

# World Journal of *Clinical Cases*

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## Cardiac rehabilitation and its essential role in the secondary prevention of cardiovascular diseases

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### Abstract

Cardiovascular diseases are the most common causes of mortality worldwide. They are frequently the reasons for patient hospitalization, their incapability for work, and disability. These diseases represent a significant socio-economic burden affecting the medical system as well as patients and their families. It has been demonstrated that the etiopathogenesis of cardiovascular diseases is significantly affected by lifestyle, and so modification of the latter is an essential component of both primary and secondary prevention. Cardiac rehabilitation (CR) represents an efficient secondary prevention model that is especially based on the positive effect of regular physical activity. This review presents an overview of basic information on CR with a focus on current trends, such as the issue of the various training modalities, utilization, and barriers to it or the use of telemedicine technologies. Appropriate attention should be devoted to these domains, as CR continues evolving as an effective and readily available intervention in the future.

**Key Words:** Cardiac rehabilitation; Secondary prevention; Cardiovascular diseases; Utilization; Barriers; Telerehabilitation

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**Core Tip:** Cardiac rehabilitation (CR) is an efficient and cost-effective secondary prevention model. It brings many benefits for patients with cardiovascular diseases but



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also acts at the medical and social system levels. Despite all of this, CR is highly underutilized across the world. There are problems in inconsistent delivery, deficient reimbursement, and further CR participation barriers in individuals. This article represents a comprehensive overview of the current situation and provides future perspectives, such as use of telerehabilitation.

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## INTRODUCTION

Cardiovascular diseases (CVDs) cause 31% of all deaths worldwide<sup>[1]</sup>. This indicator reaches 39%-47% (for females and males, respectively) in Europe<sup>[2]</sup>, and most deaths in the United States are due a CVD<sup>[3]</sup>. The annual global number of CVD deaths is 17.9 million; these mainly (85%) due to coronary artery disease (CAD) and stroke. Over 75% of mortality occurs in low-middle income countries<sup>[1]</sup>. It seems that the high mortality in poorer countries is not related to risk factors but might be related to worse access to health care<sup>[4]</sup>. Although age-standardized death rates show a decreasing trend in most countries, the absolute number of patients increases<sup>[3,5]</sup>.

CVDs constitute a common reason for hospitalization<sup>[6]</sup> and cause an inability to work<sup>[7]</sup>. Stroke and CAD are the most frequent causes of disability and are responsible for approximately 20% of age-standardized disability-adjusted life years<sup>[8,9]</sup>. According to the American Heart Association (AHA), a sum of USD 351 billion (*i.e.*, 14% of total funds spent on health care) was spent on the treatment of CVDs during 2014-2015. This amount is expected to approach USD 1100 billion in 2035<sup>[3]</sup>. This is a serious issue affecting both the social sphere and the national economy.

There are predispositions and risk factors of CVDs on a behavioral, biological, and social level. The etiology and pathogenesis of these diseases depend appreciably on the style of living. Major risk factors include smoking, lack of physical activity, and unhealthy diets (including excessive alcohol consumption<sup>[1]</sup>). Behavioral risk factors can result in hypertension, increased blood sugar/lipid levels, and overweight or obesity<sup>[2,3]</sup>. Such intermediary factors can be controlled within primary prevention. Determinants also exist at the social, economic, and cultural levels – globalization, urbanization, and population aging<sup>[1]</sup>. Additional risk factors include male gender, poverty, stress, and genetic predisposition<sup>[1]</sup>. The occurrence and development of CVDs are also related to psychological disorders such as anxiety, depression, and sleep disorders<sup>[10]</sup>. A comprehensive approach to cardiac rehabilitation (CR) can contribute favorably to the diagnosis of such conditions and the initiation of treatment<sup>[10]</sup>. According to the World Health Organization<sup>[1,11]</sup>, up to 80% of premature heart disease, stroke, and diabetes and 75% of recurrent cardiovascular events could be prevented, reinforcing the need for optimized and holistic prevention strategies.

The following text presents a review on CR basics, including its components, prescription, safety, effectiveness, and conventional and alternative training modalities. The next section contains information about CR delivery around the world, its uptake, and potential barriers. Finally, the last part offers strategies to improve CR participation, focusing on telerehabilitation (TR). This work aims to provide a comprehensive overview of contemporary CR and to outline its future perspectives.

## CR

Over time, physical activity in reference to heart disease is far from being new. Even in 1772, Heberden observed the beneficial effects in the patient he advised to saw wood for 30 min daily over 6 mo<sup>[12,13]</sup>. Despite some evidence of these particular physical activity benefits, mobility restriction was imposed on patients with acute cardiac events, often leading to serious deconditioning problems, decline in functional capacity, prolonged hospitalization, and increased mortality<sup>[12]</sup>. This wrong attitude

was furthermore reinforced after the description of myocardial infarction by Herrick in 1912<sup>[12,13]</sup>. In the 1930s, patients with acute coronary events were still advised to observe 6 wk of bed rest<sup>[12]</sup>. The “chair” therapy was introduced in the 1940s<sup>[14]</sup>, and a short daily walk of 3-5 mins was allowed 4 wk after the coronary events first in the early 1950s<sup>[12]</sup>. Concerns about measurable physical invalidism after myocardial infarction were mostly unfounded. Many healed patients had exercise capacity equal to presumably healthy, sedentary middle-aged men<sup>[13]</sup>. In 1952 the first inpatient exercise training program for patients with CAD was described by Newman *et al*<sup>[15]</sup>. Controlled physical activity began during the second week in the hospital and increased until discharge at 6 wk. In the 1960s, progressively earlier mobilization after the acute coronary event was practiced<sup>[13]</sup>. During the 1970s, the physiological basis of exercise benefits was acknowledged, which led to the development of CR programs<sup>[13]</sup>. Guidelines for CR were first established by the American College of Sports Medicine<sup>[16]</sup> and the AHA<sup>[17]</sup>. Rehabilitation and secondary prevention gained broad support as an essential component of comprehensive care in patients with CAD<sup>[13]</sup>.

CR is defined as a secondary prevention model that reduces mortality and the risk of recurrent events and improves CVD patients' quality of life (QoL)<sup>[18-20]</sup>. Systematic reviews showed a 20%-25% reduction in all-cause and cardiovascular mortality<sup>[21]</sup> and a decrease in the risk of recurrent myocardial infarctions by 38%<sup>[22]</sup>. Shepherd *et al*<sup>[23]</sup> pointed to a bilateral relationship between improved QoL and physical activity level. In the setting of CR, hospitalizations for CAD can be reduced by up to 18%<sup>[21]</sup>.

A CR program is primarily based on the favorable effects of physical exercise (exercise-based CR), but comprehensive programs also include educational sessions focusing on risk factors, lifestyle and its modification, nutritional advice, psychological support, and optimized pharmacotherapy (Figure 1). Top-class CR facilities provide this complex area multidisciplinary setting<sup>[18,19]</sup>.

Although representing an important component of follow-up care, CR is provided in < 54% countries worldwide<sup>[24,25]</sup>. It is particularly low-middle income countries staying behind (about 8% and 28% respectively)<sup>[24]</sup>, despite their broader needs<sup>[24,25]</sup>. The International Council of Cardiovascular Prevention and Rehabilitation was established in 2011 in response to this situation. This body's primary goal is to join societies (worldwide), support CVDs' prevention, and promote CR as an essential part of the care<sup>[26]</sup>.

CR consists mainly of the following phases: Hospitalization phase (Phase I); Outpatient phase (Phase II); and Maintenance phase (Phase III/IV)<sup>[27-29]</sup>. Phase I is initiated early in the hospital (in most cases till 48 h post-operation)<sup>[29]</sup> and is aimed at patient cardiovascular system adaptation to physical activity and has a crucial role in terms of discharge planning<sup>[27,28]</sup>. At least as important is the education of patients about risk factors and initiation of their lifestyle changes. A long-term secondary prevention plan is set up during that phase<sup>[27,28]</sup>.

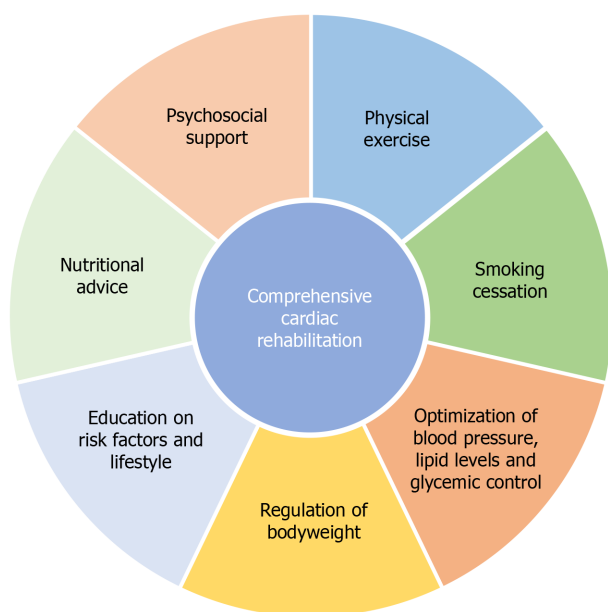
The outpatient CR program that follows (Phase II) lasts typically till week 36 after the CVD event. The main part of the outpatient program is monitored physical exercise (up to 36 training sessions), optimized based on personalized clinical assessment, with input from exercise stress testing (cardiopulmonary exercise testing; *e.g.*, spirometry or walk tests)<sup>[27,28]</sup>. The importance of functional evaluation through exercise testing before starting a training program is strongly emphasized for a physiologically comprehensive exercise intensity prescription<sup>[30]</sup>. Exercise intensity prescription is a key issue and is directly linked to both the amount of improvement (effectiveness of CR) and the risk of adverse events during exercise (safety)<sup>[30]</sup>. Phase II is considered crucial concerning the stimulation of favorable lifestyle changes and adherence to secondary prevention principles. This phase is also critical from the participation aspect, which is then mirrored in the maintenance phase<sup>[27,28]</sup>.

The aim of Phase III/IV is to maintain the established lifestyle changes under minimal professional supervision with the target of stabilization of patient's health<sup>[27-29]</sup>.

The main indications of CR (its outpatient phase) include the condition after an acute coronary syndrome, percutaneous coronary intervention, and coronary artery bypass grafting. Chronic coronary syndromes and heart failure (HF) are also indications for CR<sup>[27,28,31-34]</sup>. Peripheral artery disease of the legs is a less frequent indication<sup>[35,36]</sup>.

The safety of this approach is an essential precondition for a complete CR application. According to the retrospective study by Pavy *et al*<sup>[37]</sup>, one severe cardiac event was associated with 49565 h of physical exercise and 8484 stress tests. The cardiac arrest rate was calculated to be 1.3 per million hours of training. Low, moderate, or high risk of complications can be estimated based on the patient's overall clinical profile (including a detailed history and physical examination), ejection fraction, functional capacity, the presence of ischemia (electrocardiography ST





**Figure 1 Comprehensive cardiac rehabilitation and its core components.** Programs of cardiac rehabilitation support patients in goals of increasing levels of physical activity, healthy nutrition, optimal adherence to medication, body weight regulation, smoking cessation, and optimal psychosocial well-being, thereby helping them to reduce the risk of recurrent cardiovascular event.

segment changes; *e.g.*, during exercise stress testing), and any presence of uncontrolled cardiac arrhythmias as well as by other diagnostic tests that could be considered as relevant (on a case-by-case basis by the attending physician)<sup>[27,35,38]</sup>.

The effectiveness of CR has been well described, particularly following coronary revascularization, respectively, in patients with CAD<sup>[18,39]</sup>. Chronic HF is an increasing health problem. There are two basic types of HF: With reduced ejection fraction (HFrEF,  $\leq 40\%$ ) and preserved ejection fraction, both resulting in a smaller volume of blood pumped around the body<sup>[40]</sup>. This diagnosis is associated with a reduced tolerance to exercise, reduced QoL, and increased risk of hospitalization and death<sup>[40,41]</sup>. In this context, the publications suggest that exercise-based CR is beneficial, but the supporting evidence is less convincing<sup>[34,41–43]</sup>.

According to Long *et al*<sup>[40]</sup>, exercise-based CR makes little or no difference in all-cause mortality over the short term (but may improve it in the long-term), probably reduces all-cause/HF-specific hospitalization, and may confer a clinically significant improvement in the QoL (mainly in patients with HFrEF). In comparison, Taylor *et al*<sup>[41]</sup> show that exercise-based CR did not significantly affect the risk of mortality and hospitalization in patients with HFrEF. The study by Bjarnason-Wehrens *et al*<sup>[42]</sup> found similar results but added that programs of CR are likely to improve exercise capacity and QoL in this group of patients. O'Connor *et al*<sup>[43]</sup> further came to conflicting results. In the primary analysis, exercise training resulted in nonsignificant reductions in mortality or hospitalization. Nevertheless, after adjusting for highly prognostic predictors, exercise-based CR was associated with modest significant decreases in both all-cause mortality/hospitalization and cardiovascular mortality/HF-specific hospitalization. It seems that CR efficiency in HF also depends on the ejection fraction of the left ventricle<sup>[40,41]</sup>. In summary, exercise-based CR is an efficient and safe, supported treatment for HF patients<sup>[27,42]</sup>, but further evidence is needed to show better the effects of exercise-based CR, especially among patients with preserved ejection fraction<sup>[40]</sup>.

Comprehensive CR is safe, improves exercise capacity, QoL, and general and mental health in patients implanted with pacemaker or cardioverter-defibrillator<sup>[44]</sup>. Nevertheless, further extensive studies are needed to evaluate CR's role in this subgroup of patients. CR appears to be also safe in patients following heart transplantation, improves exercise capacity, but has no significant effect on the QoL in the short term<sup>[45]</sup>. The condition following a valve defect surgery (such as aortic stenosis) is an area where the benefits of CR are examined. CR was found to affect favorably functional capacity and QoL in such patients<sup>[46,47]</sup>. In addition to the benefits described above, CR also brings about improvements in the symptoms associated with cardiac arrhythmia (atrial fibrillation)<sup>[48,49]</sup>.

### Training modalities

Aerobic endurance exercise is the gold standard of the outpatient training program. While most European and North American guidelines recommend a moderate-high intensity, lower-intensity exercise is preferred in the United Kingdom, Australia, and New Zealand<sup>[29]</sup>. The latter countries also put less accent on technical exercise stress examination (such as electrocardiography, spiroergometry) while routinely using walk tests (*e.g.*, the 6-min walk test, shuttle walk tests) to assess the functional capacity<sup>[29]</sup>.

Timed walk tests are easy to implement, require fewer resources, do not require expensive equipment, and can be a feasible alternative to evaluate functional capacity<sup>[50,51]</sup>. In the study by Harris *et al*<sup>[52]</sup>, results from 6-min walk test highly correlated with peak oxygen uptake (peakVO<sub>2</sub>) measurement among CR patients. Due to Lelis *et al*<sup>[51]</sup>, Incremental Shuttle Walk Test (ISWT) can contribute to identifying patients at low risk for a cardiac event during exercise at moderate intensity. Hanson *et al*<sup>[50]</sup> provide support for the ISWT as a convenient field test but not as a surrogate to predict symptom-limited exercise test duration for individuals. Recently, however, there has been an increasing emphasis on comprehensive stress assessment prior to and after completing the training program<sup>[53]</sup> including technical exercise stress testing, especially for high-risk patients<sup>[30]</sup>.

Training sessions should be organized three to five times a week, and each session (main exercise) should last 20-60 min<sup>[54]</sup>. A training session should include the warm-up, main exercise, and cool-down. Preferred types of exercise include walking, jogging, cycling, or rowing<sup>[55]</sup>. The optimum exercise intensity lies within the range of 40%-70% of the heart rate (HR) reserve or 50%-80% of the exercise capacity (peak HR, peakVO<sub>2</sub>) achieved during exercise stress testing<sup>[54,55]</sup>. The incremental cardiopulmonary exercise test allows matching the different physiological responses of different exercise intensity to the individual patient pathophysiological and clinical status, maximizing the benefits from aerobic exercise training in CR<sup>[30]</sup>. Resistance training is also recommended to supplement CR<sup>[56]</sup>.

Some of the main goals of an optimally set exercise-based CR program are the achievement of improved cardiorespiratory fitness (CRF), exercise tolerance, and QoL<sup>[21]</sup>. Mounting evidence has firmly established that low levels of CRF are associated with a high risk of CVD and all-cause mortality<sup>[57]</sup>. Although different CRF parameters decrease with age and are (in terms of absolute values) lower in women, a significant beneficial effect of CR on them has been observed<sup>[57-59]</sup>. The typically measured parameter is peakVO<sub>2</sub> (mL/kg per minute) as an important prognostic indicator. Each metabolic equivalent increased by one unit (1 MET = 3.5 mL/kg per minute) was associated with a total mortality risk reduction by 8%-20%<sup>[57,60,61]</sup>, and CR induced a mean peakVO<sub>2</sub> increase by 5.4 mL/kg per minute<sup>[62]</sup>. Furthermore, the study results by Hartman *et al*<sup>[63]</sup> suggest that the changes in oxygen uptake were subject to appreciable heterogeneity, which did not correlate with improvements in other cardiovascular risk factors. In this context, De Schutter *et al*<sup>[64]</sup> referred that greater increases of peakVO<sub>2</sub> ( $\geq 2.5$  mL/kg per minute) were independently associated with improvements in survival, level of high-density lipoprotein cholesterol, weight loss, and body fat. Efforts are needed to improve CRF in secondary prevention of CVDs.

## HIGH-INTENSITY INTERVAL TRAINING

It has been demonstrated that CRF improvement is directly dependent on the intensity of the exercise. A higher intensity induces a higher peakVO<sub>2</sub> increase<sup>[65]</sup>. Such findings constitute the basis for high-intensity interval training (HIIT), in which high-intensity activity intervals alternate with lower-intensity activity (or passive recovery) intervals<sup>[66]</sup>.

Compared to the conventional continuous moderate-intensity training practice, studies have reported on HIIT being more effective in improving CRF while remaining safe<sup>[67]</sup>. In comparison, Conraads *et al*<sup>[68]</sup> observed similar improvements in CRF and peripheral endothelial function following continuous training or HIIT in CAD patients. However, the main limitations reported from the study are the lower mean HR training zone in the HIIT group (88% of peak HR) and the higher mean HR training zone in the moderate-intensity continuous training group (80% of peak HR) than was prescribed. The study by Ellingsen *et al*<sup>[69]</sup> reported an average training zone of 90% of peak HR for HIIT, where approximately half of the patients with HFrEF trained below the set target. Both studies pointed to the importance of prescribing and adjusting the HR training zone and exercise intensity according to the patient's subjective perception (*e.g.*, use of The Borg Scale). Ballesta García *et al*<sup>[70]</sup> reported a

higher efficiency of HIIT in patients with HF compared to patients with CAD and recommended using active recovery intervals. According to Wisløff *et al*<sup>[71]</sup>, exercise intensity was an essential factor for reversing left ventricular remodeling and improving aerobic capacity, endothelial function, and QoL in patients with post-infarction HF. Apart from the above diagnoses, favorable results were also achieved after heart transplantations, including the potential reduction of anxiety—a frequent health complication in such patients<sup>[72,73]</sup>.

Current HIIT research limitations include that most studies use mostly one training modality, which is not a reflection of the real world where different types of physical activity are common<sup>[67]</sup>. Besides, future research should also focus on women, as this population is a minority in the studies, and this gender bias represents a limitation in generalizing the results.

## RESISTANCE TRAINING

While resistance training was perceived as inappropriate in the past because of fear of provoked complications, this training modality is a recommended component of CR<sup>[74]</sup>. Current experience shows that a combination of endurance training and resistance training (combined training) is more efficient than either modality on its own<sup>[75]</sup>. Higher efficiency of combined training was demonstrated on improved CRF and muscle strength. Resistance exercise is an essential supplement for elderly patients in particular, resulting in enhanced self-management and QoL<sup>[76,77]</sup>. The exercise can be based on using the patient's body weight, elastic bands, free weights, or fitness machines. Intensity should be selected to enable eight to fifteen repetitions, eight to ten exercises in a two to three fashion (30%-60% of one-repetition maximum). The recommended training frequency is two to three times a week<sup>[55,56]</sup>.

## ALTERNATIVE TRAINING MODALITIES

Apart from the above-mentioned well-established modalities, research has also focused on other feasible training alternatives. The goal is to set up a selection of options and adapt the CR program to the patient's needs, experience, risk profile, and preferences; the options should be appropriately tailored to the ethnic and cultural area<sup>[78]</sup>.

Some of these alternatives include Tai Chi and yoga. Tai Chi, initially a type of Chinese martial art, includes low-moderate intensity aerobic exercise. Data suggests that this exercise brings about improved CRF, like regular activities of identical intensity. Besides, Tai Chi has favorable psychological impacts, including reduced anxiety and depression<sup>[79,80]</sup>. However, current Tai Chi experiments were performed predominantly on Chinese people. There are large differences in the environment, figure, and cultural background in different countries, and understanding the Tai-Chi approach may be different. Whether Tai Chi is generally effective on a global scale will need to be further verified in the future<sup>[81]</sup>.

Yoga as a combination of physical and respiratory exercise and meditation can also be a useful CR supplement. Yoga was demonstrated to reduce stress and improve the autonomous nervous system's function, thereby affecting cardiovascular risk factors<sup>[82]</sup>. An alternative approach through yoga has been shown to improve the subjective assessment of health status, reaching pre-infarct levels<sup>[83]</sup>. If yoga is found to be effective in CR, it has the potential to transform the care of acute myocardial infarction patients in India and other low-middle income country settings<sup>[84]</sup>.

Dance can also be used to complement CR. Urbano *et al*<sup>[85]</sup> reported several favorable effects of social dance or samba lessons—glycemia reduction, lower HR at rest, lower cholesterol, and better relaxation.

García *et al*<sup>[86]</sup> compared the effect of conventional and modified tennis training (to control the exercise intensity according to the patient's functional capacity; *e.g.*, walking slowly, walking fast, jogging, and running) in low-risk patients after acute coronary syndrome. Both groups showed improvements in QoL, lipid profile, and exercise tolerance. The development of modifications to CR programs based on alternative sports activities leads, in particular, to improved exercise adherence<sup>[87]</sup>.

Technological progress also offers the opportunity to make use of virtual reality. New generations of active video games allow the user to interact with the platform through targeted movement exercises. Several significant cardiovascular benefits in this context are demonstrated by the reviews of García-Bravo *et al*<sup>[88]</sup> and Ruivo<sup>[89]</sup>.

Besides, playing video games is fun, which improves the motivation to exercise<sup>[89]</sup>. The use of virtual reality could be considered as a complementary tool of exercise training in CR. However, it is necessary to carry out studies with adequate methodological quality to determine the ideal technological systems, target populations, and clear protocols to study their effects in the short, medium and long-term assessments<sup>[90]</sup>.

The authors agree that further extensive studies about alternative training modalities are needed to support such findings.

## RESPIRATORY TRAINING

According to the review by Wang *et al*<sup>[91]</sup>, inspiratory muscle training and respiratory exercise improved HF patients' cardiovascular function, functional capacity, and QoL. Exercise using the Threshold IMT (inspiratory muscle trainer; Respironics, Murrysville, PA, United States) resulted in a higher strength of the respiratory muscles and reduced the perception of dyspnea and depression in patients with HFrEF<sup>[92]</sup>. According to Hermes *et al*<sup>[93]</sup>, a combination of conventional training and inspiratory muscle training was more effective than endurance training and resistance training alone in that it increased the peakVO<sub>2</sub> in patients after coronary bypass. On the other hand, this hypothesis has not been proved in HF patients<sup>[94]</sup>. Adamopoulos *et al*<sup>[95]</sup> demonstrated that the addition of inspiratory muscle training to CR resulted in a supplementary improvement in respiratory muscle function, dyspnea, QoL, and inflammatory/cardiac biomarkers but not in cardiopulmonary exercise parameters (e.g., peakVO<sub>2</sub>, ventilatory threshold, exercise duration) in moderate chronic HF. There is a consensus that the inclusion of respiratory training can support the effect of conventional aerobic exercise and, hence, should become a standard option of CR<sup>[94,95]</sup>.

## PATIENTS WITH COMORBIDITIES

CR has been traditionally formed as a single disease service in Europe, North America, and other developed countries. Patients have clearly defined CR indications associated with the primary disease (post-myocardial infarction, coronary revascularization, HF, *etc.*). However, they usually suffer from comorbidities mostly related to hypertension, atrial fibrillation, and diabetes mellitus (e.g., peripheral vascular disease, chronic kidney disease, and post-stroke condition)<sup>[96]</sup>. Patients with multimorbidity are at higher risk of disability, loss in health-related QoL, hospitalization, and mortality<sup>[96]</sup>.

To reflect these complex clinical situations and improve acceptance of CR, a model of personalized multimorbidity rehabilitation should be embedded and followed. This model counts with the potential interaction of multiple diseases and their management<sup>[96]</sup>. For example, it is clinically intuitive to combine chronic obstructive pulmonary disease (COPD) and chronic HF in this model. These diseases have a common condition of dyspnea/disability and co-existing prevalence, so service could be targeted around a common disability rather than the primary organ disease<sup>[96,97]</sup>. According to Evans *et al*<sup>[97]</sup>, training program (aerobic exercise and educational lessons) focused on the improvement of exercise performance in COPD and HF patients was effective and feasible. Both groups of patients reached similar results in ISWT and were significantly higher compared to usual care. Smith *et al*<sup>[98]</sup> identified the emerging evidence to support policy for the management of patients with multimorbidity and common comorbidities in primary care and community settings.

The challenge for the indication-specific model of CR (and other services; e.g., pulmonary rehabilitation) is to evolve, building on existing successes to address more comprehensively the needs of patients with multimorbidity. Due to a lack of evidence, there is an urgent need for research into the acceptability, efficiency, and cost-effectiveness in these models<sup>[96]</sup>.

## UTILIZATION OF CR

Although representing an efficient model of secondary prevention, CR does not find as extensive utilization as would be expected<sup>[99]</sup>. Only 15%-30% of eligible patients enter the training program<sup>[100]</sup>. The participation is somewhat better, 40%-50% in high-income countries, where health care is readily available<sup>[101,102]</sup>. High heterogeneity in the availability and utilization is found in the remaining countries. Generally speaking,

CR is inadequately available and not widely used in such countries<sup>[103]</sup>.

Because of various availability and delivery worldwide, it is essential to establish and unify quality indicators at the international level (make a standardization of CR)<sup>[104]</sup>. The European Preventive Associations has recently defined the minimal and optimal standards, including core components of CR, referral and timing, patient assessment, exercise training parameters, education, long-term strategies, or CR results evaluation<sup>[74,105]</sup>. Compliance with these standards could improve CR process standardization and, hence, increase the quality of CR<sup>[106]</sup>. Resources, policy changes, and certification systems are needed to ensure that all programs meet minimum standards for CR delivery, ensuring optimal patient safety and outcomes<sup>[107]</sup>.

Adherence to the rehabilitation program is also an issue. According to the review of Oosenbrug *et al*<sup>[108]</sup>, patients who enter the program completed a median of 72% of the prescribed training sessions.

### Utilization by populations

A lower level of utilization was observed among several subgroups, such as older people<sup>[109]</sup>, patients with comorbidities, unemployed, single, and less-educated individuals<sup>[110]</sup>. Regarding gender, the level of participation and adherence was significantly lower among women than men<sup>[101,108]</sup>, although their needs are often higher<sup>[111]</sup>. Shanmugasagaram *et al*<sup>[112]</sup> found more severe barriers to CR among rural inhabitants. Among factors that adversely affect utilization are low income and low socioeconomic status<sup>[110,112]</sup>. This effect was demonstrated not only in individuals but also in the social environment<sup>[113]</sup>. Edwards *et al*<sup>[114]</sup> suggest that a lower level of adherence and completion of the rehabilitation program is associated with depression symptoms. Future research should focus on improving the participation of individuals among these specific subgroups.

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## BARRIERS TO CR

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Factors affecting the entry into CR include, in particular, patient awareness, education of physicians (other healthcare providers), availability, and inclusion of rehabilitation in the comprehensive care scheme, financial support, and timing of referral/enrolment<sup>[87]</sup>. As to participation and adherence to the training program, primary barriers include work conflicts, family responsibilities, financial costs, fear of the exercise, lack of motivation, or a long travel distance<sup>[102]</sup>. Lack of social support and comorbid conditions, such as arthritis, osteoporosis, and urinary incontinence, were also reported in a review focusing on female patients<sup>[59]</sup>.

Psychometrically validated scales assessing the utilization have been created, such as Beliefs About Cardiac Rehabilitation<sup>[115]</sup>, Cardiac Rehabilitation Preference Form<sup>[116]</sup>, and Cardiac Rehabilitation Enrolment Obstacles<sup>[117]</sup>. Their area of use, however, is somewhat limited – Beliefs About Cardiac Rehabilitation is only applicable to enrolment (not participation), Cardiac Rehabilitation Preference Form assesses only patient's perception of the CR program features importance, and Cardiac Rehabilitation Enrolment Obstacles was only validated in a sample of percutaneous coronary intervention patients. The Cardiac Rehabilitation Barriers Scale, serving to identify the barriers to the enrolment/participation at the medical system, health professional, and patient levels is an exception in this respect. The English version includes 21 items (barriers) divided into four subscales: Healthcare system factors; logistical barriers; work/time conflicts; and comorbidities/functional status. The items are assessed on a 5-point Likert scale (1 – strongly disagree, 5 – strongly agree). A higher score indicates a more substantial barrier to CR<sup>[118]</sup>. The Cardiac Rehabilitation Barriers Scale has now been translated into 15 languages<sup>[119]</sup>, and new ones are validated on an ongoing basis<sup>[120]</sup>. According to Ali *et al*<sup>[121]</sup>, higher adherence/completion, improved functional status, and reduced depression symptoms correlate with higher patient satisfaction within CR. The Patient Assessment of Chronic Illness Care scale can be used to assess the degree of satisfaction.

The causes of low utilization are very diverse among the different countries<sup>[122,123]</sup>. While the barriers to CR have been well described in developed countries (North America and Western Europe)<sup>[87,100,102]</sup>, the knowledge is minimal for the rest of the world<sup>[123]</sup>. Insight into the barriers can help develop strategies aimed at improving the utilization of CR.



## STRATEGIES TO IMPROVE UTILIZATION OF CR

Deficient use of CR is a global problem. So, strategies to improve this, including improvements in participation, are tested particularly in developed countries<sup>[124]</sup> (Figure 2). However, the countries differ in care availability, training programs, funding patterns, and patient recruitment methods<sup>[25,107,125]</sup>. For instance, according to the European Cardiac Rehabilitation Inventory Survey<sup>[126]</sup>, only 61% of European countries had national CR associations, and 57% had professional guidelines. As such, both differences and needs should be analyzed.

### CR delivery

A vast majority of the programs are funded by governments and other public sources, private resources (namely by the patient), or health insurance companies. Although financially efficient and even cost-saving<sup>[127,128]</sup>, CR is inconsistently and inadequately reimbursed<sup>[127]</sup>. Higher funding of services implies a better availability of CR. While the funds often come from national health services in Europe and Central Asia, private systems can play a more critical role in the rest of the world<sup>[125]</sup>.

According to a review by Pesah *et al*<sup>[125]</sup>, the number of participants per program lies within the range from 129 to 639 annually (median 202, more in Europe than in North America). A larger volume of a program is probably irrelevant against the quality of care provided<sup>[129]</sup>. Nevertheless, it better covers the capacity needs of CR because it is possible to increase the number of patients per program (not only the number of programs). In this context, Pack *et al*<sup>[130]</sup> pointed to the fact that the programs in the United States can cover 58% of eligible patients as a maximum (actual utilization about 34%). So the capacity of CR itself, which is insufficient in several countries, is the next issue for future policy discussion<sup>[25]</sup>.

CR was shown to be available in 54% of countries (median four programs/country)<sup>[25]</sup>. Program density concerning the population number can serve as a parameter of CR availability. The estimates are from 0.1 to 6.4 million population per program in the United States and Paraguay. Only one program in the country was identified in Bangladesh, Kenya, and Afghanistan<sup>[131]</sup>. Individual CR delivery models are being created for low-income countries<sup>[132]</sup>.

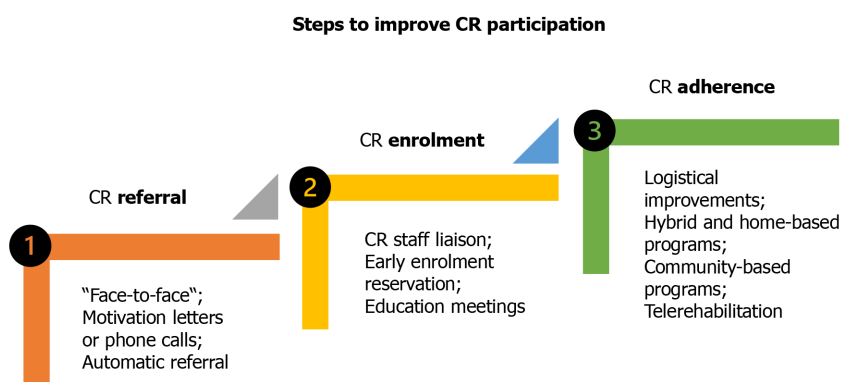
In most countries, CR is provided by a multidisciplinary team<sup>[125]</sup>. According to Supervia *et al*<sup>[107]</sup>, most programs are led by physicians, and the most common healthcare providers are nurses, nutritional specialists, and physiotherapists. A multidisciplinary team should include the program director and coordinator (cardiologist), nurses, exercise experts (physiotherapists and exercise physiologists), contributing professionals (nutritional specialists, psychologists, pharmacists, and social services experts), and consultant professionals (internists, diabetologists, *etc.*)<sup>[133]</sup>. Supervision of exercise training is performed mainly by physiotherapists and nurses<sup>[107]</sup>. While physiotherapists are a main part of the team in certain regions (*e.g.*, Australia, England, Denmark, Italy, Portugal, Spain, Mexico, Egypt, Qatar, United Arab Emirates, and Canada), exercise physiologists and kinesiologists are more common in some other regions (United States, China, and the Middle East)<sup>[125]</sup>.

On average, 24 training sessions are prescribed per program, though high international and national variability was found<sup>[134]</sup>. The frequency ranges between one to three sessions a week (average of two sessions a week, 9 wk in total)<sup>[125]</sup>. A minimum required dose of physical activity must be set to maintain adequate CR effectiveness<sup>[135]</sup>.

CR includes all the major components in most countries, particularly in the high-income ones. Exercise-based programs are most frequently provided. Patient education is frequent in North America and the Middle East, while nutritional advice is provided in East Asia and the Pacific area<sup>[125]</sup>. Alternative models to center-based programs like home-based or community-based programs are offered infrequently (12% and 10%, respectively)<sup>[25]</sup>. Mainly in residential areas, is the CR Phase II provided by Austria, Belarus, Croatia, Czech Republic, Finland, France, Germany, Hungary, Iceland, Italy, Lithuania, the Netherlands, Romania, Russia, Serbia, and Spain<sup>[125]</sup>.

The most frequently reported barrier to CR delivery worldwide is a lack of resources<sup>[125]</sup>. It is unacceptable that Class I/Level A recommendations<sup>[28,136]</sup> are inadequately funded compared to other similarly graded recommendations for the same indications<sup>[125]</sup>. Cardiology societies, foundations, and governments should make efforts to achieve better CR reimbursement<sup>[127]</sup>. The International Council of Cardiovascular Prevention and Rehabilitation recently developed and collected resources for attaining this goal<sup>[137]</sup>.

Globally, the delivery has been described in fewer than one-half of countries providing CR. The least amount of information comes from regions highly burdened



**Figure 2 Strategies to improve participation in cardiac rehabilitation.** The scheme shows efficient strategies for better participation in cardiac rehabilitation. There are three steps for implementation of these—referral, enrolment, and adherence. CR: Cardiac rehabilitation.

by CVDs: East Asia, the Pacific area, Middle East, North Africa, and South Asia. Generally, the data provided are inconsistent, and additional research is needed<sup>[25,107,125]</sup>.

### Referral strategies

Santiago de Araújo Pio *et al*<sup>[124]</sup> suggest that a referral is more convincing if provided by a health specialist (*e.g.*, nurse or physiotherapist); a physician may play an especially significant role<sup>[138]</sup>. Information of patients and health professionals (particularly general practitioners and cardiologists) is essential for increasing a level of physical activity within CR. Face-to-face contact is also important<sup>[124,138]</sup>.

Efficient strategies include personal meetings and telephone calls<sup>[139]</sup>, shortening of the time to CR appointment ( $\leq 10$  d)<sup>[140]</sup>, patient navigation/education (*e.g.*, on the bed)<sup>[141]</sup>, text messages<sup>[142]</sup>, and motivation letters based on the Theory of Planned Behaviour<sup>[143]</sup>. CR enrolment is 27% increased by introducing interventions of that type<sup>[99,124]</sup>.

The importance of initiating appropriate prevention early before hospital discharge cannot be overemphasized, as prevention treatment tends to decrease post-hospitalization<sup>[28]</sup>. It is necessary to emphasize the preventive measures (*e.g.*, education, referral to CR) directly to the patient, even during the first days after admission/cardiac event, because failure to do so may suggest that these measures are valueless<sup>[28,29]</sup>.

Grace *et al*<sup>[144]</sup> determined the attainable limit for enrolment at 70%. Subsequently, Ades *et al*<sup>[145]</sup> estimated by calculation that participation improvement from 20% to 70% would save 25000 Lives annually and prevent 180000 hospitalizations every year in the United States.

A system called "automatic referral", based on a patient's electronic record or normal discharge, is also a systematic CR call<sup>[146]</sup>. Grace *et al*<sup>[147]</sup> reported higher effectiveness of the combination of automatic/personal referral (enrollment about 73%) than of each of the strategies (60% and 50% respectively), compared to the standard recommendation (29%). Options also include an early reservation of entry during hospitalization or an educational meeting shortly after discharge from the hospital<sup>[148]</sup>. An increase in the supply of CR requires decentralization of the exercise training offer. Digital devices and the expansion of community centers can also encourage the practice of physical activity<sup>[138]</sup>.

## STRATEGIES FOR IMPROVING ADHERENCE AND COMPLETION

Successful interventions to improve adherence included, among other things, a gender-tailored CR program, because for some patients, public or mixed-gender exercise may represent a serious barrier. In this program, women completed 90% of the prescribed training sessions (77% in the standard program)<sup>[149]</sup>.

Due to review by Room *et al*<sup>[150]</sup>, focused on behavioural strategies for adherence promotion in older patients, the feedback and monitoring (*e.g.*, individualized graphic feedback on exercise goals and problem-solving support) showed positive outcomes, although there is a lack of evidence to recommend their use currently. According to Lynggaard *et al*<sup>[151]</sup>, individual patient education based on the Learning and Coping

Strategies improved adherence compared to the standard program. This type of intervention appeared to be efficient, particularly in HF patients and low-income and low-educated patients<sup>[151]</sup>. It is suggested that patients may need ongoing attention and guidance during the outpatient phase of CR but also in the long-term maintenance of their lifestyle changes<sup>[150,152]</sup>.

As it appears, strategies based on unsupervised delivery are most efficient for improving CR adherence. Due to Santiago de Araújo Pio *et al*<sup>[124]</sup>, such options result in completion improvement by 13%, although utilization measurement in different settings may be difficult to compare and unsupervised delivery is not optimal for all CVD patients (*e.g.*, high-risk patients, especially from the beginning of Phase II)<sup>[124]</sup>.

### **Home-based program**

Among frequent causes of low utilization of center-based programs are logistic barriers, such as a significant travel distance, traffic problems, and time/work conflicts<sup>[102]</sup>. The home-based program is a feasible solution; it is a CR alternative in a home setting, including exercise, monitoring, control sessions, letters, and telephone calls. Walking is a frequently recommended activity<sup>[153,154]</sup>. This program's advantages include the possibility of better adaptation to the patient's needs and relatively less time spent because of the patient need and not travel to the rehabilitation site. More detailed benefits and risks of a home-based CR program are listed in [Table 1](#).

Home-based program effectiveness has been demonstrated in patients after myocardial infarction and revascularization<sup>[21,153]</sup>, and in HF patients<sup>[154]</sup>. Like the center-based program, this option has a favorable effect on the risk factors, QoL, and risks of death or a cardiac event<sup>[21,153]</sup>. Compared to the center-based program, the home-based program was associated with a higher adherence and completion rate<sup>[153]</sup>. A home-based program may be a reasonable option for selected clinically stable low-moderate risk patients who are eligible for CR but cannot attend a conventional center-based CR program<sup>[155]</sup>.

A hybrid model combining elements (and the assets) of the center-based and home-based program is the next efficient option<sup>[156]</sup>. According to Imran and colleagues<sup>[157,158]</sup>, hybrid, home-based, and center-based CR induced similar functional capacity improvements, but only home-based programs improved QoL over usual care in HF patients.

### **TR (remotely monitored training)**

TR is defined as using information and telecommunication technologies to provide health service (rehabilitation) at a large distance. TR includes several approaches, such as remote monitoring, e-learning, and telecoaching<sup>[159]</sup> ([Figure 3](#)). They are approaches that may be used with advantage in home-based or community-based CR programs. Among the most frequently used technologies are smartphones, computers, wearable sensors (for monitoring exercise parameters; *e.g.*, HR and duration of physical activity), and the internet<sup>[160,161]</sup>.

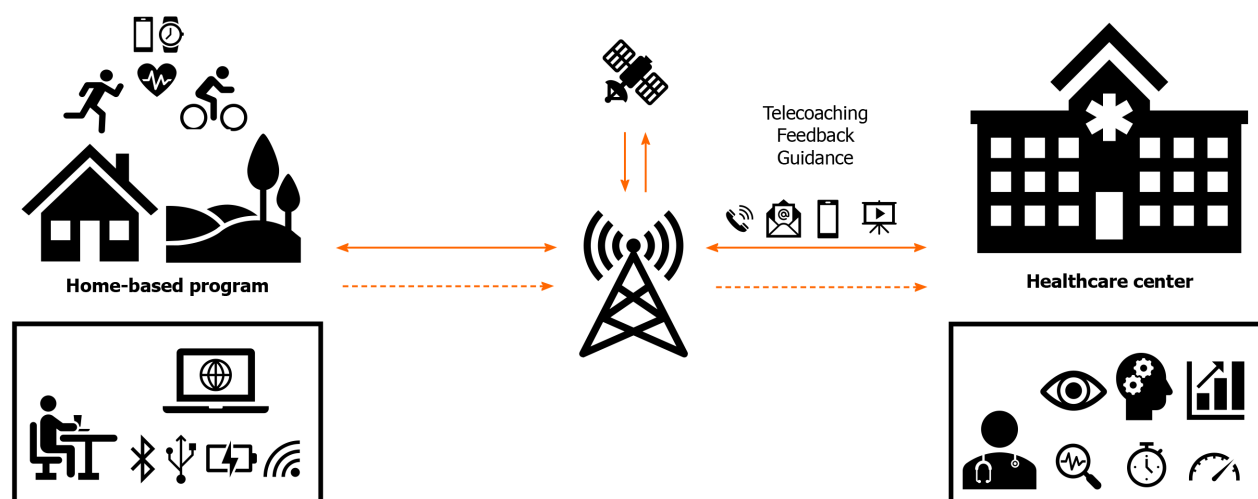
Reviews comparing the overall efficiency of telemedicine interventions and the conventional outpatient program found similar favorable outcomes, including improved functional capacity and improved QoL. TR is a suitable alternative, especially for patients for whom the center-based program is less available<sup>[159,162]</sup>, and it may increase the capacity of the CR<sup>[163]</sup>.

Physical activity in CR is often assessed using questionnaires or accelerometers<sup>[164]</sup>. The development of technologies opens new monitoring options. For example, Kraal *et al*<sup>[165]</sup> measured HR by using a watch and a chest strap. Song *et al*<sup>[166]</sup> combined a chest strap with a smartphone, while Batalik *et al*<sup>[167]</sup> used an optical sensor on the wrist. Beatty *et al*<sup>[168]</sup> tested the feasibility of using a mobile app, which included setting physical activity targets, monitoring protocols including medical metrics (*e.g.*, body weight, blood pressure, and mental condition), education, reminding, and feedback. Besides, lifestyle-focused text messages have led to improved clinical outcomes in patients with CAD<sup>[169]</sup>. However, this new alternative's promising results will require more detailed research, including data on the association between improvements in surrogates from technological devices and cardiovascular outcomes. This is an unanswered part of CR with the potential to support the use of remotely monitored training.

TR studies have been performed in almost all cardiac patients (including low- to high-risk patients). A comparable completion of TR interventions with center-based programs supports the assumption for a sufficient alternative method<sup>[155]</sup>. TR can affect barriers and is particularly suitable for those who face specific barriers and can not participate in center-based programs.

**Table 1 Benefits and risks of home-based cardiac rehabilitation program**

Advantages	Disadvantages
Low costs	Lack of "face to face" contact
Individual time planning	Deficient supervision and communication
More privacy	Absence of social interaction
Greater independence and flexibility	Worry about the safety of high-risk patients
Minimum time/travel barriers	Lack of published guidelines
Integration into daily activities	Lack of legal clarity and accountability



**Figure 3 Scheme of telerehabilitation (remotely monitored training).** The diagram describes remotely monitored exercise training and its potential use within the cardiac rehabilitation home-based program framework.

The assessment of the safety aspect of TR is based on the experience of center-based rehabilitation. Adverse events are rare in center-based programs<sup>[37]</sup>. A review of TR interventions reported no cardiovascular complication or death associated with physical training, mostly in studies that evaluated patients with low-moderate risk of cardiovascular complications<sup>[161]</sup>. Although patients at higher risk (*e.g.*, HF patients) are already better represented in remote-controlled studies to assess lifestyle changes and psychological interventions, this high-risk population is under-represented in TR exercise intervention studies<sup>[170]</sup>. For these reasons, it follows that remotely monitored exercise training as part of TR is considered a safe alternative to outpatient CR only for CAD patients with a low-moderate risk of complications<sup>[74,161,170]</sup>.

The discussion on this topic is essential because of the current global situation with the coronavirus disease 2019 (COVID-19) pandemic, where levels of physical activity, social isolation, and a closed CR center are limited<sup>[171]</sup>. This unprecedented situation does not allow many eligible patients to optimize secondary prevention and practice of physical exercise. This is an even more significant challenge to alternatives, such as TR, to provide the core components of CR for these patients<sup>[172]</sup>. The call is supported by the European Association of Preventive Cardiology, which considers TR relevant to all CVD patients who can not visit CR centers regularly, also after the end of the COVID-19 pandemic<sup>[173]</sup>.

### Community-based program

Optimum treatment of a CVD requires a healthy lifestyle sustained in the long run, including regularly practiced physical activity. Such habits are accepted and strengthened during Phase II of CR<sup>[27-29]</sup>. However, most outpatient programs are too short (4-12 wk) to fix them in the long-term. Exercise adherence eventually decreases, which may have a negative effect on cardiovascular risk factors<sup>[174]</sup>. The CR community-based program is an efficient option to bridge the period between Phase II (adoption of the new behavioral patterns) and Phase III/IV (long-term mainten-

ance)<sup>[174,175]</sup>.

Community-based programs provide similar services as hospital-based programs, including physical assessment and prescription, exercise, education, nutritional advice, and other comprehensive CR components<sup>[174,176]</sup>. Sports centers frequently organize such programs under the supervision of physiotherapists or nurses. Their advantages included better availability for patients who do not need to travel long distances to the hospital and potentially higher utilization<sup>[174,176]</sup>. At the same time, an irreplaceable role in terms of patient supervision, regular clinical assessment, and overall follow-up by a physician is needed<sup>[27,28]</sup>.

According to Mosleh *et al*<sup>[176]</sup>, community-based programs provide health benefits similar to center-based programs. Mandic *et al*<sup>[174]</sup> pointed to a higher attractiveness of community-based programs for older patients, married patients, and patients with musculoskeletal problems who live near community centers. CR programs should also support exercise beyond the regular training sessions to achieve the recommended physical activity level. The assessment of this activity is subject to additional studies. For instance, Alharbi *et al*<sup>[177]</sup> validated modern accelerometers to measure the number of steps walked and the moderate-high intensity physical activity duration.

## COST-EFFECTIVENESS

The costs associated with the treatment of CVDs are high worldwide and are growing every year<sup>[178]</sup>. For this reason, the cost of treatment, which allows for the efficient use of resources, is very crucial. Healthcare systems that are limited by budget require information on how best to use resources to increase patients' benefits<sup>[178]</sup>.

Hinde *et al*<sup>[179]</sup> examined a CR cost-effectiveness model using the current Cochrane review in relation to socioeconomic status and increased CR utilization. The results confirm the evidence that low-cost CR, which reduces the risk of reinfarction and further hospitalization, is a highly cost-effective intervention. Besides, the research noted low CR costs in a group of patients with low socioeconomic status, which increased the potential health benefits. Using England as a model, authors also estimate the expenditure that could be justified while maintaining CR's cost-effectiveness at £68.4 million per year. There is an apparent reason to support interventions that improve CR utilization. In this context, models of the home-based program have good potential. A study by Taylor *et al*<sup>[180]</sup> aimed to assess the long-term cost-effectiveness of adding home-based CR to usual care compared to regular care alone in patients with HFrEF. The intervention analysis was associated with a gain of 0.23 quality-adjusted life year points and increased mean cost of £400 compared to usual care, resulting in a cost per quality-adjusted life year gained of £1720. This cost comparison confirms that home-based CR is a cost-effective treatment option for the patient's whole life.

The above findings should support healthcare providers in funding home-based programs to improve availability and increase the CR's utilization. In summary, as currently delivered, CR is cost-effective in all groups of CVDs due to its low cost and high effectiveness in improving cardiovascular outcomes<sup>[179,180]</sup>.

## CARDIO-ONCOLOGY

In recent years, it is possible to observe rapid growth in the field of cardio-oncology. Cancer and CVDs are the leading causes of mortality in developed countries<sup>[1,181]</sup>. Cancer patients often suffer from cardiovascular complications of treatment and increased cardiovascular risk. The most common factors are reduced CRF, muscle atrophy, hypertension, and smoking<sup>[182,183]</sup>. Furthermore, the adverse effects of treatment are associated with cardiac dysfunction due to cardiovascular toxicity<sup>[183]</sup>. Prevention and mitigation of these factors are essential, and a comprehensive CR model can offer such an approach<sup>[182]</sup>.

Physical activity is a significant component in cardiovascular prevention and clinical manifestations of cardiotoxicity<sup>[182,183]</sup>. According to the AHA<sup>[183]</sup>, an individual, tailor-made exercise program is needed for oncology patients. Physical activity should be adjusted and dosed by the patient's characteristics, medication administered, anamnesis, and exercise response. Moreover, it is necessary to consider the individual training modalities, which can also be prescribed under a patient's preference<sup>[183]</sup>. In order to make the correct exercise prescription, a cardiological evaluation, including a stress test, is required for these patients<sup>[183,184]</sup>.



Recent studies showed reduced development of cancer progression as well as a reduction in cardiovascular risk following the introduction of a physical exercise<sup>[182,183]</sup>. Evidence suggested that cancer patients participating in an oncology rehabilitation program had experience improving psychological and physiological parameters<sup>[185]</sup>. Exercise effectively improved CRF, QoL, and mental well-being and reduced fatigue, anxiety, or depression<sup>[184]</sup>.

The CR model's use provides a very suitable approach to bring rehabilitation to a larger oncology population of survivors<sup>[182,185]</sup>. However, ensuring routine cardio-oncological rehabilitation is likely to require modifications to current models<sup>[184]</sup>.

## CONCLUSION

CVDs pose a severe health problem worldwide and are expected to grow in importance. The secondary prevention CR model is a useful option to reduce mortality and disability. CR brings about many benefits for the individual, including sustained self-sufficiency and improved QoL and acts at the system level, for example, by reducing hospitalizations and cutting overall healthcare costs. Despite all of its benefits, the degree of CR utilization is inadequately low. By analyzing each country's situation, barriers to CR in different population subgroups could be identified, allowing for a tailored utilization of new options emerging from current progress in both science and technology. The findings so identified could thus be used to develop even more efficient CR strategies and potential personalized alternatives.

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