

## Cardiovascular health in women: a consensus document of the Italian Cardiovascular Societies

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Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality among women, yet sex-specific and gender-specific differences in disease pathophysiology, clinical presentation, and treatment response are often underappreciated. This article presents the findings of a multidisciplinary expert consensus involving 59 specialists from cardiovascular and affine scientific societies. Experts were divided into 11 working groups, each focusing on distinct aspects of cardiovascular risk, prevention, diagnosis, and treatment in women. Utilizing a Delphi-like method, 71 key statements were developed, refined, and evaluated to establish a consensus on best practices for addressing sex-specific and gender-specific disparities in cardiovascular care. The findings underscore critical gaps in current guidelines, particularly regarding hormonal influences, pharmacological responses, and environmental and socioeconomic determinants of cardiovascular risk in women. The consensus highlights the need for improved screening strategies, individualized risk assessment models incorporating female-specific factors, and increased representation of women in cardiovascular research. Telemedicine and digital health tools offer promising solutions for bridging existing disparities. The study

reinforces the necessity for a paradigm shift in cardiovascular medicine, advocating for gender-sensitive policies and clinical guidelines. Future research should focus on integrating gender-specific considerations into all facets of cardiovascular care to optimize outcomes for women.

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## Introduction

Cardiovascular diseases (CVDs), particularly coronary artery disease (CAD), are the leading cause of death and disability for both men and women worldwide. However, the prevalence and the mortality rate of CAD vary among countries and the major impact affects low- and middle-income countries.<sup>1,2</sup> At present, sex and gender are considered as health determinants,<sup>3</sup> strictly linked to the precision medicine approach.<sup>4,5</sup>

Despite remarkable advances in cardiovascular medicine, sex-specific and gender-specific determinants of cardiovascular health remain underrecognized and insufficiently integrated into clinical research, guideline development, and daily practice. Biological factors, such as hormonal status, body composition, vascular physiology, and pharmacokinetics, interact with gender-related aspects, including lifestyle behaviors, psychosocial stress, socioeconomic status, and access to healthcare, resulting in distinct risk profiles, clinical presentations, and outcomes between women and men.<sup>6–13</sup>

In Italy, the prevalence of CVDs among women has shown a progressive increase over recent decades, in contrast to the declining trends observed in other Western European countries. This growing burden underscores the need for effective prevention, early recognition, and equitable management strategies specifically tailored to female patients.<sup>2</sup>

Although numerous scientific societies have promoted initiatives in gender cardiology, awareness of cardiovascular risk among women and even among healthcare professionals remains insufficient. Underrepresentation of women in clinical trials and guideline development

continues to limit the applicability of evidence-based recommendations to the female population.<sup>14–18</sup>

Gender disparities have a great impact on CV health in women; in fact, for female sex/gender people, stopping smoking, having healthy diet regimes, practicing regular physical activity and living in a supportive psychosocial environment are frequently influenced by their lower income and education levels, their role in family and society, and the abovementioned social issues.<sup>19–25</sup>

In response to these unmet needs, the Italian Cardiological and affiliated Scientific Societies, with the institutional support of the Istituto Superiore di Sanità (ISS), have collaborated to develop the present Consensus Document on cardiovascular health in women. Through a structured, multidisciplinary, and Delphi-like methodology, this work aims to provide a comprehensive framework for the prevention, diagnosis, and treatment of cardiovascular diseases in women, promoting the systematic incorporation of sex-specific and gender-specific considerations into clinical practice, research, and health policy.

## Method

The present work is part of an inter-society effort that aims to highlight the knowledge of the peculiarities of CVDs in women, their prevention, and treatment.

## Participants

The study was conducted as a collaborative effort involving multiple scientific societies, gathering a panel of 59 experts. This panel included 14 members of the Scientific Board, who provided oversight and strategic direction for

the initiative; the remaining 45 members were split into 11 specialized working groups, each dedicated to specific topics and subtopics relevant to women's cardiovascular health. Their diverse expertise allowed a comprehensive exploration of the multifaceted aspects of CVDs in women. For a detailed breakdown of the group composition, please refer to Fig. 1, which illustrates the distribution of members across the working groups, and Table 1, which provides an overview of the key topics addressed by each group.

### Delphi-like method

The consensus was developed through a Delphi-like methodology designed to ensure structured expert evaluation and iterative feedback. A total of 59 experts were invited to participate in the process, and 53 contributed to the final voting phase. The number of respondents for each statement is reported in the corresponding table. The procedure consisted of a structured discussion of each statement, potential reformulation based on collective feedback, and subsequent voting. Statements achieving a mean score below 4 on a 1–5 Likert scale were considered not approved and were re-discussed and revoted (voting options are detailed in Table 2 and Figure S1 in Supplementary Material, <http://links.lww.com/JCM/A768>). If, after the second round, the mean score remained below 4, the statement was regarded as definitively not approved.<sup>26–28</sup> This method facilitated interactive discussion and refinement of statements, resulting in a unified proposal that was then

subjected to anonymous voting to prevent bias from interpersonal influence.

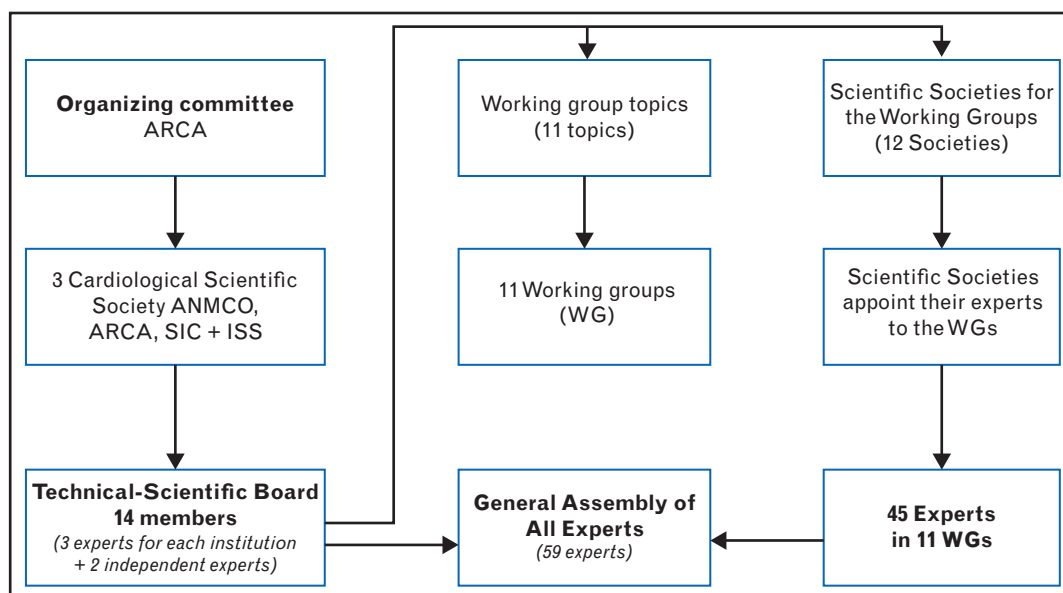
### Results

Fifty-three out of 59 (89.83%) Key Opinion Leaders agreed with the 71 statements reported online in detail. Tables 3–6 show the statements, divided into four subject areas; in each of the four tables, the topics of the Working Groups corresponding to the first 10 of those shown in Table 2 are indicated. The four subject areas are Prevention, Clinical, Therapy, and Telemedicine (Figure S1 – Supplementary Materials, <http://links.lww.com/JCM/A768>).

### Traditional risk factors, peculiar to the female sex

As reported in detail in Table 3, among the traditional and well known risk factors, hypertension has the highest prevalence, and it is more prevalent in postmenopausal women and significantly contributes to cardiovascular risk. Women have greater salt sensitivity, which exacerbates hypertension, necessitating dietary sodium restrictions.<sup>29,30</sup> Although antihypertensive treatments are similarly effective in men and women, adherence issues and a higher incidence of side effects in women require personalized treatment approaches.<sup>31</sup> Moreover, although diabetes prevalence is higher in men, women experience more severe complications, including an elevated risk of heart failure and depression-related cardiovascular risks.<sup>32,33</sup> Women with diabetes also exhibit higher platelet reactivity and inflammation, leading to increased atherosclerotic

Fig. 1



Structure and expert formation process for the Consensus Document. ANMCO, Associazione Nazionale Medici Cardiologi Ospedalieri; ARCA, Associazioni Regionali Cardiologi Ambulatoriali; ISS, Istituto Superiore di Sanità; SIC, Società Italiana di Cardiologia.

**Table 1** Working group topics

Number	Topics	Number of members
1	Traditional risk factors, peculiar to the female sex/gender	6
2	Nontraditional, nonsex/gender-specific risk factors	5
3	Nontraditional risk factors, peculiar to the female sex/gender	6
4	Chronic heart failure	5
5	Arrhythmias	3
6	Acute ischemic heart disease	4
7	Chronic ischemic cardiopathy	4
8	Principles of pharmacology and approach to therapy in women	4
9	Hormone replacement therapy and hormone therapy	5
10	Telemedicine in women's cardiovascular health	2
11	Evaluation of CVR in women	2

CVR, cardiovascular rehabilitation.

**Table 2** Selectable answers

Consensus measurement (five-point Likert measurement scale)	
1	Strongly disagree
2	Disagree
3	Neither agree nor disagree
4	Agree
5	Strongly agree

burden.<sup>34</sup> Lifestyle interventions and pharmacologic management tailored to women's metabolic profiles are critical for improving cardiovascular outcomes in diabetic women.

Moreover, women smokers have an increased risk of myocardial infarction (MI) compared with men due to hormonal interactions with tobacco-related toxins.<sup>35</sup> Passive smoking also elevates cardiovascular risk, particularly in pregnant women, leading to adverse maternal and fetal

**Table 3** Statements of working groups 1–3: prevention area

Statements about the prevention area	N	Mean	SD	Min	Median	Max
Traditional risk factors, peculiar to the female sex/gender (working group 1)						
1. In women, white-coat hypertension prevalence is higher and masked hypertension is lower.	53	4.21	0.69	2	4	5
2. The risk of cardiovascular events is significantly increased at blood pressure values lower than in men.	53	4.13	0.71	2	4	5
3. The risk of cardiovascular events is more strictly associated with night-time blood pressure values in women than men.	52	4.15	0.72	2	4	5
4. Salt sensitivity is higher in women and a low salt diet may reduce blood pressure to a greater extent in women than in men. Conversely, aerobic structured exercise reduces blood pressure to a greater extent in men than in women.	53	4.17	0.70	2	4	5
5. Renin–angiotensin–aldosterone system blockers are contraindicated in potentially childbearing women and during pregnancy.	53	4.72	0.66	1	5	5
6. In women, complaints of drug side effects are higher and adherence to antihypertensive drugs is worse in women.	53	4.38	0.71	3	5	5
7. Statin treatment is recommended for primary and secondary atherosclerotic cardiovascular prevention in women at high cardiovascular risk.	52	4.52	0.67	2	5	5
8. Lipid-lowering treatment should not be prescribed to potentially childbearing women during pregnancy and lactation.	53	4.42	0.75	2	5	5
9. Among young women with familial hypercholesterolemia, bile acid sequestrants (which are not absorbed) and/or LDL apheresis may be considered during pregnancy.	53	4.34	0.62	3	4	5
10. Women are slightly more likely (40%) than men (35%) to develop obesity which, in turn, affects several important features of women's health.	53	4.30	0.61	3	4	5
11. Pregnancy is more troublesome in obese women, which may present gestational diabetes, hypertension, and preeclampsia.	53	4.64	0.48	4	5	5
12. Women smokers have an even greater risk of developing coronary heart disease compared to men.	52	4.44	0.64	3	5	5
13. Women exposed to passive smoking have an increased risk of coronary heart disease.	53	4.23	0.78	2	4	5
14. Pregnant women exposed to passive smoking risk complications such as low birth weight and preterm birth, which increase cardiovascular risk for both the woman and the newborn.	53	4.32	0.61	3	4	5
15. Prevalence of diabetes is higher in male individuals, but in female individuals, complications of type 2 diabetes are more severe.	53	4.28	0.60	3	4	5
16. SGLT-2 inhibitors have shown similar effectiveness and cardiovascular protection in men and women. Urinary tract Infections complications are more common in women. The effect of GLP-1 receptor agonists on weight loss is greater in women.	53	4.25	0.83	1	4	5

Table 3 (continued)

Statements about the prevention area	N	Mean	SD	Min	Median	Max
Non-traditional, non-sex/gender-specific risk factors (working group 2)						
17. Socioeconomic status and ethnicity significantly influence cardiovascular risk in women, leading to disparities in disease prevalence, management, and outcomes, with those from lower socioeconomic backgrounds and ethnic minorities facing a disproportionately higher burden due to limited healthcare access, unhealthy lifestyles, and systemic discrimination.	53	4.42	0.57	3	4	5
18. Air pollution, especially indoor air pollution and particularly fine particulate matter (PM 2.5), significantly increases the risk of cardiovascular disease (CVD) in women, with studies showing a stronger link between long-term exposure and ischemic heart disease in women compared to men.	53	4.17	0.73	2	4	5
19. Migraine may be associated with an increased risk of major cardiovascular events, in particular, ischemic stroke; this association may be more evident for migraine with aura and is stronger in women than in men, particularly if under 45 years of age.	53	4.19	0.62	3	4	5
20. Autoimmune diseases have a higher prevalence and incidence in women than in men. To note, chronic autoimmune diseases are associated with a wide array of cardiac manifestations including valvular heart disease, atherosclerotic cardiovascular disease, heart failure, pericardial disease, and arrhythmias.	53	4.51	0.50	4	5	5
21. Substance abuse is high and often underdiagnosed and undertreated in women and may be frequently associated with cardiovascular risk conditions; therefore, gender-specific intervention strategies are needed.	53	4.17	0.64	3	4	5
22. CVD and mental health disorders (MHD) are, respectively, the first and second most prevalent diseases in high-income countries and the two most relevant causes of disability in the world, especially in women. The excess of cardiovascular disease-related mortality in women with MHD is multifactorial. Addressing mental health, particularly depression, in women is crucial for reducing the risk of cardiovascular disease.	53	4.36	0.52	3	4	5
23. Chronic stress significantly increases cardiovascular risk in women by contributing to hypertension, inflammation, and unhealthy behaviors, such as poor diet and physical inactivity. Women often experience stress differently from men, leading to higher susceptibility to stress-related cardiovascular diseases like heart attacks and strokes.	53	4.38	0.53	3	4	5
24. Experiencing sexual violence and abuse significantly increases the risk of CVD in women. Chronic stress and trauma resulting from these experiences can lead to disruption and dysregulation of the neuro-endocrine system that promotes cardiovascular risk mechanisms; they also lead to unhealthy lifestyles and pathological addictions.	53	4.30	0.67	2	4	5
25. The antineoplastic treatments currently available, both pharmacological and radiotherapeutic, have demonstrated a wide range of early and late cardiovascular adverse effects, included in the definition of cardiovascular toxicity related to antineoplastic therapy (CTR-CVT). The prescription of lifestyle modifications (diet, physical exercise) should be part of an integrated approach to cardiovascular prevention in cancer patients undergoing chemotherapy and in patients at high and very high risk of CTR-CVT, specific pharmacological interventions should be initiated.	53	4.43	0.57	3	4	5
Non-traditional risk factors, peculiar to the female sex/gender (working group 3)						
26. Early menarche has been associated with a higher risk of future CVD independent of sociodemographic factors.	53	4.34	0.62	3	4	5
27. Polycystic ovary syndrome (PCOS) is associated with a higher risk of overall CVD including both coronary heart disease and stroke.	53	4.47	0.50	4	4	5
28. Hypertensive disorders of pregnancy, especially preeclampsia, gestational diabetes, preterm birth, and small-for-gestational-age infant status are associated with mothers' cardiovascular disease (myocardial infarction and ischemic stroke) later in life. Intrauterine growth restriction is associated with an increased risk for hyperlipidemia, hypertriglyceridemia, and insulin resistance, a higher prevalence of diastolic dysfunction, and less cardiac reserve compared with control subjects. Women with prior pregnancy loss (miscarriage and stillbirth) are at approximately two-fold increased risk of myocardial infarction, cerebral infarction, and renovascular hypertension. Miscarriage is also associated with a 1.45-fold increased risk of CVD, and more than 1 miscarriage was associated with a two-fold risk of CVD.	52	4.42	0.61	3	4	5
29. Menopause is a cardiovascular risk factor. Recognizing menopause as a specific cardiovascular risk factor is essential for the clinical management of postmenopausal women (PMW). Premature natural, iatrogenic, and surgical menopause as well as premature ovarian failure are associated with incident cardiovascular disease and stroke.	53	4.45	0.57	3	4	5
30. Vasomotor symptoms (VMS) could serve as biomarkers for increased CVD risk in PMW. Health professionals should monitor women with severe or persistent VMS more closely for cardiovascular risk factors and implement preventive strategies, such as lifestyle modifications and, where appropriate, hormonal or nonhormonal therapies.	53	4.23	0.58	3	4	5
31. The transgender population has a higher cardiovascular risk for reasons that have yet to be well defined; probably caused by hormonal therapies and partly by psycho-social factors.	53	4.23	0.61	3	4	5

I, number of votes; Max, maximum vote; Min, lowest vote; LDL, low-density lipoprotein; SD, standard deviation.

**Table 4** Statements of working groups 4–7: clinical area

Statements about clinical area	N	Mean	SD	Min	Median	Max
<b>Chronic heart failure (working group 4)</b>						
32. Numerous studies demonstrate that women with chronic heart failure (CHF) show better survival than men but they suffer from a worse quality of life. Anxiety and depression, prevailing among women, could be a cause of this difference, and an integrated plan of cure (according to multidisciplinary specialists and general physicians) is also needed to treat these comorbidities.	53	4.30	0.67	2	4	5
33. Women benefit from drug therapy in a sex-specific way, potentially due to different pharmacodynamic and pharmacokinetic properties, and in a sex-specific and gender-specific way due to socio-economic, cultural, and religious factors.	53	4.38	0.66	2	4	5
34. Women could be underrepresented both in pharmacological and nonpharmacological therapy trials; therefore, also in clinical practice there could be a gender bias regarding ICD/CRT/VAD implantation and transplants, in particular: sex difference in the access to transplants and prognosis after transplant need to be detailed; women seem to have less access to LVAD implantation, either as destination therapy and as a bridge to transplant; women could have higher mortality risk after LVAD implantation.	52	4.35	0.65	2	4	5
35. The treatment of peripartum cardiomyopathy depends on the period of observation of the ventricular dysfunction, established the pharmacological specifics for pregnancy, and the postdelivery/breastfeeding period.	52	4.23	0.67	2	4	5
36. Takotsubo syndrome (TTS) is more frequent in women in the postmenopausal period than in men, but it has a worse prognosis in men.	51	4.39	0.53	3	4	5
37. The causal factor of TTS is more often emotional in women and physical stress in men.	52	4.38	0.72	1	4	5
38. Epicardial or microvascular coronary spasm in association with endothelial dysfunction may also contribute to TTS. This could explain the higher incidence in postmenopausal women, in whom endothelial dysfunction seems to be more prevalent.	53	4.32	0.61	3	4	5
<b>Arrhythmias (working group 5)</b>						
39. Fluctuations in estrogen and progesterone levels, blood volume, and blood pressure can affect electrophysiological stability leading to an increased incidence of arrhythmias in different conditions such as different times of the menstrual cycle, pregnancy and pregnancy diseases, perimenopause, and menopause.	53	4.25	0.59	3	4	5
40. Women are more likely to be affected by A-V node reentrant tachycardia (AVNRT) than men; a relationship with the monthly cycle has been suggested, and episodes are more frequent during pregnancy in women with preexisting SVT. The converse is true for AVRT, accessory pathways, atrial fibrillation (AF), and atrial flutter, which are more frequent in men.	53	4.11	0.64	3	4	5
41. Female sex is currently recognized as a 'thromboembolic risk factor modifier', because it independently increases the risk of stroke in AF, particularly in older women, when other risk factors are present.	53	4.23	0.82	1	4	5
42. Inherited Long QT syndrome (LQTS) is more prevalent in women, with major age-dependent gender differences regarding the risk of Torsade de Pointes (TdP). Before puberty, arrhythmic risk is higher in males, but after puberty, there is gender risk reversal, and females become at a three-fold higher risk of TdP. The role of sex hormones, particularly that of testosterone in males, has been invoked to explain the sex/age-related behavior of repolarization and the gender differences in propensity towards the risk of TdP in both congenital and acquired LQTS.	53	4.26	0.56	3	4	5
43. Differences in pharmacokinetics and pharmacodynamics may lead to variations in the efficacy and safety profile of antiarrhythmic drugs between genders. Women are generally more susceptible to the side effects of antiarrhythmic drugs.	53	4.36	0.56	3	4	5
<b>Acute ischaemic heart disease (working group 6)</b>						
44. In acute recognition and management of chest pain syndromes in women, it is necessary to define a chest-pain assessment protocol, addressing (a) symptoms, (b) EKG, (c) female-specific, traditional, and female predominant risk factors, (d) sex-specific thresholds for high-sensitivity cardiac troponin (hs-cTn); (e) risk stratification of acute coronary syndromes (ACS) in women and unique aspects of the pathophysiological spectrum of ACS in women.	53	4.42	0.60	3	4	5
45. Pregnancy and the postpartum period present a unique challenge in the definition of acute chest pain: the differential diagnoses include asthma, valvular heart disease, pulmonary edema, peripartum cardiomyopathy, aortic dissection, coronary dissection, gastrointestinal reflux disease, and acute coronary syndrome.	53	4.36	0.65	2	4	5
46. In women, the predominant clinical pictures are those of (angina)-ischemia with nonobstructive coronary artery disease, today defined as INOCA (ischemia with nonobstructive coronary arteries). Other noncoronary cardiopulmonary causes of acute chest pain in women include Takotsubo cardiomyopathy, aortic dissection, coronary dissection, pericarditis, pulmonary embolism, heart failure, arrhythmias, valvular disease, and hypertensive emergencies.	53	4.55	0.57	3	5	5
47. The electrocardiogram (EKG) component of exercise stress testing has a lower sensitivity and specificity for women compared to men and may lead to nondiagnostic EKG interpretation. In contrast, stress echocardiographic imaging has been shown to have high sensitivity, specificity, and prognostic value in women, comparable to that obtained in the male population. Stress myocardial perfusion imaging is recommended to diagnose ischemic heart disease (IHD) in women with intermediate to high risk who have resting EKG abnormalities. Coronary computed tomography angiography can assess many causes of IHD, CMR (cardiovascular magnetic resonance imaging) is an essential diagnostic tool that can reveal the diagnosis of myocarditis and stress (TTS) cardiomyopathy.	53	4.43	0.57	3	4	5

Table 4 (continued)

Statements about clinical area	N	Mean	SD	Min	Median	Max
48. Invasive testing with evaluation of coronary blood flow reserve or the index of microcirculatory resistance at the time of coronary angiography are essential tools for the diagnostic work-up of female patients.	53	4.25	0.73	2	4	5
49. Pregnant women with STEMI should be treated regardless of pregnancy status due to the high mortality associated with STEMI in pregnancy. Primary angioplasty is preferable to fibrinolysis. The management of pregnant women with ACS must be multidisciplinary (cardiologists, obstetricians, anesthesiologists, and neonatologists). Patients must be monitored in the neonatal intensive care unit at the same time as obstetric monitoring, and if necessary, the treatment must be carried out without delay. Delivery should be postponed for at least 2 weeks after ACS as the risk of maternal mortality increases during this period. Coronary dissection is the most common cause of myocardial infarction in pregnancy and occurs more frequently in the late gestation period or the early postpartum phase.	53	4.42	0.57	3	4	5
Chronic ischemic cardiopathy (working group 7)						
50. Concerning gender and sex biases in cardiovascular disease research, there is a need for developing more inclusive and equitable healthcare approaches to improve the cardiovascular health of all individuals.	53	4.25	0.85	1	4	5
51. Gender and sex significantly influence the epidemiology, clinical presentation, and progression of chronic coronary syndromes (CCS), resulting in the need for more personalized and sex-specific treatment strategies.	53	4.45	0.54	3	4	5
52. Gender and sex may influence the clinical presentation of chest pain and ischemia in patients with angiographically normal coronary arteries. Specifically, women are notably more affected by ischemia without obstructive CAD.	53	4.51	0.58	3	5	5
53. In chronic coronary syndromes a gender paradox is widely recognized, as women often have worse outcomes compared to men despite having a lower prevalence of traditional risk factors.	53	4.40	0.57	3	4	5
54. There is a growing need for evidence-based research that includes both genders to provide more accurate and comprehensive data, thereby improving the understanding of gender-specific responses to treatments and optimizing therapeutic strategies for all patients.	52	4.33	0.62	3	4	5

Max, maximum vote; Min, lowest vote; N, number of votes; LDL, low-density lipoprotein; SD, standard deviation.

Table 5 Statements of working groups 8 and 9: therapeutic area

Statements about therapeutic area	N	Mean	SD	Min	Median	Max
Principles of pharmacology and approach to therapy in women (working group 8)						
55. Gender/sex differences in pharmacokinetics significantly impact drug absorption, distribution, metabolism, and clearance, affecting drug efficacy and toxicity. Despite evidence of these differences, sex-specific dosing recommendations remain largely absent, thus showing the need for more personalized approaches to pharmacological therapy.	53	4.51	0.50	4	5	5
56. Women and men respond differently to antihypertensive drugs due to variations in drug metabolism, distribution, and clearance, influenced by sex hormones. Women are more prone to certain side effects, such as cough when on ACE inhibitors, or hyponatremia when on diuretics, highlighting the need for sex-specific considerations in hypertension treatment.	53	4.45	0.50	4	4	5
57. Women have higher plasma levels of beta-blockers like metoprolol and propranolol due to slower clearance, leading to a greater reduction in heart rate and blood pressure. Despite these differences, beta-blockers offer similar survival benefits in both sexes for heart failure and postmyocardial infarction treatment.	53	4.26	0.59	3	4	5
58. The effectiveness of antiplatelet therapy in women could be reduced, caused by a greater platelet reactivity than in men, likely due to higher fibrinogen-binding receptor density, increased expression of signaling proteins, and elevated levels of inflammatory markers.	53	4.25	0.59	3	4	5
59. Sex hormones significantly influence platelet behavior, with estrogen and progesterone generally reducing platelet aggregation and inflammation in women, while testosterone in men may increase platelet aggregation through thromboxane A2 pathways.	53	4.30	0.64	3	4	5
60. Women on aspirin therapy exhibit higher platelet reactivity and aspirin resistance compared to men, with aspirin primarily benefiting women through reduced stroke risk rather than myocardial infarction. Despite similar overall bleeding risks, gastrointestinal bleeding may be more common in women.	53	4.28	0.60	3	4	5
61. Although in the real-world setting, discontinuation of PCSK9 mAbs is similar between sexes, LDL-cholesterol PCSK9 mAbs reduction is less in women compared to men. No sex differences are observed in the reporting side effects due to PCSK9 mAbs.	53	4.21	0.79	2	4	5
Hormone replacement therapy and hormone therapy (working group 9)						
62. Combined oral contraceptives carry a higher risk of venous and arterial thromboembolism, particularly in women with additional risk factors. Progestin-only methods and long-acting reversible contraceptives generally present lower cardiovascular risks but are not completely risk-free. Individualized contraceptive counseling and careful monitoring are essential to optimize cardiovascular health while effectively managing reproductive health. The most up-to-date gynecological guidelines on contraceptives do not suggest preliminary thrombophilia screening in healthy women.	53	4.32	0.64	2	4	5

Table 5 (continued)

Statements about therapeutic area	N	Mean	SD	Min	Median	Max
63. Hormone stimulation during medically assisted pregnancy involves significant hormonal changes with short-term cardiovascular risks, particularly thromboembolic events. Current evidence about long-term cardiovascular risks is not definitive. Women considering or undergoing assisted reproductive technologies should discuss potential risks with their healthcare providers and consider ongoing monitoring of cardiovascular health.	53	4.36	0.59	2	4	5
64. Hormone therapy during gender transition is associated with both potential benefits and risks for cardiovascular health. Regular monitoring and a personalized approach to managing these risks are crucial to ensure overall health and safety. More research is needed.	53	4.21	0.74	1	4	5
65. Hypogonadism in men and women, as well as PCOS in women, are conditions that significantly impact cardiovascular health through mechanisms like altered lipid profiles, increased insulin resistance, obesity, and endothelial dysfunction. Comprehensive management strategies, including lifestyle modifications and medical treatment, are essential to mitigate these cardiovascular risks. Regular monitoring and individualized care are key to improving long-term cardiovascular outcomes in these populations.	52	4.29	0.57	3	4	5
66. Hormone replacement therapy can have a role in cardioprotection among women, particularly if initiated early in the postmenopausal period. However, the overall benefits and risks vary based on individual factors and HRT is not universally recommended for cardiovascular prevention, yet. Women considering HRT should discuss their specific health circumstances with their healthcare provider to make an informed decision.	53	4.30	0.64	3	4	5

Max, maximum vote; Min, lowest vote; N, number of votes; SD, standard deviation.

outcomes.<sup>36</sup> Although electronic cigarettes are marketed as safer alternatives, their long-term cardiovascular impact remains uncertain, warranting caution and further research.<sup>37</sup>

Finally, authors highlighted that obesity is a major cardiovascular risk factor, with women being more affected than men.<sup>38</sup> Postmenopausal women experience a surge in LDL cholesterol, further increasing their CVD risk.<sup>39</sup> Obesity is associated with hypertension, diabetes, and metabolic disorders, all of which contribute to CVD development.<sup>40</sup> Lifestyle interventions, including weight management and physical activity, remain primary strategies for mitigating obesity-related cardiovascular risk in women.<sup>19,39</sup>

### Nontraditional, nonsex-specific risk factors

In Table 3, authors have reported all these risk factors in detail; among them, socioeconomic and ethnic factors significantly impact cardiovascular risk among women. Women from lower socioeconomic statuses experience a higher prevalence of CVDs due to limited healthcare access, lower health literacy, and increased exposure to risk factors like poor nutrition and chronic stress.<sup>41</sup> Additionally, ethnic minority women, particularly African American and Hispanic populations, display elevated rates of hypertension and diabetes due to genetic, cultural, and systemic healthcare barriers.<sup>42,43</sup> Addressing these disparities requires improved healthcare accessibility and targeted public health interventions. Moreover, violence

Table 6 Statements of working group 10: telemedicine

Telemedicine in women's cardiovascular health (working group 10)	N	Mean	SD	Min	Median	Max
67. Gender-Specific and Sex-Specific Challenges in Cardiovascular Care: Women experience different cardiovascular disease patterns, symptoms, and outcomes compared to men, necessitating gender-specific approaches in telemedicine applications.	53	4.23	0.64	3	4	5
68. Rapid Remote Diagnosis and Emergency Triage: Telemedicine facilitates rapid remote diagnosis of acute cardiovascular events in women, who often present with atypical symptoms that differ from the classic presentations seen in men.	53	4.15	0.72	3	4	5
69. Continuous Management of Chronic Conditions: Telemedicine provides continuous management for chronic cardiovascular conditions in women, such as heart failure, and coronary artery disease, through regular remote monitoring and consultations. Telemedicine provides remote symptom/signs tracking and early identification of exacerbations, helping to prevent hospitalizations and improve the quality of life for women.	53	4.23	0.61	3	4	5
70. Technological and Accessibility Barriers: Challenges such as limited internet access and digital literacy can impede the effective use of telemedicine, particularly for women in underserved areas.	53	4.26	0.65	3	4	5
71. Development of Gender-Specific and Sex-Specific Protocols: Developing and implementing gender-specific telemedicine protocols can improve the effectiveness of remote care for women by addressing their unique cardiovascular health needs.	52	4.13	0.74	2	4	5

Max, maximum vote; Min, lowest vote, N, number of votes; SD standard deviation.

and abuse contribute to long-term cardiovascular risk by triggering chronic stress responses that elevate blood pressure, inflammation, and hormonal imbalances.<sup>44</sup> Victims of intimate partner violence are at increased risk of hypertension and stroke due to prolonged exposure to stress hormones such as cortisol and adrenaline.<sup>45,46</sup> Additionally, survivors often develop unhealthy coping mechanisms like smoking and poor diet, exacerbating cardiovascular risk.<sup>47</sup> Screening for abuse and integrating mental healthcare into cardiovascular prevention is essential for mitigating this risk.<sup>48</sup> In addition, mental health disorders, particularly depression, are strongly associated with cardiovascular risk in women. Depression contributes to CVD through behavioral (smoking, sedentary lifestyle, etc.) and biological mechanisms (inflammation, autonomic dysfunction).<sup>33,49–51</sup> Women with depression display increased levels of inflammatory cytokines, leading to endothelial dysfunction and atherosclerosis.<sup>34</sup> Pharmacological treatments such as selective serotonin reuptake inhibitors can also influence cardiovascular risk, necessitating careful management of mental health in cardiovascular prevention strategies.<sup>52</sup>

Similarly, chronic stress activates the hypothalamic–pituitary–adrenal axis, elevating cortisol and inflammatory markers, which contribute to hypertension, atherosclerosis, and MI.<sup>53,54</sup> Women experience heightened vasomotor reactivity and microvascular dysfunction in response to stress, increasing their susceptibility to conditions such as Takotsubo syndrome and spontaneous coronary artery dissection.<sup>15,55–57</sup> Incorporating stress management techniques, including cognitive–behavioral therapy and mindfulness, is crucial for reducing cardiovascular risk.<sup>44</sup>

Likewise, metabolic dysfunction-associated steatotic liver disease (MASLD), previously named nonalcoholic fatty liver disease (NAFLD), is increasingly recognized as a cardiovascular risk factor. MASLD is linked to insulin resistance, systemic inflammation, and atherogenic dyslipidemia, exacerbating cardiovascular risk.<sup>58,59</sup> Screening for CVD in MASLD patients is crucial for early intervention and risk mitigation.<sup>60</sup>

Furthermore, migraine, particularly with aura, doubles the risk of ischemic stroke in women, especially in those younger than 45 years.<sup>61</sup> Smoking and oral contraceptive use further amplify this risk. Sleep disorders, including obstructive sleep apnea, contribute to hypertension and arrhythmias, increasing cardiovascular events.<sup>62,63</sup> Identifying and managing sleep disorders in women through lifestyle modifications and targeted interventions are essential for cardiovascular prevention.<sup>62,64</sup>

Additionally, pollution is still a disregarded risk factor, with a great impact on the cardiovascular health of both sexes, but with different outcomes.<sup>65</sup> Environmental pollution,

particularly fine particulate matter (PM 2.5), has a sex-specific impact on cardiovascular risk. Women exposed to high levels of air pollution exhibit increased susceptibility to ischemic heart disease due to heightened inflammatory responses and endothelial dysfunction.<sup>66,67</sup> Public health policies should prioritize reducing pollution exposure to mitigate cardiovascular risk in women.

In addition, women exhibit higher rates of autoimmune diseases, which contribute to increased cardiovascular risk. Hormonal fluctuations, immune system hyperreactivity, and chronic inflammation play key roles in this association.<sup>68</sup> For example, systemic lupus erythematosus and rheumatoid arthritis are linked to higher incidences of coronary artery disease due to endothelial dysfunction and chronic inflammation.<sup>69,70</sup> Monitoring cardiovascular health in women with autoimmune diseases is crucial for early intervention and risk reduction.

Finally, authors have highlighted that the antineoplastic treatments currently available, both pharmacological and radiotherapeutic, have demonstrated a wide range of early and late cardiovascular adverse effects, included in the definition of cardiovascular toxicity related to antineoplastic therapy (CTR-CVT). The prescription of lifestyle modifications (diet, physical exercise) should be part of an integrated approach to cardiovascular prevention in cancer patients undergoing chemotherapy and, in patients at high and very high risk of CTR-CVT, specific pharmacological interventions should be initiated.<sup>71–73</sup>

#### **Nontraditional risk factors, peculiar to the female sex**

Authors have dealt in detail in Table 3 with the recently emerged nontraditional cardiovascular risk factors. Among them, early menarche has been identified as an independent CVD risk factor, increasing susceptibility to coronary heart disease and stroke. Similarly, polycystic ovary syndrome (PCOS) is associated with an elevated risk of CVD, with mechanisms linked to insulin resistance, dyslipidemia, and hypertension.<sup>74,75</sup> Hypertensive disorders of pregnancy, including preeclampsia and gestational diabetes, significantly increase the likelihood of MI and ischemic stroke in later life. Intrauterine growth restriction further predisposes women to metabolic dysfunctions, including hyperlipidemia, hypertriglyceridemia, and insulin resistance, leading to cardiac dysfunction.<sup>76</sup> Women with a history of pregnancy loss, including miscarriage and stillbirth, face approximately twice the risk of MI, cerebral infarction, and renovascular hypertension, with multiple miscarriages doubling the likelihood of CVD.<sup>77</sup>

Menopause is another significant cardiovascular risk factor, influencing endothelial function, lipid metabolism, and arterial stiffness.<sup>78</sup> Premature menopause, whether natural,

iatrogenic, or surgical, as well as primary ovarian failure, is associated with increased incidence of CVD and stroke.<sup>79</sup> Vasomotor symptoms such as hot flushes and night sweats are related to incident coronary artery disease, higher blood pressure levels and atherosclerosis; therefore, in postmenopausal women, they may serve as biomarkers for heightened cardiovascular risk, necessitating enhanced clinical monitoring and preventive strategies such as lifestyle interventions and tailored hormonal therapies.<sup>80,81</sup> Additionally, the transgender population faces increased cardiovascular risk, likely due to hormonal therapy and psychosocial factors, necessitating further research to clarify mechanisms and optimize risk mitigation strategies.<sup>82</sup> These findings underscore the need for comprehensive, sex-specific and gender-specific cardiovascular risk assessment and management to improve long-term health outcomes.

### Heart failure and sex differences

As reported in Table 4, authors have also dealt with heart failure in women, which presents unique characteristics, with evidence suggesting a better prognosis in terms of mortality, hospitalizations, and sudden death risk compared with men.<sup>83,84</sup> The Framingham study reported a lower mortality rate in women (45%) than in men (59%) during the 1990–1999 period.<sup>85</sup> More recently, data from the Olmsted County study confirmed higher cardiovascular mortality and hospitalizations in men compared with women, despite similar overall mortality rates.<sup>86</sup>

Sex-based differences are also evident in heart failure with preserved ejection fraction (HFpEF), where women demonstrate a nearly 20% lower risk of mortality and hospitalization than men, as indicated by the I-PRESERVE study.<sup>87</sup> Despite this survival advantage, women with heart failure often receive less intensive pharmacological and nonpharmacological treatments.<sup>88</sup> This disparity is influenced by multiple comorbidities, anatomical and physiological differences, and hormonal variations, which impact disease progression and treatment response.<sup>89</sup> Additionally, pregnancy-related cardiovascular adaptations may confer some degree of resilience against heart failure pathophysiology, though further research is needed to validate this hypothesis.<sup>90</sup> Prognostic stratification in heart failure remains a challenge for women, as most risk scores have not been validated in female populations due to their underrepresentation in clinical trials<sup>91,92</sup> and in real-life registries. This limitation underscores the necessity for gender-specific risk assessment tools to improve clinical decision-making. Despite their longer survival, women with heart failure often report a poorer quality of life, characterized by greater physical disability, more severe symptoms, and higher rates of psychological distress, including anxiety and depression.<sup>93,94</sup> The increased prevalence of age-

related comorbidities further complicates management and therapeutic interventions.

Given these differences, further studies are warranted to determine whether psychosocial interventions could improve the quality of life and psychological distress in women with heart failure and whether such interventions could impact the overall prognosis.<sup>95</sup> HFpEF, which is more prevalent in women, is particularly complex and necessitates a multidisciplinary approach that considers both clinical and psychosocial dimensions.

These findings highlight the urgent need for a more tailored approach in the prevention, diagnosis, and treatment of heart failure in women, ensuring equitable access to evidence-based care and research inclusion.

### Arrhythmias and cardiovascular risk in women

Sex differences in cardiac electrophysiology contribute to variations in arrhythmia susceptibility and clinical outcomes.<sup>96</sup> Women exhibit higher intrinsic heart rates, shorter atrioventricular block cycle lengths, and shorter anterograde atrioventricular node slow pathway effective refractory periods compared with men.<sup>97</sup> They also present with a longer corrected QT interval, which predisposes them to late repolarization arrhythmias, including Long QT syndrome and Torsades de Pointes, whereas men are more prone to early re-entry arrhythmias like atrial fibrillation and short QT syndrome.<sup>98</sup>

Hormonal fluctuations significantly influence arrhythmic risk across different life stages.<sup>99</sup> During the menstrual cycle, estrogen peaks in the follicular phase and can prolong the QT interval, while progesterone in the luteal phase may have a stabilizing effect.<sup>100</sup> Pregnancy, with increased estrogen and progesterone levels, further prolongs the QT interval and heightens autonomic tone, exacerbating arrhythmic susceptibility.<sup>101</sup> Menopause introduces a decline in estrogen, leading to increased atrial fibrillation prevalence and structural cardiac changes.<sup>102</sup>

Sex-specific differences are also evident in ECG parameters. Women demonstrate shorter PR intervals, narrower QRS complexes, and a longer QTc interval than men. These differences underscore the need for sex-stratified ECG interpretation and arrhythmia risk assessment.<sup>103</sup> Furthermore, women are twice as likely as men to develop supraventricular tachycardia (SVT), particularly A-V nodal re-entrant tachycardia, due to sex-related electrophysiological properties.<sup>104</sup> The occurrence of SVT is influenced by hormonal status, with higher prevalence during pregnancy.<sup>105</sup>

Atrial fibrillation presents differently between sexes.<sup>106</sup> Women with atrial fibrillation are typically older and have

a higher prevalence of hypertension and HFpEF, but lower coronary artery disease incidence. They report greater symptom burden and reduced quality of life compared with men. Whereas female sex was previously considered a risk factor for cardioembolic stroke and included in the CHA<sub>2</sub>DS<sub>2</sub>-VASC, recently, it has been reconsidered as a risk modifier and not a risk factor at all; thus, CHA<sub>2</sub>DS<sub>2</sub>-VA Score for Atrial Fibrillation stroke risk does not consider female sex among its items.<sup>107</sup>

Notably, female patients are less likely to receive rhythm control therapies, including catheter ablation, and tend to be undertreated with anticoagulation therapy.<sup>108,109</sup>

Sex differences also extend to ventricular arrhythmias.<sup>110</sup> Women have lower susceptibility to ischemia-induced ventricular arrhythmias but higher rates of idiopathic right ventricular outflow tract tachycardia, which may be linked to hormonal influences.<sup>82</sup> Women with inherited Long QT Syndrome are at greater risk of Torsades de Pointes postpuberty, while men predominantly experience J-wave syndromes such as Brugada syndrome due to testosterone-mediated ion channel effects.<sup>111,112</sup>

Understanding these sex-based disparities is critical in tailoring arrhythmia prevention and treatment. Future research should prioritize gender-specific therapeutic approaches, including individualized risk stratification and targeted pharmacological interventions, to optimize arrhythmia management in women.<sup>113–115</sup>

### Acute and chronic coronary syndromes

As reported in Table 4, CVDs remain the leading cause of mortality worldwide, yet a gender-biased and sex-biased approach in research and clinical practice has significantly impacted outcomes for women. Acute<sup>116</sup> and chronic coronary syndromes<sup>117</sup> (ACS and CCS, respectively) present distinct challenges for women due to differences in pathophysiology, risk factors, clinical presentation, and treatment responses.<sup>118</sup>

Women with ACS are more likely to experience atypical symptoms, such as radiation to the back, jaw, or epigastric region, nausea, and dyspnea, leading to misdiagnosis and delays in treatment.<sup>12</sup> Younger women with MI have a seven-fold higher risk of being discharged from the emergency department with a misdiagnosis compared with men.<sup>119</sup> Lack of awareness among healthcare professionals regarding sex-specific risk factors and symptoms contributes to these disparities.<sup>15</sup>

Recent evidence has further clarified the pathophysiological spectrum of ischemic heart disease in women, particularly the conditions of ischemia and MI with nonobstructive coronary arteries (INOCA and MINOCA).<sup>117,120</sup> Both are

considerably more frequent in women and are now recognized as distinct clinical entities rather than benign findings. The 2024 ESC Chronic Coronary Syndromes Guidelines recommend a mechanism-oriented diagnostic approach, including coronary functional testing, cardiac magnetic resonance, and intracoronary imaging, to identify underlying causes such as microvascular dysfunction, vasospasm, or plaque disruption.<sup>121</sup> Management should likewise be tailored to the identified mechanism, combining optimal medical therapy with lifestyle and risk-factor control. Recognizing and appropriately treating INOCA and MINOCA represent a crucial step toward precision and equity in women's cardiovascular care.

Percutaneous coronary intervention (PCI) is less frequently performed in women with ACS due to differences in coronary anatomy, smaller vessel size, and a higher prevalence of plaque erosion and vasospasm rather than plaque rupture.<sup>122</sup> When PCI is performed, women experience increased rates of vascular complications, bleeding, and radial artery spasm, making procedural success more challenging.<sup>123</sup> The underrepresentation of women in clinical trials evaluating drug-eluting stents and advanced interventional techniques further limits the optimization of percutaneous treatments for female patients.<sup>124</sup>

Pregnancy and the peripartum period introduce unique cardiovascular risks, including spontaneous coronary artery dissection, the leading cause of MI in pregnancy.<sup>125</sup> Managing ACS in pregnant women requires a multidisciplinary approach, incorporating obstetricians, anesthesiologists, and neonatologists to ensure optimal maternal and fetal outcomes.<sup>126,127</sup> Primary PCI is preferred over fibrinolysis due to the high mortality associated with STEMI in pregnancy.<sup>128</sup>

In CCS, women are often diagnosed later in life, frequently after menopause when estrogen's cardioprotective effects decline.<sup>129</sup> This hormonal shift exacerbates metabolic dysfunction, leading to increased central obesity, low physical activity, dyslipidemia, and endothelial dysfunction.<sup>130</sup> Traditional risk assessment models such as the Framingham Risk Score tend to underestimate cardiovascular risk in women due to their reliance on male-centric data.<sup>131</sup> There is an urgent need for gender-specific risk stratification tools that incorporate factors such as hormonal status, psychosocial influences, and microvascular dysfunction.

### Therapeutic area

#### *Principles of pharmacology and approach to therapy in women*

Authors have analyzed sex differences in pharmacokinetics and pharmacodynamics influence cardiovascular

drugs' efficacy (Table 5). Sex differences influence all phases of drug disposition, including absorption, distribution, metabolism, and excretion.<sup>132</sup> Women generally have a lower body weight and organ size but a higher percentage of body fat, affecting drug pharmacokinetics.<sup>133–135</sup> Although these differences exist, they do not significantly alter drug absorption.<sup>136</sup> However, women's higher body fat content increases the volume of distribution (Vd) for lipophilic drugs, leading to prolonged drug action, while hydrophilic drugs exhibit a smaller Vd, resulting in higher plasma concentrations and greater effects.<sup>137</sup>

Metabolic clearance varies due to sex-specific expression of enzyme systems. Women demonstrate increased activity of CYP3A4, CYP2A6, and CYP2B6 but reduced activity of CYP1A2 and CYP2E1, influencing drug metabolism.<sup>138,139</sup> Additionally, renal clearance is lower in women due to a reduced glomerular filtration rate, impacting drug excretion.<sup>140</sup> Pharmacokinetics fluctuate across the menstrual cycle due to hormonal variations, which affect drug efficacy and toxicity.<sup>141</sup>

Regarding antihypertensive therapy, sex-related differences impact drug metabolism, distribution, and clearance. Women metabolize angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers differently,<sup>142</sup> often requiring lower dosages for effective blood pressure control. However, they experience more side effects, such as cough with ACE inhibitors and diuretic-induced hyponatremia.<sup>143</sup> Women also have higher plasma levels of beta-blockers, leading to greater heart rate and blood pressure reduction but increased risk of adverse effects.<sup>144</sup>

In antiplatelet therapy, women exhibit higher platelet reactivity, which may reduce aspirin's protective effects against MI while maintaining stroke prevention benefits.<sup>2,145,146</sup> Further research is needed to refine sex-specific dosing recommendations to optimize efficacy and safety in cardiovascular treatment.

#### **Hormone replacement therapy and hormone therapy**

As is known, hormones significantly influence cardiovascular health across different populations. Estrogens, progesterone, and testosterone exert direct effects on the cardiovascular system, with estrogens playing a key role in cardio protection by stimulating endothelial nitric oxide (NO) production and inhibiting the renin–angiotensin–aldosterone system.<sup>147,148</sup> Estrogen receptors (ER), particularly ER $\beta$ , mediate protective activities on the endothelium, reducing oxidative stress and enhancing vasodilation.<sup>149</sup> The decline in estrogen levels postmenopause contributes to increased CVD incidence in women.<sup>150,151</sup>

As reported in Table 5, throughout a woman's reproductive life, exogenous hormones can impact cardiovascular

health. Hormonal contraceptives, especially combined oral contraceptives, increase the risk of venous thromboembolism, MI, and ischemic stroke, particularly in women with additional risk factors.<sup>152,153</sup> Progestin-only methods and long-acting reversible contraceptives present lower but not negligible cardiovascular risks.<sup>154–157</sup> Individualized contraceptive counseling is essential for balancing reproductive and cardiovascular health.<sup>158</sup>

Hormonal therapies in medically assisted pregnancy and gender-affirming care also carry cardiovascular implications.<sup>159,160</sup> While the long-term cardiovascular effects of assisted reproduction remain uncertain, short-term thromboembolic risks are well documented.<sup>161,162</sup> Gender-affirming hormone therapy (GAHT) introduces varied cardiovascular risks<sup>163</sup>: transgender men face an increased risk of MI and hypertension due to testosterone therapy, while transgender women on estrogen therapy are more prone to stroke and venous thromboembolism.<sup>164,165</sup> Regular cardiovascular monitoring is crucial for individuals undergoing GAHT.<sup>166</sup>

Endocrine disorders such as hypogonadism, Turner syndrome, and PCOS further elevate cardiovascular risk.<sup>167–170</sup> Hypogonadism in men is linked to increased CVD risk, and testosterone replacement therapy may ameliorate the cardiometabolic risk profile.<sup>171–173</sup> Women with PCOS often develop obesity and insulin resistance, contributing to hypertension and atherosclerosis.<sup>174,175</sup> Turner syndrome patients face congenital heart defects and early-onset atherosclerosis, necessitating comprehensive management strategies.<sup>176</sup>

Hormone replacement therapy (HRT) offers potential cardiovascular benefits, particularly when initiated early in menopause, reducing all-cause mortality and CVD incidence.<sup>177,178</sup> However, HRT requires individualized risk assessment to optimize benefits while mitigating potential adverse effects. Further research is needed to refine hormone-related cardiovascular risk management strategies.<sup>179</sup>

#### **Telemedicine and cardiovascular health in women**

Telemedicine provides a novel approach to addressing gender disparities in cardiovascular care. It facilitates remote risk assessments, enhances adherence to treatment, and allows continuous monitoring of chronic conditions.<sup>180</sup> Wearable technologies and artificial-intelligence-driven analytics further improve personalized care for women, enabling early detection and intervention.<sup>82,181</sup> However, technological barriers, digital literacy, and data privacy concerns must be addressed to maximize the benefits of telemedicine.<sup>182,183</sup> In Italy, several initiatives<sup>184</sup> – such as the MACAP-AI project for artificial-intelligence-based prognostic ECG analysis and the TeleCheck-AF<sup>185</sup> program for

remote atrial fibrillation management – demonstrate the growing integration of telemedicine into cardiovascular care. European networks like *ESC e-Cardiology*<sup>186</sup> and *SmartCARE* promote digital platforms for remote monitoring and rehabilitation,<sup>187</sup> with a special emphasis on improving access for women and older adults. These models highlight telemedicine's potential to reduce diagnostic delays and enhance adherence, particularly among underserved populations.

## Discussion

This consensus underscores the need for a paradigm shift toward sex-sensitive and gender-sensitive cardiovascular medicine. The clinical implications are clear: hormonal status, reproductive history, and sex-specific physiological differences must be systematically integrated into cardiovascular risk assessment, diagnostic algorithms, and therapeutic decision-making.

Clinicians should recognize that cardiovascular risk in women evolves dynamically across life stages, particularly during pregnancy and menopause, and that preventive strategies must reflect these transitions. Tailored pharmacological approaches are also required, given the well documented differences in drug metabolism and adverse-event profiles between women and men.

Bridging these gaps demands inclusive research designs and equitable female participation in clinical trials to generate evidence that can inform sex-specific recommendations. At a population level, policies addressing social and environmental determinants of health are essential to reduce the disproportionate burden of cardiovascular disease among women.

Future directions should prioritize the validation of diagnostic and therapeutic pathways for conditions that are more prevalent or distinctive in women – such as HFpEF, INOCA, and MINOCA – and the integration of telemedicine and digital health tools to enhance access, adherence, and continuity of care. Collaborative national and European initiatives will be key to translating these goals into measurable improvements in women's cardiovascular outcomes.

## Conclusion

Cardiovascular risk in women is shaped by a combination of biological, hormonal, environmental, and pharmacological factors. A sex-specific approach is crucial to optimize prevention, diagnosis, and treatment strategies. As a direct extension of precision medicine, gender medicine emphasizes the importance of tailoring healthcare based on sex and gender differences. Future efforts must focus on translating this knowledge into actionable clinical pathways and public health initiatives that ensure the timely

recognition and optimal management of cardiovascular disease in women.

## Limitations

This consensus has some limitations. The selection of experts, although multidisciplinary, may reflect institutional and regional heterogeneity and introduce potential selection bias. The Delphi-like approach, while structured, depends on available evidence and expert interpretation. Additionally, some emerging clinical topics may evolve as new evidence becomes available.

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## Conflicts of interest

There are no conflicts of interest.

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GRAPHICAL ABSTRACT

**Cardiovascular Health in Women:  
A Consensus Document of the Italian Cardiovascular Societies**

 <p><b>TRADITIONAL RISK FACTORS, PECULIAR TO THE FEMALE SEX/GENDER</b></p>	<p>Hypertensive disorders, dyslipidemia, obesity, smoking habits and diabetes have peculiar risk profile in women and have to be properly screened and treated.</p>	<p>Peculiar signs and symptoms identification and accurate risk stratification should be considered. Pregnancy and peripartum period must be included in risk stratification. Prevalence of microvessels damage and INOCA require reserve flow evaluation. Treatments must not be delayed in presence of not typical signs and symptoms.</p>	 <p><b>ACUTE ISCHEMIC HEART DISEASE</b></p>
<p>Socioeconomic status, ethnicity, pollution exposure have a stronger impact on cardiovascular women's health than in men, as well as, mental health issues, autoimmune disorders, chronic stress, abuse and violence conditions.</p>	 <p><b>NON-TRADITIONAL, NON-SEX/GENDER-SPECIFIC RISK FACTORS</b></p>	 <p><b>CHRONIC ISCHEMIC HEART DISEASES</b></p>	<p>Gender and sex significantly influence epidemiology, clinical presentation and progression of chronic ischemic cardiomyopathy. "Gender paradox" implies worse outcomes with lower traditional risk factor burden.</p>
 <p><b>NON-TRADITIONAL RISK FACTORS, PECULIAR TO THE FEMALE SEX/GENDER</b></p>	<p>Early menarch, PCOS, hypertensive disorders in pregnancy, vasomotor symptoms during menopause and gender transition should be carefully evaluated during cardiovascular anamnesis.</p>	<p>Gender and sex strongly influence the pharmacokinetics, absorption, distribution and therapeutic compliance of all categories of drugs used for cardiovascular diseases. The platelet activation and the coagulation system are highly influenced by the presence of estrogens.</p>	 <p><b>PHARMACOLOGY AND APPROACH TO THERAPY IN WOMEN</b></p>
<p>Women show peculiar symptoms, better outcomes, worse quality of life and good therapeutic adherence. Frequently underrepresented in CHF clinical trials, women have less access to transplantation and devices implantation.</p>	 <p><b>CHRONIC HEART FAILURE</b></p>	 <p><b>HORMONE REPLACEMENT THERAPY AND HORMONE THERAPY</b></p>	<p>Hormone replacement therapy has demonstrated several advantages against cardiovascular risk in post-menopause. Contraceptive therapy has demonstrated high safety profiles at therapeutic doses. In pharmacological treatment of gender transition, no significant cardiovascular risks related to therapy have been demonstrated at the moment, but further studies are needed.</p>
 <p><b>ARRHYTHMIAS</b></p>	<p>Hormones' fluctuations and hormonal profile during lifetime could explain some differences in cardiac rhythm disorders between sexes. Female sex is a risk factor/modifier for atrial and ventricular arrhythmias, stroke, LQTS. Women suffer from antiarrhythmic drugs side effects more than men.</p>	<p>Telemedicine applied to cardiology in women can make diagnoses quicker, treatments easier to access, even in underserved areas. Teleconsultation can allow to overcome socioeconomic barriers and to provide answers to women's unic cardiovascular needs.</p>	 <p><b>TELEMEDICINE IN WOMEN'S CARDIOVASCULAR HEALTH</b></p>

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