making process will lower the patient's adherence to medication prescription.[44] The lack of adherence to medication prescription should not be confused with difficult-to-treat hypertension, which is BP not optimally controlled despite adherence to an appropriate regimen of three antihypertensive drugs of different classes (including diuretics) in which all drugs are prescribed at appropriate antihypertensive doses.[13] In this regard, pseudo-resistance (such as inaccurate BP measurement, extracellular volume expansion, intake of NSAIDs or

stimulants known to elevate BP) as well as a secondary cause of hypertension should be excluded before this diagnosis is accepted.

Dyslipidaemia

Low-density lipoprotein (LDL) cholesterol is a key causal factor of CVD.[45,46] Lipid-lowering medications are often prescribed to decrease the risk of micro- and macro-cardiovascular complications related to dyslipidaemia, in both primary and secondary CVD prevention,[13] including patients who have undergone heart transplantation.[47] Despite widespread prescription of lipid-lowering drugs, including statins, adherence to therapy is a challenge worldwide, in particular in primary prevention.[48] Statins reduce the risk of recurrent ischemic stroke and myocardial infarction (MI) and better adherence to outpatient statin prescriptions lowers the rates of subsequent CVD events.[49] The following characteristics/factors predict a greater adherence to statin prescription: male sex, older age, history of MI or stroke, presence of diabetes, hypertension or co-morbidities, positive patients' beliefs about medicines, and very recent treatment initiation.[48,50,51] However, the adherence to medications for treatment of a symptomless condition, such as dyslipidaemia, is a great challenge: lipid-lowering agents may be discontinued sooner than other oral medications for chronic therapy because of a lack of sensation of improvement in symptoms or benefit. A substantial proportion of patients do not achieve adequate reduction in LDL-cholesterol levels despite intensive statin treatment, cannot tolerate statins, or remain at high residual risk despite being on statin therapy.[52,53] For high-risk patients in whom statin therapy alone is insufficient, add-on treatment with non-statin medications, ezetimibe and proprotein convertase subtilisin/kexin-9 inhibitors (PCSK9i) is a valuable option.[54,55] Importantly, appropriately identifying and characterizing barriers to PCSK9i access, and developing approaches to overcome them, will reduce the clinical and economic burden for patients who are likely to benefit from PCSK9 inhibition and likely result in more cost-effective policies.[56,57]

Diabetes

The current management of diabetes in the secondary prevention of CVD remains suboptimal,[1] notwithstanding the well-established clinically significant relation between a worse glycaemic control and greater risk for adverse CVD events.[58] Sometimes, the treatment of diabetes can be even more challenging when not only glycaemic control is targeted, but also the lipid profile, body weight and blood pressure of the patient with diabetes.[13] This often leads to the need to take different medications in combination with important lifestyle adjustments (e.g. nutrition, quit smoking, and physical activity/exercise training), and stepwise approach is recommended by guidelines,[13] which should be better settled by a shared-decision

making process. In this process, health education can be offered: very often the health literacy is low in diabetic patients, which negatively affects adherence to treatment. In addition to the intensiveness of treatment, there are additional predictors for a lower adherence to treatment: anxiety, diabetes distress, older age, poor communication with healthcare professionals, stress, concerns about medicines, cognitive impairment, and low levels of self-care. [26] In particular the experience of frequent hypoglycaemia can significantly lower the adherence to prescriptions of glucose-lowering medications. As a result, it is important to provide a close/regular follow-up of the patient with diabetes, in which such side effects can be remediated timely. On the other hand, a high self-efficacy, social and family support, and the acceptance of illness have a beneficial effect on medication and lifestyle adherence.[26]

Coronary artery disease and heart failure

Poor adherence to prescribed regimens is pervasive and results in preventable hospitalisations, premature deaths and unnecessary healthcare expenditure in CAD and heart failure (HF), regardless of the underlying CVD etiology.[5,14,59–67] Non-adherence to treatment remains high.[68–70] Many factors contribute to medication non-adherence, such as lack of social support, absence of symptoms, cognitive decline, adverse reactions, depression, poor attention span, poor knowledge about medication or treatment, the prescription of multiple medications, difficulty with swallowing (large) pills, and inconveniences of urinary frequency with diuretics.[64] Healthcare providers should continue to provide education, constantly reinforce the importance of taking medication as prescribed, and when feasible, utilize one of the successful evidence-based strategies to increase adherence.[64] In this regard, shared decision making and applying a stepwise approach based on the capacities and preferences of the patient could be of vital importance. A multidisciplinary team approach, such as cardiac rehabilitation (CR) programs, would be the best way to improve medication adherence, since the patient would receive education and resources from every discipline.[14] In addition, a close monitoring/follow-up of the patient may assist in keeping the adherence to treatment high.[11] Telehealth and remote consultations are excellent options to consider.[71]

Stroke

The burden of stroke is immense and rapidly growing and recurrence is a major risk factor since recurrent stroke is more likely to cause death and disability. Medication adherence and persistence rates are low in patients after suffering a stroke as well as adherence to exercise programs. [72,73] Nevertheless, there is a lack of a uniform method of measurement of adherence to exercise or physical activity recommendations in the stroke population.[73] Further research using clear, standardized and objective assessments is needed to

clarify the association between cognitive impairment, psychological determinants and medication adherence in stroke survivors.[74,75]

Atrial fibrillation

The impact of atrial fibrillation is increasing and an a holistic care approach for atrial fibrillation patients, the 'Atrial fibrillation Better Care' (ABC) pathway has been proposed.[76] The ABC pathway stands on three main pillars: 'A': Avoid stroke (with Anticoagulants); 'B': Better symptom management; 'C': Cardiovascular and Comorbidity management and it is recommended in the recent European Society of Cardiology atrial fibrillation management guidelines.[77,78] Adherence to the ABC pathway is associated with a reduction inthe risk of major adverse outcomes, however adherence to the ABC pathway is suboptimal, being adopted in one in every five patients.[79]

COPD

COPD is a common disease that, if not managed appropriately, causes an enormous strain on health services.[80] Optimal medication adherence in patients with COPD assists in improving disease management and reducing health care costs and patients who adhere to treatment have a lower risk of exacerbating their medical condition as compared to those with poor adherence.[80] Nevertheless, adherence to COPD medication is generally low, with the majority of studies identifying the presence of depression and subjects' concern about the harmful effects of the medicine as barriers to adherence.[80]

Elderly patients

Despite the beneficial effects of secondary prevention, including CR, on clinical outcome in elderly patients with CVD, participation and adherence significantly decrease with age (next to its negative impact on guideline-directed medical therapy adherence).[81,82] The main reasons include transport difficulties and a lack of referral by healthcare providers. Also, elderly patients are more likely to assume that lifestyle changes would not improve their health.[82,83] Key factors that have previously been identified as relevant to increase exercise adherence in elderly patients include supervision, social support from staff and peers, and individualization.[84] Moreover, it is important to provide adequate information about benefits and potential risks, identifying perceived barriers and facilitators, as patients with realistic expectations of change are more likely to be adherent.[84] This may also increase patients´ self-efficacy which is related to achieving lifestyle goals. Enjoyment is an immediate reward that is closely related with intrinsic motivation and could lead to better adherence than delayed rewards, such as health benefits in the long-term.[84] Many secondary prevention services have not specifically been designed for the elderly and the implementation requires a high

degree of individualization. A comprehensive geriatric assessment including not only CV function, but also peripheral functional evaluation (strength, balance, coordination, aerobic capacity), assessment of disability and comorbidities, nutritional, cognitive and psychosocial components are suggested.[11] Interventions should be tailored to target the main goals of CR for the elderly, including preserved independence, prevention of sarcopenia and frailty, improvement in quality of life and encouragement of social adaptation.[11] Only those programs that are in line with the preferences of patients, improving them globally, can become an actual long-term sustained habit.[84]

Bringing it all together: the five dimensions of adherence to treatment (patient, disease, healthcare provider, therapy, healthcare system) – barriers and strategies

The non-adherence to (non)-pharmacological treatment is common.[1–5] Based on the above-mentioned information, combined with insights from research in the psychology of non-adherence to treatment, barriers and motivators to adherence are presented, originating from the patient him/herself, the (type of) disease, the healthcare professional, the therapy and the healthcare system (see Table 2 and Figure 2).[85–87]

Improving the adherence to treatment requires an active process of behavioural change, which is nearly always a challenge. It requires education, motivation, tools, support, monitoring, and evaluation.[88] Multifactorial interventions are more effective,[89] tailored solutions addressing a patient's specific adherence barriers (precision medicine), scaled to the population level (population health), may be a successful strategy to facilitate improved medication adherence on a larger scale.[90]

The patient

Sex/gender

There is a significant impact of sex/gender on adherence rates to secondary prevention measures, which need to be considered in clinical practice. For example, among 9.283 patients with ACS (in Australia), it was discovered that women had lower odds of attending CR than men (OR [95% CI] 0.87) and at 12 months after discharge, women were less likely to be on ≥75% of the indicated medications (OR 0.84).[91] This sex difference in secondary prevention of CVD is a global phenomenon, as also in China it was found that women with established CVD were significantly less likely than men to receive BP-lowering medications (OR 0.79), lipid-lowering medications (OR 0.69), antiplatelets (OR 0.53), or any CVD prevention medication (OR 0.62).[92] Women were less likely to achieve physical activity targets (OR 1.92), but also were less likely to smoke (OR 13.89).[92] In the USA, very similar findings were reported.[91] It is also noted that next to a lower referral rate to CR, also the drop-out during CR seems to be greater in women.[93] Potential barriers to women's

participation in CR could be greater psychological distress, pressure as the primary caretaker of the family, and the lack of financial resources and social or emotional support.[94]

Hence, secondary prevention interventions should be adapted accordingly, and caregivers should be more aware of the issues, to meet these needs and to maximize women's adherence to treatment and participation rates in structured secondary prevention and CR programs.

The psychosocial health status and the barriers to their appropriate management

To enhance secondary prevention and ensure the best possible prognosis for patients with CVD, it is paramount to treat not only the underlying disease and ensure management of traditional risk factors, but also to treat mental disorders/issues, such as anxiety, depression, and post-traumatic stress disorder. The sudden confrontation with chronic and potentially life-threatening disease may trigger the onset of one or more mental disorders/issues or increase symptom levels that warrant treatment. Hence, not surprisingly, 20% of CVD patients suffer from depression, anxiety, or both.[95] It is not sufficient to screen patients for mental health problems only at the time of the index event, as the incidence of new-onset anxiety and depression are 14% and 11% during 24 months of follow-up in patients without anxiety and depression at baseline.[96] In addition, mental disorders are often undetected and undertreated.[97] Irrespective of whether patients receive a clinical diagnosis or report subthreshold levels, the impact on patient prognosis is potentially large. Mental disorders comprise barriers for lifestyle changes, impair patients' quality of life and health status, increase the risk of refusal or drop-out from CR, non-adherence, hospitalisation, premature death, and increased costs.[98–102]

Several barriers exist for the provision of appropriate management of mental disorders in patients with CVD at the patient, society, and healthcare system levels. One barrier is the current organisation of our healthcare system, with its primary focus on treatment of the underlying heart disease, while largely ignoring the interaction between heart and mind and how they through biological and behavioural pathways interact to influence patient and clinical outcomes.[98] Generally, the adherence rate of healthcare providers to the implementation of guideline-based psychosocial interventions in medical settings is poor. Luckily, in some countries and in some healthcare settings (i.e. CR) mental health professionals are part of the multi-disciplinary team At the patients' and society level, while some CVD patients are interested in receiving psychological support and therapy even before the onset of CR,[103] others still feel the stigma associated with going to a psychologist or other mental health professionals; others may lack confidence in these interventions or lack the financial means to go to a psychologist due to lack of reimbursement..

Psychological treatments, such as cognitive behavioural therapy, help in reducing psychological distress and increase quality of life in patients with CVD,[104–106] and mental healthcare is effective for the treatment of mental disorders.[13,107] Observational studies with large sample sizes revealed that remission of mental disorders is associated with improvement of cardiac prognosis.[13,107] Nevertheless, some uncertainties remain regarding the magnitude of psychological intervention effects in patients with CVD,[108] and the areas of the mental healthcare impact on cardiovascular outcomes in CVD patients. A systematic Cochrane review and meta-analysis found that psychological interventions had important health benefits among people with CAD, reducing the rate of cardiac mortality and alleviating the psychological symptoms of depression, anxiety, and stress. However, no effects were observed for total mortality, myocardial infarction, or revascularisation. The mixed effects of interventions may also be attributed to a "one-size-fits-all" therapeutic approach in RCTs rather than a precision-medicine approach that is targeted to patients' specific needs and preferences.[109]; in addition, trials should avoid an over-representation of well-educated and motivated patients.[110] Therefore large-scale trials are still warranted.[108]

Impact of psychological determinants of non-adherence

The ability of a patient to adhere to medical treatments and healthy behaviour changes depends on complex cognitive-emotional capacities and interaction with his or her social environment (e.g., the healthcare system). Emotional factors are symptoms of mental disorders such as anxiety, depression, and other signs of emotional dysregulation.[107] Emotional factors, knowledge (health literacy), and the belief about the consequences of medications strongly influence medication adherence.[111] Other, less essential elements are displayed in Table 3.[111]

These factors are all closely related to the level of personality functioning, i.e., the mental capacity of persons to do something good for themselves (self-care), their capacity of self-directedness, and interpersonal skills (communication, being able to ask for help, to cooperate effectively, to trust doctors and to depend on them). Psychological determinants of non-adherence in themselves are a medical problem that has to be tackled explicitly in the treatment.

Health literacy

Health literacy can be defined as the knowledge, motivation, and competencies of people to access, understand and apply health information to make judgments and decisions in daily life about health matters. These skills include reading, writing, numeracy, communication, and increasingly the use of electronic

technology. Health literacy therefore plays an important role in CVD secondary prevention, encompassing some of necessary skills, such as understanding health information and active interaction with health professionals, needed to improve self-care.[112,113] Low levels of health literacy have been associated with low educational attainment, low income, and ethnic minority status and have less favorable CVD risk profiles.[114,115] Inadequate health literacy is highly prevalent in patients with CVD and it is associated with poorer control of CVD risk factors and poorer adherence to drugs and changes in lifestyle.[116,117] A high level of health literacy is associated with a lower readmission rate after MI and may be a factor influencing dropout in CR.[116–118] Poor health literacy can be modified through the development of knowledge and skills related to self-care.[119,120] The most commonly used strategies include attention to printed patient educational materials, including elimination of medical jargon by using plain language with clear and concise messages , to ensure that patients understand the advice of healthcare professionals.[121] Digital solutions can improve health literacy by providing patients the opportunity to be a more active participant in their own healthcare. Digital solutions will provide a more person-centred approach in which individuals will have more control over health and data, while staying connected to their healthcare team.[122]

From the "awareness" state to the "empowerment" state

The efficacious promotion of treatment adherence requires patients to acquire a solid awareness of their status and then they move to an active engagement in managing their disease. The awareness of the disease and of its potential risks is critical for patient adherence: patients' awareness level is not always high.[123–125] Such a lower awareness is usually associated with various factors, including age, familiar history for a specific risk factor, and unhealthy behavioral habits like poor physical activity, smoking, and heavy alcohol use.[126] The educational status also plays an important role.[127] The sources of information mostly reported are traditional ones and digital media, including social media, print information in newspapers and magazines, healthcare professionals, and family members.[128,129] Educational and informative programs are primarily suggested to promote patients' awareness of their condition and are suitable for interventions directed to large communities, particularly those that consider patients' information needs and offer tailored content and communication strategies.[130] Despite increased knowledge, awareness is insufficient to guarantee prolonged adherence to the treatment. The association between awareness and behavior is usually modest, suggesting that awareness alone does not motivate individual action.[131] Self-management programs are needed to enable patients to have a major role in coping with their condition, controlling their symptoms, understanding and accepting their prescribed treatment, recognizing the time they need medical follow-up, in other words: exerting control over their own situation. This process has been defined as «empowerment»,

namely, “the process through which people gain greater control over decisions and actions affecting their health”.[132] Digital solutions are largely employed to enhance patients’ empowerment by providing a large variety of opportunities to be active and engaged in managing their health.[133]

Maintenance self-efficacy and recovery self-efficacy

Unhealthy lifestyles are difficult to change, and, when changes occur, it is hard to maintain them over time. People could make multiple attempts to move from intention to a healthy actual behavior. However, relapses could happen anytime, especially in complex and chronic disease conditions requesting multiple behavioral changes. Maintenance self-efficacy refers to the confidence in one's capability to maintain the behavior despite potential barriers and obstacles. A self-efficacious person responds confidently with efficacious strategies, more effort, and greater perseverance. Greater maintenance self-efficacy correlates with higher medication adherence among CR patients.[134] Patients with a first coronary event and CV high-risk who feel more self-efficacious in coping with potential difficulties related to behavioral changes, are more likely to improve their physical activity over time,[135] while a lower self-efficacy in CVD patients is associated with higher hospitalisation rates and all-cause mortality.[136] Programs focusing on self-efficacy increase patients’ engagement in managing their condition with an improvement in clinical outcomes, such as lower blood pressure levels and reduced hospitalizations.[137] A poor self-efficacy can be improved through the sources originally identified by Bandura in psychological counselling programs.[138] The direct experience of mastery and success in increasing difficulty tasks is the primary source of self-efficacy beliefs. Furthermore, self-efficacy could be improved by vicarious experiences. Patients may observe significant and competent patterns, for example, by sharing CR sessions with a practiced patient who serves as a model. A further source of self-efficacy is verbal persuasion by others (doctors, nurses, physiotherapists) to help patients in gaining confidence and esteem.

The disease

Condition/disease-related factors

Among barriers to adherence co-morbidities adversely impact treatment adherence in case of linked conditions (e.g. CVD and diabetes) or when conditions co-exist (e.g. CVD and orthopaedic limitations), particularly when drug regimens are complex, costly, and influencing activities of daily life. Non-cardiovascular comorbidities play a major role in determining unsatisfactory adherence levels, both to medications and lifestyle, especially in the elderly.[139] Although it is difficult to establish which disease combinations are at highest risk of non-adherence, several situations should be carefully monitored, such as atrial fibrillation and renal impairment

after MI.[140] Co-morbidities could also lead to the prescribing cascade, i.e. a situation in which a first drug administered to a patient causes adverse signs and symptoms, that are misinterpreted as a new condition, resulting in a new medication prescription.[141]

The duration of disease has an uncertain impact,[142] even though chronic conditions or long duration of acute illnesses reasonably increase the risk for low adherence.

The absence of current signs of symptoms (i.e. the "asymptomatic" patient) constitutes per se a condition potentially interfering with adherence, since patients may believe they do not need the medication and might not even follow their prescription.[143] This kind of intentional non-adherence primarily affects dyslipidaemia, hypertension, and subclinical atherosclerosis treatments.

The healthcare provider

Avoid information overload and forgetfulness

Many patients, families and caregivers are exposed to 'information overload', often far more than they can remember, exacerbated by the widespread use of social media, emails, and online communications, and the pressure to simultaneously read, produce and exchange information. This is likely to affect the assimilation, understanding, retention and recall of information,[144] which may have an adverse impact on adherence to therapy and lifestyle changes. Therefore, improving access to and delivery of information is important for increasing transparency, patient autonomy and engagement, and improving safety.[145,146]

Most patients prefer a written lay summary of health information,[147] but, to avoid information overload and forgetfulness, healthcare professionals should consider the relevance, timing, content, duration, presentation and readability of information and information-processing abilities of patients. Improving recall, understanding and adherence to treatment involves: i) using plain, simple, uncomplicated, and consistent language and terminology, ii) being specific, using some repetition, minimizing jargon and iii) checking a person's understanding. This can be aided by a variety of information and educational media formats and modes of delivery, encouraging note-taking, clarifying with questions, and using techniques like teach-back and 'chunk and check'.[148] Shared decision-making [149] taking account of patients' self-efficacy and autonomy and experience in risk factor modification, can help patients have a more active role and more accurate risk perceptions.[150] How information is portrayed can influence perceptions and adherence.[151]

Enhance communication: ask, tell, ask

The physician-patient relationship is critical for establishing a good working alliance and hereby improve the adherence to treatment.[152] Therefore, medical training is supposed to include education in interpersonal

and communication skills aiming at effective collaboration with patients, their relatives, and other healthcare professionals.[153] Concerning non-adherence, its detection and effective treatment also depends of physician-patient communication. However, problems with adherence are rarely addressed and recognized by physicians.[18] One teachable method of patient-centred communication is the Ask-Tell-Ask method. This method aims at increasing the involvement of the patient in the treatment process. It consists of asking the patient's understanding of his/her disease and treatment. Based on this information, the physician tells the patient what is needed and then asks again what the patient received and his/her further informational needs. There is continuous feedback between physician and patient to ensure that the patient has understood the information and grasped its meaning and consequences. The physician should use a language style adapted to the health literacy and the emotional state of the patient. The sentences should be short and digestible.[18,154] The Ask-Tell-Ask method needs to be embedded in basic patient-centred communication skills, including active listening and attending to the patient's emotions.[155]

Improve patients' risk perception

Risk perception may be defined as individual thoughts and feelings about the risks they face in behaving in certain manners. The greater the perceived risk for one's health, the greater the motivation for taking protective action.[156] Therefore, risk perception, both absolute ('How I am at risk') and comparative ('How I am at risk comparing to people around me'), is an integral part of many major health behaviour theories, aimed at describing, explaining, and modifying human habits. About 40% of the general population underestimate their risk for developing CVD, while 20% overestimate it.[157,158] Risk underestimation is very common among individuals with CVD. This dysfunctional belief essentially compromises the adoption and the maintenance of healthy habits,[159,160] diminishing the success of CVD secondary prevention. On the other side, excessive overestimation may cause a significant psychological burden. Complex explanations of CVD risk appear insufficient to motivate behaviour change. Providing more medical information to patients may not mitigate the impact that prevailing beliefs have on patients' views on medical issues. They seek personal, meaningful information that can be helpful in making healthcare and lifestyle decisions and a tailored approach should be adopted.[161] Online calculators (such as the ESC CVD Risk app) can be used to estimate the average lifetime benefit of smoking cessation, lipid lowering, and BP lowering on an individual patient level expressed as extra CVD-free life-years. Average lifetime benefit is easy to interpret and may improve the communication of potential therapy benefits to patients in a shared decision-making process. This may increases patient engagement, self-efficacy, and motivation to adhere to lifestyle changes and drug treatment.[13]

Enhance patients' self-efficacy

Self-efficacy is extensively treated above, here is only to be emphasised that each healthcare provider should consider the patient's self-efficacy. It is important to incorporate self-efficacy as a key element in CVD self-management programs. These programs should have a multidisciplinary approach, should be patient-driven and should have a theoretical basis for behaviour change. More research is needed to investigate the causal relationship between self-efficacy, self-control, and clinical outcomes.[137]

Healthcare professional: Don't be inert!

Clinical inertia is defined as the failure to initiate or intensify therapy when treatment goals are not met and is a well-recognized barrier to improving patient care and clinical outcomes.[162] The lack of treatment intensification and goal achievement is multifactorial, involving not only healthcare professionals, but also patients, healthcare system, and policy/regulatory factors.[162] One key contributor to therapeutic inertia is poor guideline implementation and slow integration of new knowledge into practice.[162] Educating healthcare professionals on practice guideline changes through continuing education programming is one approach, however, evidence supporting the effectiveness of this strategy is limited.[163] A more effective approach is to provide education outreach visits in which a trained individual provides face-to-face education and feedback on healthcare professional performance. This methodology improves clinical outcomes while also reducing costs. (6) A healthcare professional-patient discussion that helps patients navigate medical misinformation found in online and published media is also extremely important,[164] and educational outreach visits may help healthcare professionals in implementing this in their daily practices. There is also an urgent need to increase guideline dissemination improving readability and dissemination also by smartphone applications and social media.[162] Multidisciplinary team-based care models are more likely to achieve CVD risk factor control and can reach high-risk populations successfully.[162,165] A key aspect of such models is a guideline-based algorithmic approach to treatment, which can significantly reduce therapeutic inertia. Regarding systems approach, the creation of quality improvement programs that incorporate feedback metrics provides healthcare professionals with data needed to drive improvement. In some institutions, these data are available on dashboards where healthcare professionals can compare their control rates for a particular disease, such as hypertension, with others, with the intent to use this information to improve their performance metrics.[162] In a general view of this important topic, patient preference must also be included, as not all patients desire treatment intensification or change, owing to concerns about side effects or personal convictions about prescription-medication use. This underlines the importance of shared decision making with patients to guide treatment decisions that are consistent with the patient's wishes and goals.[162] Finally,

studies and efforts aimed to the improvement of therapeutic inertia should be based in implementation science, which is a scientific area focused on determining the best methods for increasing the integration of research findings into clinical practice, with the goal of improving the quality of health services.[166]

Promote and use a slogan in your facility: "I am with my therapy!"

According to the Oxford English Dictionary, a motto is “a maxim or saying adopted by a person, family, institution, etc., expressing a rule of conduct or philosophy of life”. It's usually simple, catchy, timeless, and easy to remember as well. So defined, the “I am with my therapy!” motto could apply to patients suffering from CVD and was created for the purposes of this consensus statement as a tool to promote treatment adherence. It is not trademarked for protection and could be enriched by an accompanying logo created at a local level. These five words evoke personal empowerment and engagement (“I am”, i.e. taking control of own life, and making positive decisions), appropriate relationship between the patient and prescription/prescriber (“with”), and finally recognition of the importance of individualised treatment regimens, tailored to patients' views and embracing all aspects of pharmacotherapy and lifestyle (“my therapy”). This declaimed alliance between patient and therapy definitely overcomes the old concept of passive “compliance” by shifting towards a mutually agreed treatment programme, best appreciated in terms of “concordance” and “persistence”. The motto is offered to providers and prescribers, communities, institutions, and healthcare policy makers. By way of example, it could be systematically adopted by multidisciplinary teams for counselling activities during secondary prevention and CR programmes. It could be inserted among educational (posters, pamphlets, booklets, audio tape, tutorial videos) materials prepared for patients. It could be conveyed by websites, apps, and digital health tools, also during telemedicine activities. It could be utilized as slogan for campaigns at a population level or for community activities during phase III CR programmes. It could be even reproduced on T-shirts or presented as jingles for enhancing memory and recall. In other words, it could support the “brand” of CV prevention to 360°, by expanding patient-centred thinking and action.

The therapy

Many medications have side effects, require additional monitoring, and serve as a consistent reminder of the patient’s illness. All these factors might reduce the patient’s persistence/adherence [167]. Furthermore, complicated dosing regimens can lead to inconvenient administration times and contribute to forgetting to take medications. Individuals with multiple medical conditions or conditions that require a large pill burden must adhere to complex regimens and may experience medication interactions and polypharmacy leading to non-adherence. Therefore, the number of diseases as well as the number of prescribed drugs can reduce

adherence and adversely affect both secondary prevention of CVD and comorbidity trends. The financial cost of medication can also act as a barrier to adherence and persistence, especially in healthcare systems that have a higher patient cost burden.[5,168] Finally, frequent changes in medication plan pose a greater risk for non-adherence, especially during transition phases between acute and primary care or routine follow-up visits. Medication changes during hospitalization are common and those patients, particularly in the elderly, who are not aware of the changes, may have higher rates of non-adherence.[169] Further, also prolonged disease could lower the adherence to pharmacologic therapy, as well as the absence of symptoms (i.e. the "asymptomatic" patient). [142,143]

The Polypill: focus on therapy simplification:

A polypill is a medication that combines multiple active pharmaceutical ingredients. In the prevention of CVD, the types of treatment can be classified into three groups: i) single-pill combinations containing aspirin, a statin and BP-lowering agents mainly focused on prevention and treatment in patients with established atherosclerotic CVD; ii) fixed-dose combinations containing a statin at different dosages and ezetimibe or three or four BP-lowering medications at low doses; and iii) two-drug or three-drug combinations currently on the market, such as two-drug combinations of a BP-lowering drug and a statin, metformin and a statin, and other combinations.[170] The polypill approach aims at controlling multiple risk factors and diseases and it addresses adherence simultaneously, particularly among certain high-risk populations (e.g. low- and middle-income countries, low socioeconomic status).[171] It substantially differs from a precision medicine approach which is individualized and tailors guideline-directed medical therapies, based on measurement of CVD risk factors.[172] However, for secondary prevention of CVD, both approaches could be combined. Patients should be prescribed the components of the polypill according to best medical practice, but providing these components in a combined polypill format simplifies the administration of therapy and improves adherence.[173] In patients with, or at high risk of, CVD polypill-based care with all the three formats described above is more likely than usual care to achieve therapeutic targets for BP, LDL-cholesterol and adherence to antiplatelet therapy simultaneously. [173–175] [176]

Digital technologies: m-Health/eHealth

The rapidly growing interest and advances in digital technologies such as mHealth (mobile-Health) and eHealth (electronic-Health) are gaining universal popularity and coverage and have the potential to address the challenge of poor adherence to CVD therapy and lifestyle changes, hereby improving outcomes.

m-Health

The WHO defines m-Health technology as "a medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants, and other wireless devices".[177] mHealth provides access to multiple resources and allows monitoring and real-time analysis of health data, and enable patients to become more engaged in the self-management of their condition. For example, mHealth appears to improve health behaviours and medication adherence and to be generally preferred by patients and healthcare professionals to other interventions.[178–180] It is becoming more user-friendly for older adults and an adjunct to manage CVD risk and improve overall cardiovascular health.[181] In older adults, mHealth is particularly effective when there is a short message service (texting) component involved. However, there remain distinct barriers to the use of mHealth, such as affordability, usability, privacy, and security issues.[181] Also, mHealth interventions that incorporate personalized features other than content (e.g. format/visualisation of screen) may improve effectiveness.[182]

eHealth

eHealth refers to the organisation and delivery of health services and information using the Internet and related technologies, such as web-based technology and mHealth.[183] eHealth interventions are emerging as an effective alternative model for improving secondary prevention of CVD, where patients receive access to resources at their discretion. For instance, eHealth could be offered to patients who cannot attend traditional CR programmes or as an adjunct and may decrease non-participation and dropout rates due to better adaptation to patients' needs and preferences.[184] Utilising eHealth technology in education delivery, which might be more popular among the youngsters, provides easier access for patients and permits them to self-pace through educational materials. An additional advantage of remote delivery of interventions through eHealth platforms is that patients can receive treatment and information during pandemics, such as covid-19. However, it is important to acknowledge patient-related barriers, such as low eHealth literacy, which might inhibit patients' ability to apply knowledge, make appropriate decisions and achieve better self-management.[184] To improve health outcomes, eHealth should be designed to foster effective interactions at a distance between patients and healthcare professionals, closer to those which are presential. However, little is known about whether social support offered through eHealth programmes has the same effect on self-management behaviour and psychosocial outcomes as traditional secondary prevention programs. Thus, while eHealth interventions offer the potential of more flexibility, which can overcome barriers of work schedule or geographical distance, further research is needed regarding their acceptability, feasibility, content, delivery and

impact, in particular in the elderly and in patients with low socio-economic status and low health/eHealth literacy.

The healthcare system

The epidemiological shift in disease burden from acute to chronic diseases has rendered acute care models of health service delivery inadequate to address the health needs of the population.[14] The healthcare delivery system has the potential to affect patients' adherence behavior.[14] Healthcare systems control access to care. For example, health systems control providers' schedules, length of appointments, allocation of resources, fee structures, communication and information systems, and organizational priorities.[14]

The following are examples of the ways in which systems influence patients' behavior:[14]

- Systems direct appointment length, and providers report that their schedules do not allow time to adequately address adherence behavior;
- Systems determine fee structures, and in many systems (e.g. fee-for-service) the lack of financial reimbursement for patient counselling and education seriously threatens adherence-focused interventions;
- Systems allocate resources in a way that may result in high stress and increased demands upon providers which, in turn, have been associated with decreased adherence in their patients;
- Systems determine continuity of care. Patients demonstrate better adherence behavior when they receive care from the same provider over time;
- Systems direct information sharing. The ability of clinics and pharmacies to share information on patients' behavior regarding prescription refills has the potential to improve adherence;
- Systems determine the level of communication with patients. Ongoing communication efforts (e.g. telephone contacts) that keep the patient engaged in healthcare may be the simplest and most cost-effective strategy for improving adherence.

Unless variables such as these are addressed, it would be expected that the impact of the efforts of providers and patients would be limited by the external constraints.[14] .

Social media

Social media, defined as "electronic communication, especially applications and websites, through which users create and share information, ideas, and personal messages in an online community", is increasing exponentially. [185,186] Reported social media use by American adults has gone from 5% in 2005 to 69% in 2018, and the impact of social media on both adults and youth is both mixed and incompletely

understood.[185]. Over recent years, social media have gained powerful influence globally and throughout society. Although initially cautious, healthcare professionals and organizations are increasingly present on social media platforms, with young professionals in particular viewing social media as an integral component of communicating, networking, and keeping up to date with the latest science. While potential problems need to be considered, responsible social media use is likely a beneficial addition to traditional means of obtaining and disseminating medical and scientific education. Healthcare professionals and organizations are advised to actively engage in social media to counterbalance un-reviewed and biased information [7,8]. Future investigations of social media effects should focus on best practices, patient-oriented research, and the costs-benefit of using certain tools or platforms in varying healthcare settings.[187,188]

The role of informal caregivers in adherence to CVD management

Family members and friends can provide practical (e.g., prepare meals, bring a patient to an appointment) and emotional support to improve patients' mood, encourage compliance, and reward them for their efforts. Involving social networks can improve patients' quality of life, self-efficacy and relationship quality and at the same time lower the risk of hospitalisations.[189,190] However, informal carers most often report problems such as lack of time for care and the need for institutional and personal support. In addition, caregivers require information and training (e.g., emergency first aid, practical advice on caring for a bed rest, simple medical procedures, administering medications, patting to prevent pressure ulcers, basic massage and rehabilitation treatments, blood pressure measurement, among others) as well as counselling and the availability of respite care.[191,192] Targeting informal caregivers with behavioural interventions and training may be cost-effective. Carers could help with the multifactorial origin of adherence such as reminding patients to take the medication even if asymptomatic and motivating them to continue with treatment leading to lower rates of hospitalisations or lower use of additional medical resources.[70] Adherence to medication is increased with the support of paid carers. Therefore, providing informal carers with the knowledge of paid professional carers may lead to more successful patient management. [193] Caregivers feel powerless and ignored if they do not engage in relationships with healthcare professionals. This lack of coordination between health caregivers, as well as the lack of access to information, was clearly highlighted in research and stakeholder consultations.[191,194] Therefore, psychosocial support for patients and caregivers can lead towards a more successful management of patients.[195] Adherence to smoking cessation for secondary prevention can be improved by involving family members and friends, with such as a 67% probability for smoking cessation if the spouse of the patient takes the steps to stop smoking.[196]

The role of integrated care: community-based projects

The most common intervention is education (41%), followed by counselling or support (38%), and exercise (28%). Half of the interventions are multi-component. The most common interventionists are health workers. Interventions to lower BP are the most promising, with behaviour change interventions being the most challenging. There is a pattern of successful educational and supportive interventions, initially a more intense phase individual or group based, followed by a less intense phase that often involves individual telephone support or support groups.[197] Increasing accessibility to pharmacists and integrating them in community programs with general practitioners for screening of CVD risk factors or for monitoring patients who have been already diagnosed and require monitoring has proved to be effective in increasing early diagnosis, adherence and follow-up by physicians.[198] The most important barriers are lack of adequate funding, qualified personnel, equipment and material resources, technical support in the field of data management and analysis, training for providers, political support of local authorities and approval of the proposed intervention by the authorities in the local community. The facilitators are motivated local leaders, cross-sector participation and seizing local resources. The evaluation of the project should be based on the process, not on the results indicators.[199] However, the patient adherence to treatment over time seems to be a more complex process in which factors such as individual motivation and professional-patient interaction play an important role.[200] Getting closer to the neighbourhood has proven to be effective. For example, an improved adherence to therapy and management of high BP can be achieved through the involvement of barbershops in CVD prevention.[165]

Future directions/research

Regarding future research, suggestions from a recent Policy Statement of the American Heart Association are available (see Table 4).[201] The currently available studies are relatively small and of short duration, and few information about how study designs were performed are provided. These facts significantly limit their ability to be replicated in other settings and with other populations. Several studies used a multi-component interventional design compared to usual care arm. Therefore, it is very difficult to identify the relationship between each intervention and the outcome. The implementation in clinical practice of a policy to improve adherence to optimal therapy is still often disregarded, due to the complexity of the problem and its multidimensional nature. A great hope is in e-Health as a tool to improve adherence by facilitating the relationship and communication between patients and healthcare professionals in the long term. In future studies, it will be of particular importance to isolate the contribution of each component, in order to identify the best target to test in future e-Health tools.

Conclusions

Adherence to pharmacological treatments and healthy lifestyle behaviours is poor in secondary CVD prevention. However, adherence to therapy is an extremely complex problem. Probably, it is because of this complexity that, despite the large size of the available literature and the widespread awareness of its importance, effective approaches to address this problem are lacking in daily clinical practice. Since a complex problem necessarily does not have a simple solution, in daily clinical practice every healthcare provider is needed to increase sensitivity to the fact that without considering the future patient's adherence to therapies, every effort done to improve the patient's health status can be insufficient. Each healthcare professional must therefore apply a multidisciplinary approach, focused on adherence to guideline-directed medical therapy and a heart-healthy lifestyle, based on present knowledge. This approach might be based on the following steps: i) the identification of patients at risk of non-adherence, ii) the development of a multidisciplinary intervention pathway useful to support adherence in the long-term, and iii) develop an adequate follow-up strategy in the long term.

Author's contribution

RFEP conceived the idea for paper, led the work group, drafted sections of the text, and provided editorial oversight. DH co-led the work group, drafted sections of the text, and provided editorial oversight. MA/MB/MCF/CPZ/AG/DK/MM/EO/SP/RES/MS/PS/DRT/MW/AA drafted sections of the text, reviewed and commented on a final draft of the paper. CV/CHD/DW/IF reviewed and commented on a final draft of the paper. All authors agreed to the final version of the paper.

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Table 1 Take-home messages and consensus statements

° In the secondary prevention of CVD, it is crucial to optimize the adherence to therapy since most CVD risk factors and lifestyle measures are far from optimally controlled in many patients.

° Considering the multifactorial process that can lead to suboptimal adherence to treatment, secondary CVD prevention should be deployed in a multidisciplinary setting or context.

° In general, a low self-efficacy, poor health literacy and risk perception, and certain psychosocial issues (e.g. depression, anxiety, cognitive decline, poor social support and socio-economic status) predict a low adherence to therapy. Hence, these factors should be screened at entry of a secondary prevention program and targeted accordingly.

° For each CVD risk factor or condition separately, additional specific predictors for a low adherence to therapy are established, and should thus be taken into account by healthcare providers.

° To optimize the adherence to therapy, it is important to work on its five dimensions simultaneously, including: the patient, the disease, the healthcare provider, the therapy, and the healthcare system.

Table 2 General barriers to adherence to treatment

Patient-centred barriers to adherence to treatment
Low education level
Low health literacy with poor knowledge of illness and medication
Lack of competence in self-management
Misbeliefs (alternative belief systems as media and neighbours medication information
Lack of motivation
Fear for medication side-effects
Low economic status
Depression or cognitive disturbances
Old age
Poor vision
Alcohol or drug abuse
Disease-driven barriers to adherence to treatment
Absence of symptoms
Chronicity
Good prognosis
Healthcare professional-centred barriers to adherence to treatment
Not enough time for consults (short consult period)
Poor practitioner-patient relationship
Unsatisfactory skills in coaching self-management treatment
No satisfactory full list of medication review (too time-consuming)
Difficulties to obtain the accurate knowledge of home medication (generics, past medication maintained)
Healthcare professional authoritarian approach to patients
Medication-driven barriers to adherence to treatment
Complexity of medication
Polypharmacy
Doubts on duration of medication (temporary, chronic)

Medication withdrawal
Drugs adverse effects and toxicity
Drug-to-drug interaction
Existence of different generic drugs (different names and boxes for the same drug)
Costs (economic, personal, social)
Inconvenience
Time
Unavailability
Healthcare system-driven barriers to adherence to treatment
Provided poor access to healthcare (distance, costs, reimbursement)
Poor communication within the system
Problems in keeping the list of medication up-to-date
Lack of enough healthcare professionals with multitask appointments and short time for consults

Table 3 Psychological determinants of non-adherence

• Skills (language skills, planning, and organization skills): Poorer skills yield worse adherence • Beliefs about capabilities: Helplessness impairs adherence, perceived control improves adherence • Memory: Memory deficits were related to poorer adherence • Social Influences: Perceived discrimination due to race, ethnicity, education, or income was linked to a higher risk of non-adherence. Increasing inertia appeared was related to increased non-adherence

Table 4 Gaps in current knowledge – need for future studies

° Which interventions have the broadest impact on maximising adherences to therapy across patient groups or health conditions? Which interventions work best for which component of the CVD therapy?

° What is the direct impact of improved adherence to medication and improved adherence to lifestyle in specific patient populations or health conditions on actual healthcare outcomes and costs?

° Does the adherence to medications for multiple medical conditions differ from adherence if only one medical condition is present? If yes what additional tools, resources needed?

° Are there patient subgroups for whom spending on adherence interventions yields more benefit in terms of reducing future healthcare costs than other patient subgroups?

° What healthcare provider-patient communication strategies mostly impact adherence to heart healthy therapies (i.e medication and lifestyle) in a positive direction?

° To what degree does payment reform and incentives impact medication adherence rates on the long-term?

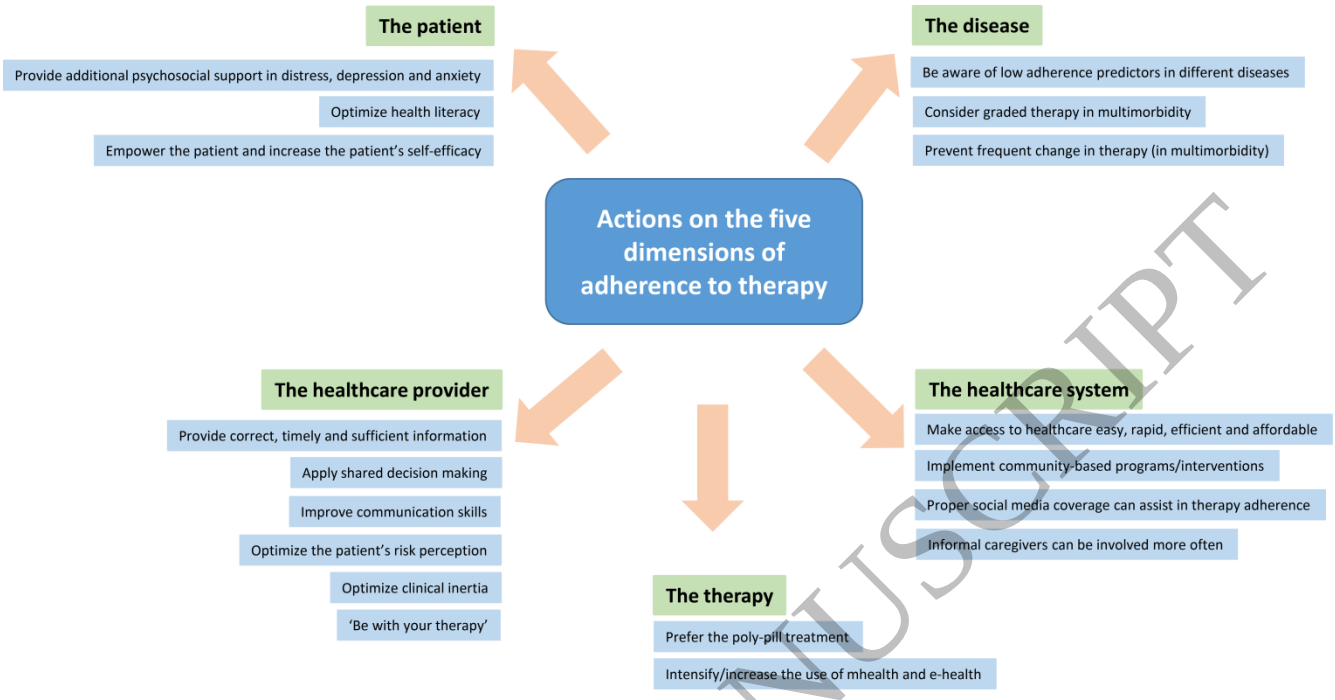

Figure 1 How to optimize therapy adherence in CVD

Figure 1
305x173 mm (x DPI)

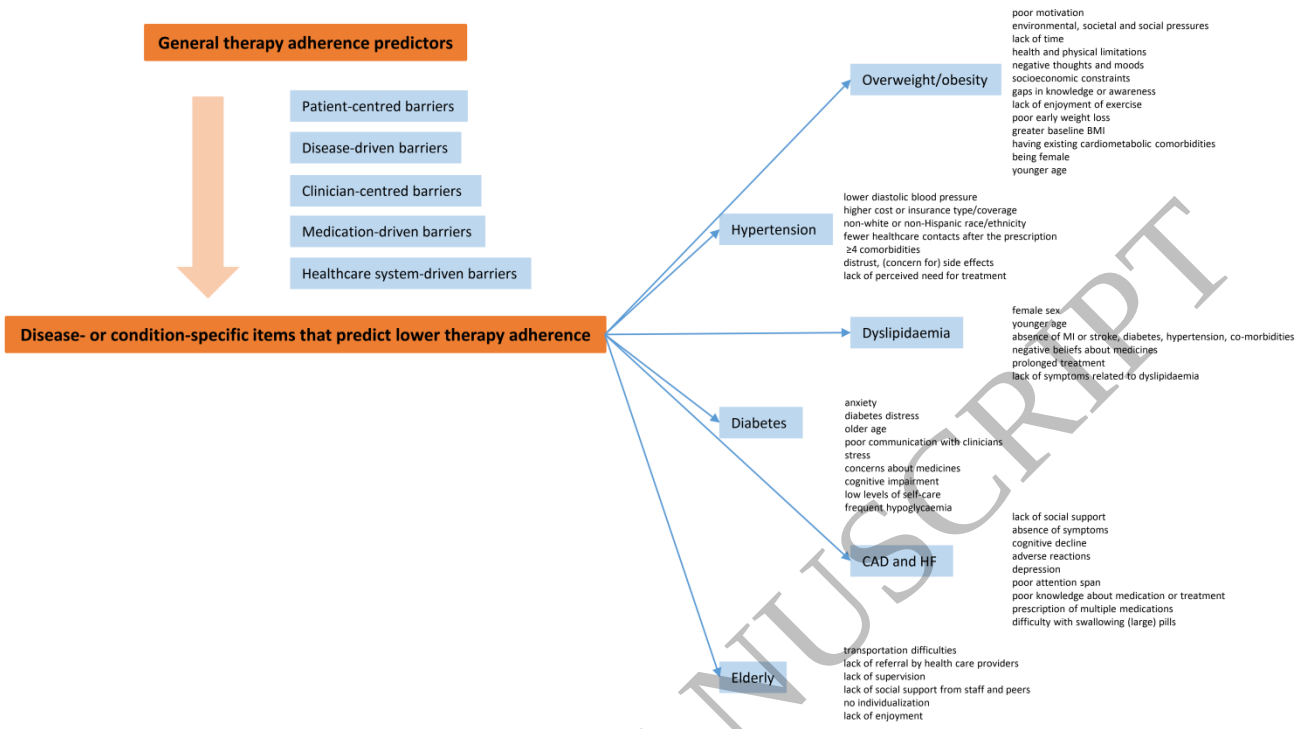

Figure 2 Predictors of therapy adherence in specific CVD's or risk factors

Figure 2
301x187 mm (x DPI)

Figure 3 Graphical abstract

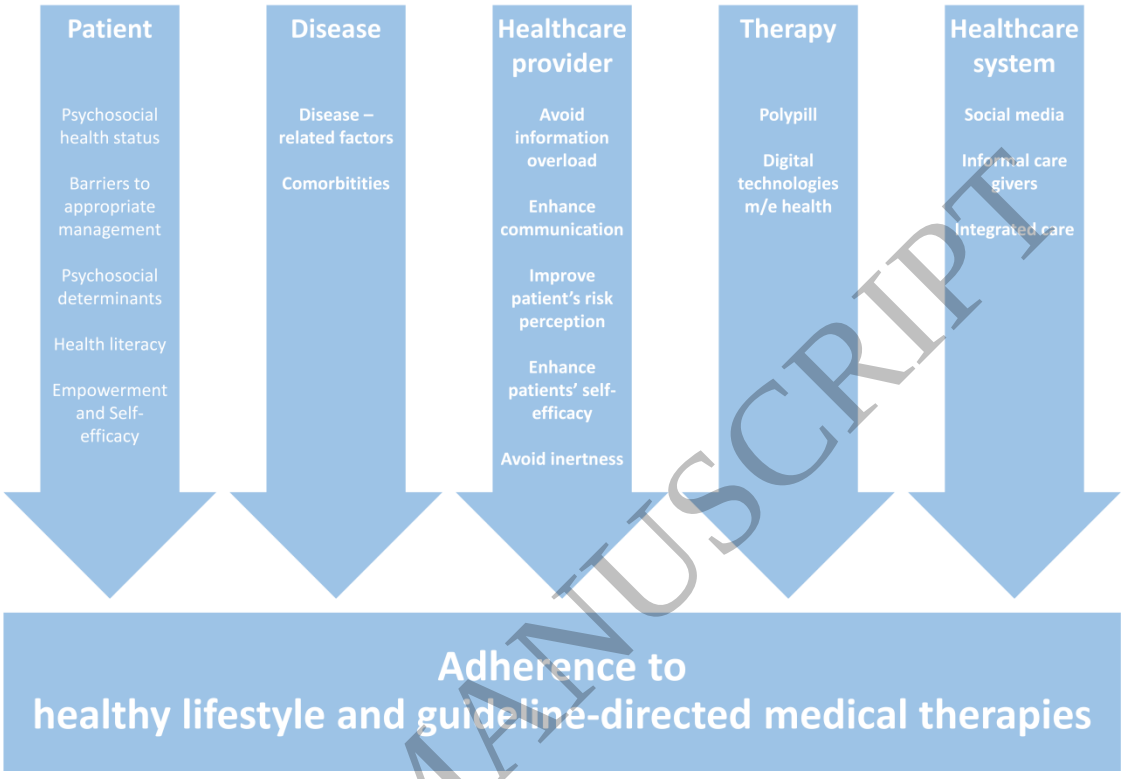

Figure 3
295x180 mm (x DPI)