

Sex and gender specific pitfalls and challenges in cardiac rehabilitation: a working hypothesis towards better inclusivity in cardiac rehabilitation programmes

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Notwithstanding its acknowledged pivotal role for cardiovascular prevention, cardiac rehabilitation (CR) is still largely under prescribed, in almost 25% of patients owing an indication for. In addition, when considering differences concerning the two sexes, female individuals are underrepresented in CR programmes with lower referral rates, participation, and completion as compared to male counterpart. This picture becomes even more tangled with reference to gender, a complex socio-cultural construct characterized by four domains (gender identity, relation, role, and institutionalized gender). Indeed, each of them reveals several obstacles that considerably penalize CR adherence for different categories of people, especially those who are not identifiable with a non-binary gender. Aim of the present review is to identify the sex- (i.e. biological) and gender- (i.e. socio-cultural) specific obstacles to CR related to biological sex and sociocultural gender and then envision a likely viable solution through tailored treatments towards patients' well-being.

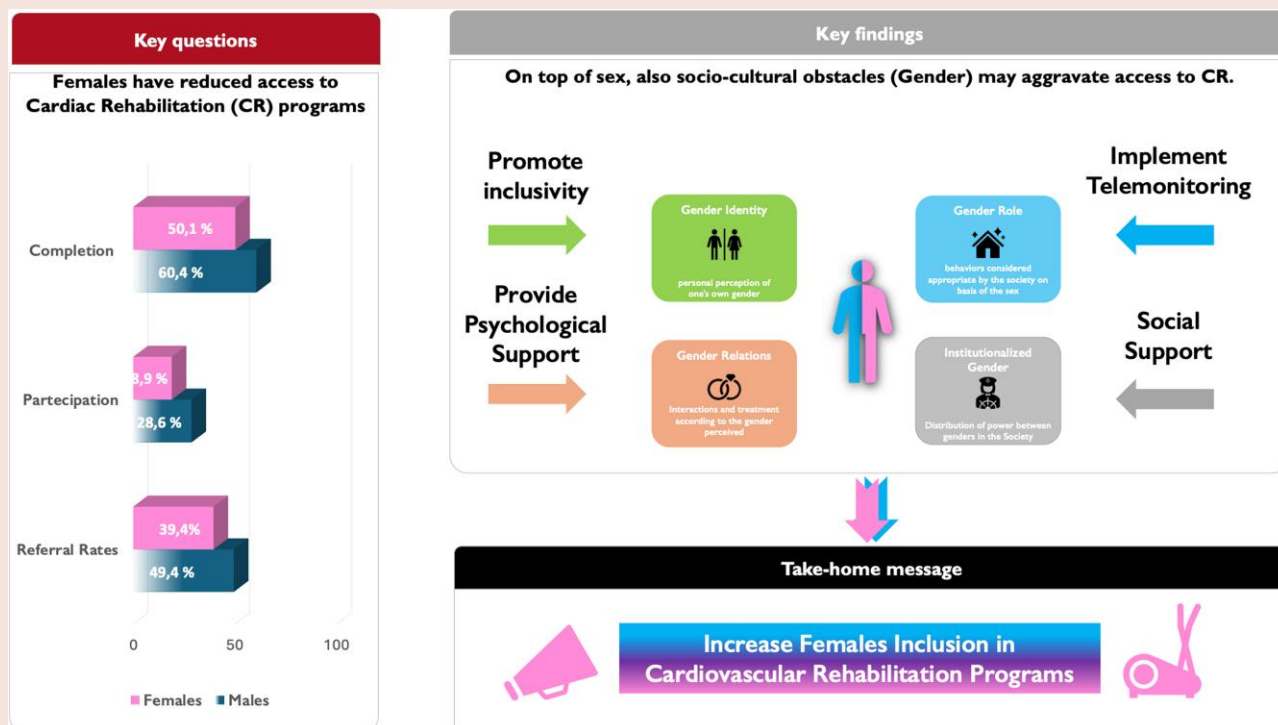
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Graphical Abstract



Keywords

Gender • Sex • Cardiac rehabilitation • Cardiovascular diseases • Health disparities

Introduction

Cardiac rehabilitation (CR) is defined as an interdisciplinary comprehensive programme based on physical training, with a concomitant complementary counselling made by trained physiotherapists, changes in modifiable cardiovascular (CV) risk factors, psychosocial support, and patient education about nutritional assessment.^{1,2} CR represents a pivotal tool in improving exercise capacity, quality of life, and clinical outcomes in different CV diseases (CVD), through different mechanisms (Figure 1). Following evidence from epidemiology and clinical studies, the most recent European Society of Cardiology (ESC) and American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend CR in patients with several CVD, enlisted in Table 1; in brief, CR is recommended by guidelines in coronary artery disease in order to reduce CV mortality and rehospitalisations,^{3–5} in patients affected by acute myocardial infarction (MI), coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), pulmonary arterial hypertension,^{6,7} and in chronic heart failure (HF) to improve exercise capacity and quality of life and reduce HF hospitalisation.^{8,9} In addition, despite the lack of a specific guideline-based recommendation, a recent position paper made by Ambrosetti et al.¹⁰ suggests CR also for valve surgery, both for minimally invasive cardiothoracic surgery and aortic valve replacement, to improve short-term physical activity.

Nevertheless, CR is still globally largely under prescribed. For instance, among 366 103 eligible Medicare beneficiaries in 2016, it has been reported that only 89 327 (~24%) attended CR, of which ~57% completed more than 24 CR sessions and around 27%

completed 36 CR sessions, implicating missed opportunities to potentially improve health outcomes.¹¹

As reported in the most recent position paper of the Italian Association for Cardiovascular Prevention and Rehabilitation (formerly GICR-IACPR),¹² based on the findings of a multi-centre survey,¹³ the total offer remains still very low, involving no more than 30–35% of the potential patients despite an increase in a 5-year period of around 20% of the number of facilities addressing CR.

In this context, the lack of accessibility to CR programme with clear sex-based disparities is a matter of immediate concern¹⁴; women are less likely to be enrolled and complete CR compared with men.^{11,15,16} In addition, the lower attendance of women to CR programme has been reported to be dependent on a gendered cluster of vulnerability which include specific socio-economic, psychological, and cultural patterns. Indeed, gender is a complex socio-cultural construct characterized by four domains (gender identity, relation, role, and institutionalized gender). Beyond biological sex, sociocultural gender represents a major driver of the disparities in the access to CR programme.¹⁷

Therefore, the aim of the present review is to shed light upon sex and gender differences in CR, their underlying causes, their effects on clinical outcomes, and the possible strategies to improve this trend.

Cardiovascular rehabilitation programmes: why sex and gender matter

In recent years, there has been an increasing awareness on how 'sex' and 'gender' capture different aspects of people and constantly intersect to

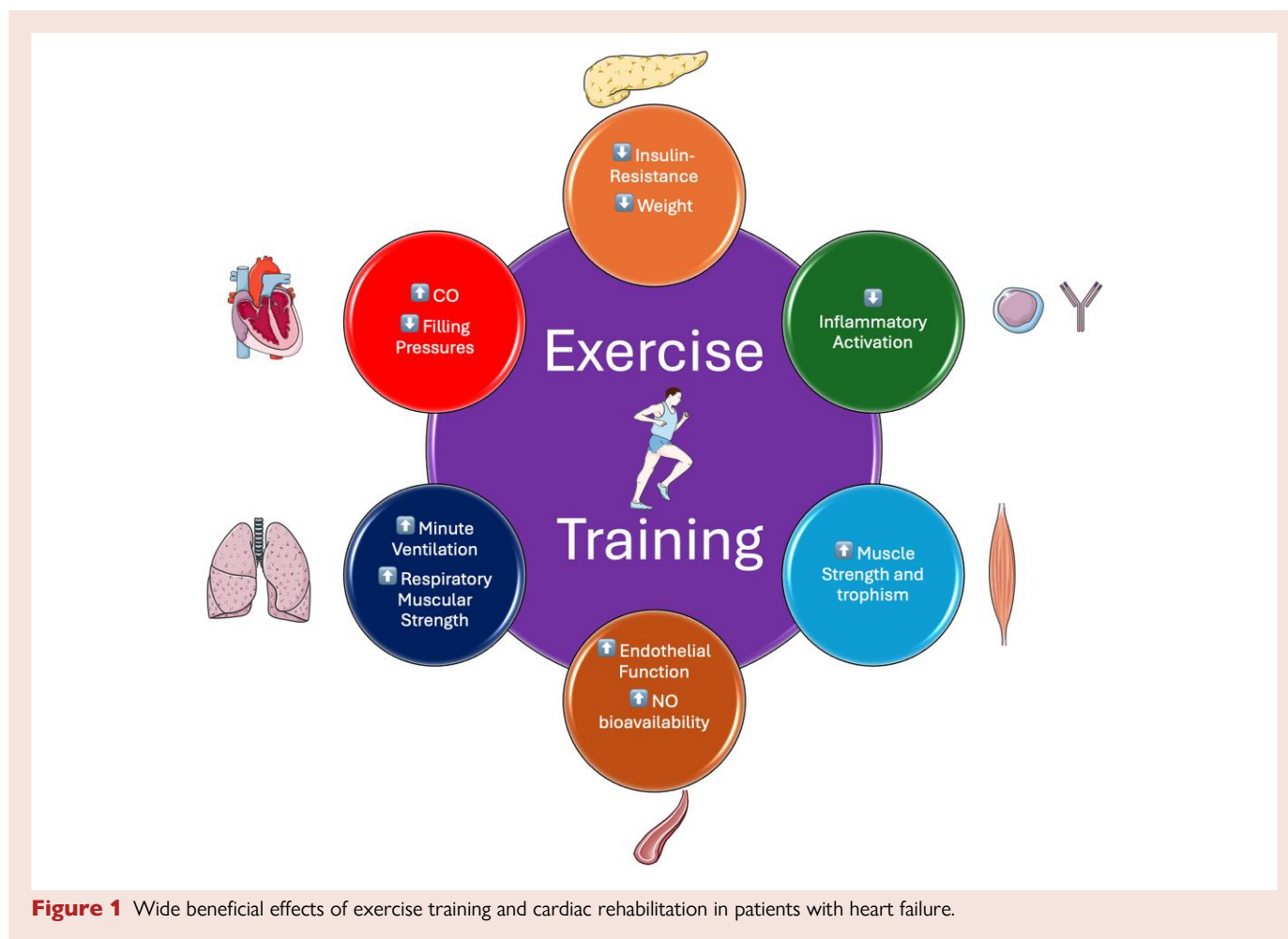


Figure 1 Wide beneficial effects of exercise training and cardiac rehabilitation in patients with heart failure.

shape health and diseases.¹⁸ While sex identifies the biological attributes (that are dependent on chromosomes, genes, reproductive, and endocrine systems), 'gender' is a multi-dimensional concept that comes from social science that can be broken down in four main domains: (i) gender identity, that is the personal perception of one's own gender (which might be different from the sex a person is assigned at birth), (ii) gender roles, which include behaviours and attitudes considered appropriate by the society on basis of the sex, (iii) gender relations, that consist on how one interacts with others and how is treated according to the sex and gender, and (iv) institutionalized gender, that mirrors the structural distribution of power between genders in the political, educational, religious, medical, cultural, and social institutions of a society^{18,19}—see *Figure 2*. Sex and gender might be difficult to tease apart and frequently they are interconnected. The main goal of sex and gender informed medicine is to deliver fair and equitable, patient-specific treatments to improve and strengthen both therapy and patients' prognosis. In the CV clinical setting, the awareness on the impact of sex and gender as modifiers of patient outcomes has increased overtime and recently guidelines have been provided on how to integrate sex and gender in CV research.²⁰ Furthermore, reporting of SOGIE (sexual orientation and gender identity and expression) data have been strongly recommended to guarantee equity, inclusion, and diversity in evidence that guide CV clinical work.²¹

In the context of CR, it has been demonstrated that there are remarkable sex disparities in CR referral, participation, and completion.²²

Generally speaking, there is a lack of facilities dedicated to CR represented by only one spot for every seven patients in need, with a great

need for developing countries.²³ To date, it is not understood how much gender, broadly viewed as a set of the four constituent domains, influences reduced therapeutic adherence to CR. Therefore, in the absence of evidence, it is appropriate to parcel out its domains to postulate its importance. The difference in CR referral and participation among sexes is consistent with several evidence showing key distinction in clinical presentation, diagnosis, treatment, and clinical outcomes of CV patients.²² In a recent review Arcopinto *et al.*¹⁹ highlighted the involvement of sex-specific factors, such as role of oestrogens and pregnancy-related cardiomyopathies, in the incidence of different HF patterns, with women affected more frequently by HF with preserved ejection fraction and higher number of comorbidities. Instead, male individuals showed a predisposition of developing HF with reduced ejection fraction (HFrEF), due to a higher incidence of coronary artery disease and MI. In this regard, the large under-representation of women in clinical trials leads to an incomplete characterisation, and thus knowledge, of a large group of patients. This clinical scenario is further tangled by the presence of gendered socioeconomic and cultural differences between men and women that transcend the mere biological sex.

Specifically, lower rates of women in comparison with men (18.9% vs. 28.6%) have been reported in CR participation, with a decrease as age increases.¹¹ Due to the greater burden of CV risk factors and the higher mortality rate,²⁴ it has been suggested that theoretically women would benefit the most from secondary prevention through CR; yet, they are still less likely to receive a proper CR referral, with a significant impact on their health status. With this regard, among 48 993 patients of the American Heart Association Get with The Guidelines Coronary Artery Disease

Table 1 European Society of Cardiology (ESC) and American College of Cardiology/American Heart Association (ACC/AHA) recommendations for cardiac rehabilitation in cardiovascular diseases

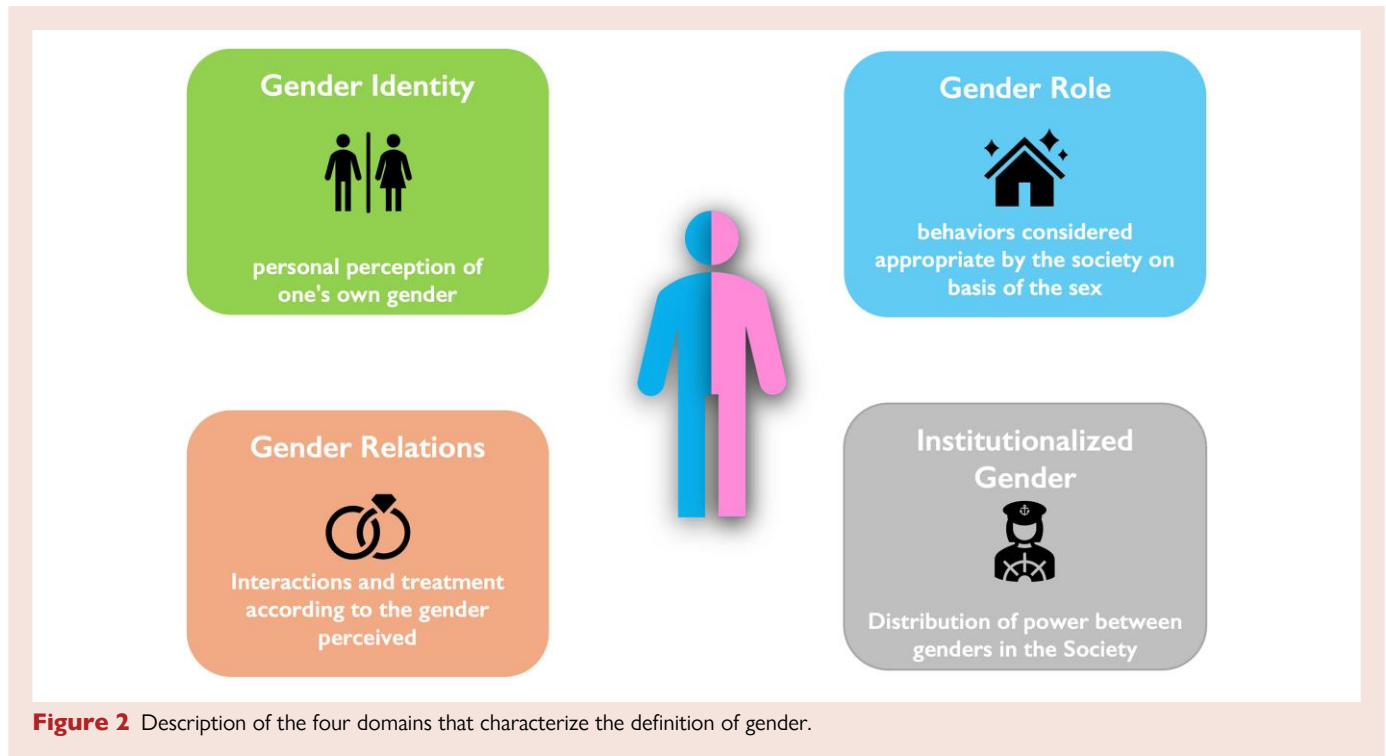
	ESC guidelines	ACC/AHA guidelines	Notes
Heart failure	IA (2021)	IA (2022)	
Acute coronary syndromes			
Persistent ST-segment elevation	IA (2023)	IB*(2014)	*Either Before Hospital discharge or during first outpatient visit
Unstable angina	IA (2023)	IB* (2014)	°Exercise-based cardiac rehabilitation/secondary prevention programmes are recommended for patients with STEMI (Level of Evidence: B)
Patients with ST-segment elevation	IA (2023)	IB° (2013)	
Chronic coronary syndromes	IA (2019)	I [§] (2023)	§All patients with chronic coronary disease and appropriate indications should be referred to a cardiac rehabilitation programme to improve outcomes. Level of evidence (LOE) A: After recent MI, percutaneous coronary intervention, or CABG; LOE B-R: With stable angina or after heart transplant; LOE C-LD: after recent spontaneous coronary artery dissection event
Myocardial revascularization:			
Coronary artery bypass graft surgery (CABG)	IA (2018)	IA [§] (2021)	§Either before hospital discharge or during first outpatient visit
Percutaneous coronary intervention	IA (2018)	IA [§] (2021)	
Aortic disease		IC [£] (2022)	£For patients who have undergone surgery for aortic aneurysm or dissection, post-operative cardiac rehabilitation is recommended
Peripheral arterial disease	IA (2017) [^]	IA (2016)	[^] For supervised exercise training in patients with intermittent claudication. I C for unsupervised exercise training when supervised exercise training is not feasible or available. IIa C when daily life activities are compromised despite exercise therapy, revascularization should be considered. IIa B when daily life activities are severely compromised, revascularization should be considered in association with exercise therapy
Pulmonary hypertension	IA (2022) ^{''}		^{''} Supervised exercise training is recommended in class IA for patients with PAH under medical therapy

registry, Li et al.¹⁵ found that women were 12% less likely to be referred to CR than men, even though the CR referral was associated with a reduction of 40% in 3-years all-cause mortality, and women with a CR referral at hospital discharge showed a lower mortality when compared with those who did not. It is not known whether the reduced participation in CR depended on a lack of physician referral or whether, after the CR prescription, patients decided not to participate. Despite a slight increase in CR referral rate overtime, this positive trend involved men more than women as depicted in a study among Medicare beneficiaries with HF rEF from the 2014 to 2016.¹⁶ In fact, among 11 696 hospitalized HF patients, only 4.3% participated in CR within 6 months of HF hospitalisation, with lower participation in women vs. men (3.3% vs. 5%; $P < 0.001$). The same picture was obtained for outpatients with HF: among 11 832 patients with outpatient encounters for primary HF diagnosis without a hospitalization event, only 2.2% participated in CR within 6 months of the outpatient encounter.¹⁶ Samayoa et al.²⁵ showed that <40% of women with acute coronary syndrome (i.e. MI or unstable angina), chronic stable angina, stable chronic HF, or undergoing PCI, CABG surgery, cardiac valve surgery, cardiac transplantation, or cardiac resynchronization therapy eligible for CR were enrolled, highlighting a 36% lower enrolment rate in women compared with men. In a meta-analysis, Colella et al.²⁶ showed that CR referral rates for women were 39.6% on average compared to 49.4% for men. Colbert et al.²⁷ in a recent study demonstrated that, in a cohort of 25 958 patients with coronary artery disease, 6374 were women and there was a lower rate for females than males of CR referral (31.1% vs. 42.2%) and completion (50.1% vs. 60.4%). The survival was greater among patients who attended CR compared to those who were referred but did not

participate; moreover, women not referred to CR exhibited the highest mortality of all subjects and a higher mortality when compared with men not referred.²⁷ In fact, women referred to CR, even if they did not attend, showed a significantly improved survival when compared to those not referred and even more whether they completed the programme; likewise, men exhibited survival benefits derived from referral and even more so from participation in CR. However, the relative survival benefit derived from the completion of CR was larger in women than in men.²⁷ Therefore, the benefits from CR are known among women, but difficulties related to transportation and family responsibilities often may affect their participation in CR programme. A recent retrospective study from the United States on patients enrolled in intensive-cardiac-rehabilitation (ICR) from January 2016 to December 2020 stressed the importance of not exercise-related components of CR in order to reduce the barriers in participation and the gap between sexes.²⁸ Among 15 613 patients the rates of participation in ICR were about 44% for women ($n = 6788$) and 56% for men ($n = 8825$), demonstrating a lower women-disparity than in previous studies.²⁸ Furthermore, the difference in ICR completion was lessened with an exhibited rate of 63.3% for women and 65.9% for men.²⁸ The adherence to CR shows sex differences: men and women enrolled in CR adhered to 68.6% and 64.2% of prescribed sessions, respectively.²⁹ (Table 2).

Gender issues in cardiac rehabilitation

The drivers of the abovementioned sex disparities in CR utilization might be influenced by the socio-economic, psychological, and cultural



differences, which are part of the 'gender' concept.^{31,32} Specifically, barriers for accessing CR have been reported to be strongly dependent by both individual and structural levels.² Although there are still no specific studies directed towards understanding the impact of various gender domains on CR, the application of a gender-based framework to understand obstacles and challenges of CR among patients eligible for it can be very informative.

Gender identity and sexual orientation

Among the concept of gender identity, a vast spectrum of self-perception exists (girls, women, boys, men, and gender diverse people). With the term 'transgender' it is defined a person who does not identify with the sex assigned at the birth in contrast to 'cisgender', in which sex and gender match. According to the minority stress theory, the transgenders represent a minority of population characterized by disparities in the access to healthcare system, due to social barriers, namely gender non-affirmation (e.g. being called by incorrect pronoun or name), stigma, discrimination, rejection, hypervigilance, concealment, and victimization that influence negatively their mental and physical health.³³ In the report of the 2015 U.S. transgender survey³⁴ came to light numerous difficulties for transgender people in terms of adequate access to health care due to economic up to social aspects. In fact, the insurance coverage was often denied due to being transgender or because of care related to gender transition. A higher rate of poverty and unemployment was frequent among this population and one-third of them showed in the previous year at least a negative experience related to the gender identity in terms of verbal harassment or treatment refused. 23% of them rejected to see a doctor due to the fear of mistreatment for being transgender. Moreover, a great number of transgender people wanted counselling at certain point of the life, and discrimination and marginalization contribute to the psychological distress that could result in a high rate of suicide attempts. Alzahrani *et al.*³⁵ depicted that men who are transgender had a significant higher prevalence of MI compared to cisgender women and cisgender men; conversely women who are transgender showed a significant higher prevalence of MI compared

with cisgender women but not when compared with cisgender men.³⁵ In a recent review Connelly *et al.*³⁶ collected some retrospective studies carried on adult transgenders to investigate the CV effects of hormonal therapy. The authors underlined that, in contrast with current evidence, there were discrepant results regarding the relationship between the use of oestrogens by transgender females (TGFs) that are individuals assigned to male sex who identify themselves as female, and an increased risk of MI and ischaemic stroke. Furthermore, studies on transgenders are limited and contradictory and often it remains unclear if CV morbidity and mortality are only ascribable to the hormonal therapy or if there is a component related to the natal sex. In addition, the results are subordinated to the rate of traditional CV risk factors, unhealthy behaviours and additional risk factors (i.e. HIV infection) in this population.

Gender roles

For female caregivers, familial and household responsibilities represent an influential obstacle to CR.³¹ More frequently women put forward familial responsibilities as obstacles for CR, having difficulties to make time for their prevention. Moreover, sometimes, women consider exercise training as an inappropriate behaviour for a lady.^{37,38} Additionally, because of logistic problems such as dependence on others for transportation and, differently from men, less encouragement from the spouse, women's attendance at CR decreases.³⁷ To this extent, it would be appropriate for health care authorities to be made aware and alerted to these disparities so that appropriate corrective measures may be placed.

Gender relations

In a meta-analysis, it has been demonstrated that being married/partnered is associated with a significant higher attendance at CR in patients with coronary heart disease.³⁹ Among these patients, those married or with a partner were 1.5–2 times more likely to attend at outpatient CR. Among patients referred to CR after acute MI the baseline

Table 2 Main studies highlighting the under-representation of women in cardiovascular rehabilitation programmes

Study	Main results
Ritchey MD, 2020. ¹¹ Observational study. 366.103 CR-eligible beneficiaries	89 327 (24.4%) participated in CR, of whom 24.3% initiated within 21 days of event and 26.9% completed CR. Participation: women (18.9%) vs. men (28.6%)
Samayoa L, 2014. ²⁵ Systematic review and meta-analysis of 26 eligible observational studies. 297 719 participants (128 499 [43.2%] women)	45.0% of men and 38.5% of women enrolled in CR. Women 36% less likely to be enrolled in a rehabilitation programme
Colella TJ, 2015. ²⁶ Meta-analysis of 19 observational studies. 241 613 participants (80 505 [33.3%] women)	In the pooled analysis (39.6%) significantly less likely to be referred to CR compared to men (49.4%)
Colbert JD, 2015. ²⁷ Retrospective cohort study. 25 958 subjects (6374 [24.6%] women) with at least one vessel CAD.	Among females reduced rates of CR referral (31.1% vs. 42.2%) and completion (50.1% vs. 60.4%). Women completing CR experienced the greatest reduction in mortality with a relative benefit greater than men.
Hussain Jafri SH, 2023. ²⁸ Retrospective cohort study. 15 613 patients (6788 [44%] women) enrolled in 46 Ornish-intensive cardiac rehabilitation (ICR) programmes	ICR completion rates were 64.7% overall and nearly equal between men and women (63.3% women vs. 65.9% men)
Oosenbrug E, 2016. ²⁹ Meta-analysis including 14 studies. 8176 participants (2234 [27.3%] women).	Cr adherence ranged from 36.7% to 84.6% of sessions, with a mean 66.5 ± 18.2% (median, 72.5%). Men and women enrolled in CR adhered to 68.6% and 64.2% prescribed sessions, respectively.
Ghisi GLM, 2023. ³⁰ Cross-sectional study. 2163 patients (916 [42.8%] women) from 16 countries across all 6 WHO regions.	1239/57.8%) patients referred to CR. Differences in referral rate to CR according to sex: 368 women (40.4% of the female group) vs. 866 men (71.0% of the male group). 571 (27.8%) patients participated in CR. Differences in participation rate in CR according to sex: 284 women (34.1% of the female group) vs. 283 men (23.5% of the male group).

characteristics of non-participants compared with participants were more likely to be elderly, female, and with more CV risk factors and comorbidities.^{40–42} One hypothetical intervention that could be implemented would be to provide psychotherapeutic-relational support, especially for those individuals whose CV risk is remarkably high.

Institutionalized gender

Unemployed and less educated people and those with lower income had a lower participation.⁴¹ In the literature, there are several qualitative studies on women's barriers to CR and on sex differences in relation to these obstacles, but only few quantitative studies. Three quantitative studies on sex differences in CR barriers used a validated scale, the cardiac rehabilitation barrier scale (CRBS).⁴³ One of them, carried on patients of a high-income and very gender-equal Canadian country, showed no sex differences in total number of CR barriers, but a diverse nature of barriers according to sex.⁴⁴ Conversely, another study, conducted on patients of middle-income and gender-unequal Iranian country, exhibited significantly greater overall barriers among women and in addition to the sex differences of the former study showed some differences related to the socioeconomic status (i.e. cost, transportation, and distance).⁴⁵ Ghisi et al.³⁰ in a landmark cross-sectional study carried on 2163 patients, of which 916 were women (42.8%), from 16 countries across six WHO regions from October 2021 to March 2023, had shown that women's barriers to CR were greatest in the Western Pacific and South East Asian regions and, in both cases, had individuated the lack of CR awareness as major responsible. The CRBS was used to assess the barriers perceived by patients to CR enrolment and adherence.³⁰ Furthermore, women's unemployment increased barriers to CR. On one hand, among non-enrolled referred women, obstacles were lack of awareness of CR, absence of contact by the programme, cost, and the belief that exercise would be tiring or painful. On the other hand, enrolled women identified as

greatest barriers to adherence the distance, transportation, and family responsibilities.³⁰

Summarizing, some of the most frequent issues reported by patients in relation to reduced CR attendance are anxiety to exercise, overburden due to medical appointments, barriers in the interaction with CR staff, lack of awareness or skepticism about the resulting benefits, logistical problems due to distance from the hospital, costs, transportation/parking, employment, and social and familial responsibilities^{31,46} (Figure 3). The lack of CR referral and the hesitation of women due to emotional, relational, economic, cultural, and logistical barriers contribute to a lower level of participation or adherence to CR.^{46,47} Several studies had examined the principal barriers that women mentioned for non-attendance at CR. Some of these are related to personal issues (e.g. insufficient time, lack of motivation, religious conflicts, economic, and logistical difficulties), whereas others are associated with interpersonal aspects, linked to inadequacy in social and familial support—which correlates with the domain of gender relations and employment—correlated with the domain of institutionalized gender.⁴⁸ In a secondary meta-synthesis, Angus et al.³⁷ observed that gender issues and socioeconomic status are involved in sex disparities when accessing rehabilitation. More precisely, on the one hand difficulties related to employment duties and transportation, especially if there is a lack of financial resources, are more frequently mentioned by men as a cause of non-attendance. On the other hand, women advocate more frequently domestic, familial, and economic responsibilities; in addition, even in the case of no enrolment fees, women have to make time for their prevention, paying for a housekeeper or family caregiver.³⁷ In a recent systematic review, Galati et al.⁴⁹ underlined that women who do not complete the CR programme were significantly younger, affected by more risk factors, and with greater rate of anxiety and depression in comparison with women who complete CR. Lastly, physicians play a crucial role in addressing candidate patients to rehabilitation, yet often they are perceived as barriers to referral.⁵⁰



Figure 3 Some of the gender issues on the attendance at cardiac rehabilitation. Access to CR can become cumbersome in the presence of several superposed gender-related issues which result in a burden too great to be carried, ultimately leading to drop out of this secondary prevention.

How to assess the gender?

The lack of a standardized measure of gender might be an obstacle for the integration of sex and gender in research and clinical practice. Several operational frameworks for integrating gender in clinical studies have been published.^{20,51–53}

Based on the recently published guidelines in CV research, efforts should be made to prospectively collect gender-related variables as pertinent to their research hypothesis/questions and explore retrospectively available datasets using the GOING-FWD methodology.⁵⁴

The gender working group of the Italian Society of Internal Medicine (SIMI), funded in 2019, have conceptualized based on the evidence available^{51,52} a list of variables that should be collected through questionnaire that capture gender domains in the clinical studies.⁵³ Specifically, the gender core dataset consists of data regarding personality traits (gender identity), occupation, caregiver status, household responsibilities, condition of primary earner (gender roles), marital status, social support and discrimination (gender relations), and educational level, personal income and living area (institutionalized gender).

Possible tools to enhance inclusivity in cardiac rehabilitation

Several solutions might be available to fill the gap of lower rates in CR participation; however, first it would be beneficial to increase physicians' awareness of the essential benefits related to this strategy of prevention.^{10,12} Moreover, it would help to invest substantial resources in the healthcare system to ensure high-quality and high-capacity rehabilitation centres.^{10,12} Improvements in counselling and social support may be necessary for major attendance to therapy.

Regarding specific sex and gender-issues that limit participation to CR, a more tailored programmes based on women attitude and needing, that may lead to an increase in CR participation, and correct the modifiable barriers, through flexibility of timetable (with both morning and afternoon sessions) and strategy to manage stress might be helpful.⁴⁹ Another important issue would be to promote the knowledge, between the physicians, of the four main domains (e.g. gender identity,

gender roles, gender relations, and institutionalized gender) in line with the statement recently made by a panel of experts on an open-access CR education resources to support women in CV prevention through their participation in CR.⁵⁵ As a benchmark of possible strategies, the million hearts initiative strive to prevent up to one million CV events through CR.⁵⁶ Especially for women, with the aim of overcoming logistic problems, such as those related to transportation or the impossibility of leaving their houses, home-based programmes controlled by rehabilitation staff through telemedicine have been proposed and developed.⁵⁷ The flexibility of this strategy allows physicians to follow the patient's progresses in a partially or completely remote way, thereby facilitating their adherence through individual management regarding location and time. Likewise, smartphone-based CR used to monitor digitally the improvements in exercise capacity, symptomatology and changes in lifestyle is a promising tool to be considered, leading to a possible additional improvement in communication between patients and CR staff.^{57–59} A recent meta-analysis, collecting studies carried on patients with coronary heart disease, acute coronary syndrome who underwent cardiac revascularization procedures, or valvular replacement surgery, showed a favourable adherence to CR through digitalization instead of traditional programmes.⁶⁰ The support by the healthcare system is another aspect that might help. In fact, the reduction of the costs related to rehabilitation positively encourages participation in the programme. Another specific aspect is the need for searching neuropsychiatric disorders (i.e. depression and anxiety) that may hardly limit the women participation to CR programmes; in addition, the inclusion in CR programmes of exercises to manage stress or anxiety (e.g. yoga techniques and mindfulness) demonstrated to increase the CR attendance.⁶¹ Another possible solution may be to identify CR strategies more pleasant for women; for instance, it has been described that exercise programmes based on dance classes and with a high level of aggregation are usually appreciated by women.⁴⁹

Finally, an international panel of experts published a women focused CV rehabilitation clinical practice guideline, aimed to better engage women in CR programmes and to provide guidance on how to deliver women-focused CR programme. As a result, 15 final recommendations for women-focused CR have been proposed, relate to CR referral,

Table 3 Specific obstacles to perform research on barriers due to sex and gender in cardiovascular research

Obstacle type	Specific obstacles	Reference
Biological (sex-specific) obstacles	<ul style="list-style-type: none"> • Atypical symptom presentation in women • Higher prevalence of comorbidities such as osteoporosis autoimmune diseases and arthritis in women 	Ades et al., ⁵⁶ Joseph et al., ⁶⁴ Angum et al., ⁶⁵ and Sanderson and Bittner ⁶⁶
Socio-cultural (gender-specific) obstacles	<ul style="list-style-type: none"> • Greater caregiving responsibilities among women • Reduced social support for physical activity among women • Lower awareness of CR benefits and underestimation of heart disease risk among women • Lower incomes, less health insurance coverage, and greater difficulty accessing healthcare services among women 	Daponte-Codina et al. ⁶⁷ and Daher et al. ⁶⁸

setting, and delivery. Notably, of these recommendations, only two have a 'high' certainty of the evidence based on the grading of recommendations assessment, development, and evaluation criteria and 10 have been suggested with a strong level of recommendation,⁶² further supporting the need for sex and gender specific investigations.

Gaps in evidence

A profound gap in knowledge about the development of CR dynamics in the last decade still exists. For instance, in Italy, the more recent survey about the cardiac prevention and rehabilitation programmes dates to 2013.¹³ Here, it was highlighted that the total number of CR facilities amounted to 221 (1 for every 270 000 inhabitants), with 31.7% of programme response rate and at least 280 771 patients with an unmet need.^{12,23} Considering the broadening of the spectrum of CV disease for which CR has been now recommended in the most recent updates by the European Guidelines,¹⁰ the pool of potential patients has been extended, further widening the gap between supply and demand. Several issues are worth to be acknowledged regarding the difficulties to understand the gender related obstacles in ensuring gender equality and inclusivity in CV rehabilitation. Among sex-related differences, presentation of cardiac disease and comorbidities pose challenges specific to each sex. Women often exhibit atypical symptoms and are more likely to suffer from conditions like auto-immune diseases, osteoporosis and arthritis, which can complicate their participation in CR programmes.^{63–65} On the other hand, current society do not allow women to take care of their health properly. It is a matter of fact that women commonly face greater barriers due to caregiving responsibilities, reduced social support for physical activity, and different health beliefs. Women are often less aware of the benefits of CR and underestimate their heart disease risk.^{66,67} Socioeconomic factors further impact, considering that women are more likely to have lower incomes, less health insurance coverage, and greater difficulty accessing healthcare services.⁶⁸ Higher prevalence of depression and anxiety among women can hinder their participation in CR.³⁰ Addressing these obstacles require tailored interventions that consider both biological and socio-cultural dimensions to improve CR utilization and outcomes for women (see Table 3).

Finally, there are no specific analyses regarding the proper role of sex and gender and no definite strategies to increase women adherence to CR programme.

Conclusions

Despite its role as prevention tool to improve clinical outcomes of patients affected by CV diseases, to date CR is still underused, particularly by women. The identification of patients' obstacles to attend CR

related to sex and gender differences has a non-neglectable impact. In fact, every subject should be considered beyond the biological sex in agreement with the four gender domains, to craft tailored therapies.

Every patient identifies his/her own gender, while the society considers and interacts with him/her on basis of the sex. Furthermore, the institutionalized gender might represent the distribution of power between genders in the political, educational, religious, medical, cultural, and social institutions. All that should be considered in the management of the individual to improve clinical outcomes. According to CR, possible tools to optimize patients' participation are represented by increased referral rate related to physicians' awareness of the essential benefits of CR, strengthening in healthcare system facilities' information after hospital discharge, tailored rehabilitation programmes, and the use of telemedicine and tel-monitoring to allow a stricter connection between CR staff and patient and to contrast socio-economic problems or familial and logistic obstacles. International scientific societies and ministerial governance should be involved in this process to reduce sex and gender inequality in CR attendance.

Lead author biography



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Data availability

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