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Review
Canadian Women's Heart Health Alliance

The Canadian Women's Heart Health Alliance ATLAS on the Epidemiology, Diagnosis, and Management of Cardiovascular Disease in Women — Chapter 9: Summary of Current Status, Challenges, Opportunities, and Recommendations

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ABSTRACT

This final chapter of the Canadian Women's Heart Health Alliance "ATLAS on the Epidemiology, Diagnosis, and Management of Cardiovascular Disease in Women" presents ATLAS highlights from the

RÉSUMÉ

Dans ce chapitre final de l'ATLAS sur l'épidémiologie, le diagnostic et la prise en charge de la maladie cardiovasculaire chez les femmes de l'Alliance canadienne de santé cardiaque pour les femmes, nous

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perspective of current status, challenges, and opportunities in cardiovascular care for women. We conclude with 12 specific recommendations for actionable next steps to further the existing progress that has been made in addressing these knowledge gaps by tackling the remaining outstanding disparities in women's cardiovascular care, with the goal to improve outcomes for women in Canada.

présentons les points saillants de l'ATLAS au sujet de l'état actuel des soins cardiovasculaires offerts aux femmes, ainsi que des défis et des occasions dans ce domaine. Nous concluons par 12 recommandations concrètes sur les prochaines étapes à entreprendre pour donner suite aux progrès déjà réalisés afin de combler les lacunes dans les connaissances, en s'attaquant aux disparités qui subsistent dans les soins cardiovasculaires prodigués aux femmes, dans le but d'améliorer les résultats de santé des femmes au Canada.

This is the ninth and final scheduled chapter in the Canadian Women's Heart Health Alliance (CWHHA) "ATLAS on the Epidemiology, Diagnosis, and Management of Cardiovascular Disease in Women." The overall goal of the ATLAS was to create a living document that will help health care providers and the public recognize the unique aspects of cardiovascular (CV) care in women and provide policy makers with the information they need to ensure equitable care for women with CV disease (CVD). These chapters have been published serially in *CJC Open* and are housed collectively on the journal's website at: https://www.cjcopen.ca/womens_heart_health_alliance.

In this last chapter, we summarize the ATLAS highlights from the perspective of current status and challenges, opportunities, and recommendations for the next steps to further the progress that has been made in addressing the knowledge gaps and disparities in women's heart health care (Fig. 1). We plan to follow-up with regular updates on these recommendations and report on advances in women's CVD research and implementation in clinical practice as we collectively "move the dial forward" to improve CV outcomes for women. Going forward, it is our intention that the repository of critical information contained within the ATLAS serves as foundational evidence for guideline-directed CV care in women. We would like to sincerely thank the editors of *CJC Open* for their support in the creation of this opportunity and the CWHHA Secretariat for their support in the publication of these documents.

In the foregoing chapters, consistent themes have emerged confirming disparities in CV care for women including:

1. Underdiagnosis across all CVD conditions, often due to the failure to recognize sex and gender differences in disease presentation and/or the failure to use sex-specific diagnostic thresholds in standard laboratory testing;
2. Undertreatment including not only the failure to apply evidence-based therapies, but the failure to recognize sex differences in the efficacy of therapies;
3. A paucity of research, including clinical trials that inform clinical guidelines, as well as the inconsistent application of sex and gender in the design, analysis, and reporting of research.

To capture the landscape of CVD in women in Canada as a basis for proposed recommendations going forward, we sought to develop, through a sex- and gender-focused lens a summary of the current status of challenges and opportunities to diagnosis, treatment, guideline development, and access to care within a national and global context.

Current Status and Challenges: The Influence of Sex and Gender in CVD Presentation, Diagnosis, Treatment, and Prognosis

We refer the reader to each of the designated ATLAS chapters for a detailed analysis regarding sex and gender disparities in the diagnosis, treatment, and prognosis of CVD, but for convenience, highlight some the major findings according to the 3 most common CVD-based presentations of acute coronary syndromes (ACS), heart failure (HF), and valvular heart disease (VHD).

1. Acute coronary syndromes

Certain distinct underlying pathophysiologies are more often identified in women with ACS, including spontaneous coronary artery dissection (SCAD) and myocardial infarction with no obstructive coronary arteries (MINOCA). SCAD, a nonatherosclerotic angiographic diagnosis, is considered to be a diagnosis distinct from MINOCA, although missed SCAD (not recognized on initial angiographic testing) can fall under the label of MINOCA, until recognized. SCAD accounts for at least 4% of myocardial infarctions overall, but approximately 50% of the myocardial infarctions in women younger than 50 years of age.[1] More than 90% of patients with SCAD are women, approximately 20% are peripartum, and in approximately 50%, associated fibromuscular dysplasia is identified when appropriate screening is performed, suggesting an underlying vasculopathy interfacing in approximately 50%, along with acute extreme stress (most often emotional, less often physical) as contributing precipitants.[1] It is important to recognize the diagnosis of SCAD, because treatment is different than that for an ACS caused by atherosclerotic plaque rupture or erosion. Unless hemodynamic compromise is present, SCAD is treated conservatively, without percutaneous intervention or surgery. Recently reported registry data suggest that recurrence rates, initially thought to be 15%-20% overall, are observed at 5%-10% with appropriate management.[2] MINOCA is 2-5 times more likely to occur in women than in men and can be caused by atherosclerotic (plaque rupture or erosion), and nonatherosclerotic (vasospasm, thromboembolism, coronary microvascular dysfunction) processes.[3] Recent trials suggest thorough evaluation using multimodality diagnostic tools (such as optical coherence tomography, intravascular ultrasound, and cardiac magnetic resonance imaging) can lead to the identification of an underlying cause in $>$ 80% of MINOCA cases.[4] The prognosis of MINOCA is not benign, and the occurrence of major adverse cardiac events (MACE) has been observed to be twice that of matched individuals having no

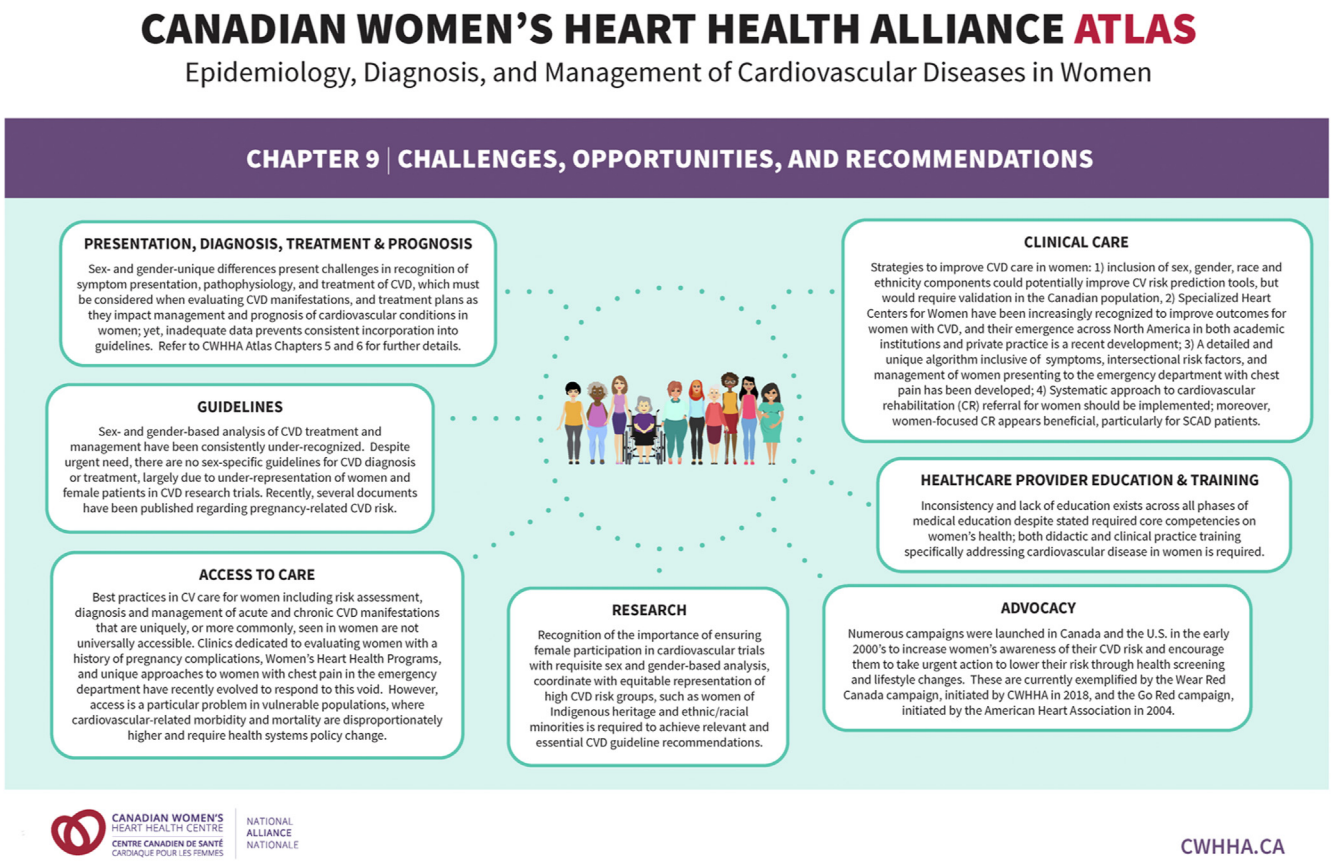

Figure 1. Summary of challenges, opportunities, and recommendations to further the progress that has been made in addressing the knowledge gaps and disparities in women's CV care. CR, cardiovascular rehabilitation; CV, cardiovascular; CVD, cardiovascular disease; CWHHA, Canadian Women's Heart Health Alliance; SCAD, spontaneous coronary artery dissection.

CVD and one-third that of those with obstructive coronary artery disease.[5]

The recognition of these unique and/or more common pathophysiologic causes of ACS in women is imperative, to improve the comparatively worse outcomes as manifested by higher event rates for MACE in women, especially young women, compared with that in men. Through this clinical recognition of the expanded diagnosis of ACS in women, knowledge has been generated and the CWHHA has led a Canadian Cardiovascular Society (CCS) clinical practice update on the epidemiology, diagnosis, and management of MINOCA that is presently under review with an anticipated publication in spring of 2024. Next steps must include continued and increasing awareness, systematic workup, and use of appropriate diagnostic pathways to identify causes of myocardial infarction in women, and more clinical trials aimed at providing high-quality evidence regarding specific pharmacologic and nonpharmacologic treatments.

Several randomized controlled trials (RCTs) have recently been conducted, including Randomized Evaluation of **B**eta Blocker and **A**CE-Inhibitor/Angiotensin Receptor Blocker **T**reatment (ACEI/ARB) of **MINOCA** patients' (MINOCA-BAT; NCT03686696), and Statin and Angiotensin-converting Enzyme Inhibitor on Symptoms in Patients With SCAD (SAFER-SCAD; NCT02008786). In hs-**c**Tn—**O**ptimizing the **D**iagnosis of Acut**e** **M**yocardial **I**nfarction/Injury in Women CODE-MI; NCT03819894), investigators are seeking to evaluate the effect of routine use of hs-troponin on CV outcomes in women who present with chest pain syndromes.

2. Heart failure

Nearly half of the patients who present with HF have HF with preserved ejection fraction (HFpEF), and women, especially those with advanced age and multiple comorbidities, comprise most HFpEF patients.[6] Sex-based differences have been observed in the response to certain medical therapies in large clinical trials, including **T**reatment **o**f **P**reserved **C**ardiac Function Heart Failure With an **A**ldosterone An**t**agonist (TOPCAT) and **P**rospective Comparison of **A**ngiotensin **R**eceptor Neprilysin Inhibitor With **A**ngiotensin Receptor Blocker **G**lobal **O**utcomes in **H**eart **F**ailure and Preserved Left Ventricular Ejectio**n** Fraction (PARAGON-HF), in which aldosterone antagonists and sacubitril-valsartan benefited women more compared with men.[7] The mechanisms for these sex-based differences is currently unknown; dose-response relationships, microvascular inflammation, variation in natriuretic peptide deficiency, and differential regulation of constitutive nitric oxide synthase have been proposed.[7] Interestingly, no sex differences were shown in patients with HFpEF who were receiving sodium-glucose cotransporter-2 inhibitors, for the clinical outcomes of rehospitalization, CV death, or quality of life.[8,9]

Although more prevalent among men, HF with reduced ejection fraction (HFrEF) is still notable in women. Peripartum, Takotsubo (stress), and chemotherapy-induced cardiomyopathy, are causes of HFrEF that occur exclusively, or more frequently, in women.[10,11] Importantly, there is a lack of robust, clinical trial evidence to guide treatment of these conditions, and although biomarkers have been observed to differ according to age and sex, there are no sex-specific thresholds for HF biomarkers such as N-terminal pro hormone brain natriuretic peptide.[12]

Sex-based differences in response to the medical management of HFrEF with β-blockers, and neurohumoral agents are inconsistently reported across large clinical trials, and vary in subgroup analysis, dosing regimens, and outcome variables.[13-17] Newly emerging therapies such as the soluble guanylate cyclase stimulators and cardiac myosin activators in the **Ver**i**c**igua**t** Gl**o**bal Study in Subjects With Heart Failure With **R**educed Ejec**t**i**o**n Fr**a**ction (VICTORIA)-HF and **G**lobal **A**pproach to **L**owering **A**dverse **C**ardiac Outcomes **T**hrough **I**mproving **C**ontractility in **H**eart **F**ailure (GALACTIC-HF) trials respectively, showed no sex-based differences in heart failure hospitalizations or CV death.[18]

There are clear sex differences in HFrEF management outcomes when using device therapies. Women consistently report better clinical outcomes after cardiac resynchronization therapy (CRT), and at lower QRS duration.[19] However, research on sex-based differences in outcomes after implantable cardioverter-defibrillator (ICD) implantation have conflicting results.[20-23] Thus, international guidelines informing ICD and CRT device implantation lack sex-specific recommendations regarding the indications for and outcomes of these therapies.[24,25] Such ambiguity highlights the longstanding disparity in sex-based representation across RCTs as a significant barrier to generating concrete evidence and recommendations; women remain under-represented by 4:1 across CRT and ICD RCTs as participants and as investigators.[23,24,26]

Similarly, women are referred less often and later in their disease trajectories for advanced therapies including temporary mechanical circulatory support, durable left ventricular assist device (LVAD), or heart transplantation compared with men, and concerns exist regarding bias in consideration of female patients for advanced therapies.[27-30] Survival rates are lower in women after LVAD implantation further stratified according to race/ethnicity,[31] but not after heart transplantation.[32] However, women are more prone to post-LVAD (eg, ischemic and hemorrhagic stroke, pump thrombosis, device malfunction, and right ventricular failure) and post heart transplantation (eg, allograft failure and antibody-mediated rejection, but not malignancy or cardiac allograft vasculopathy) complications.[29,32-34] The persistent issue of under-representing female patients in clinical trials might be attributable to factors including the lack of female investigators leading knowledge generation and dissemination, ineligibility of individuals of childbearing age, and lower referral rates of women to cardiology clinics, because women are approximately 3 times less likely to receive CRT or ICD therapy.[35,36]

3. Valvular heart disease

Sex differences are also apparent in the context of VHD, whereby women remain equally under-represented in landmark studies of VHD interventions to inform guideline development and care.[37,38] This has resulted in crucial metrics for grading severity of VHD and guiding the timing of interventions being developed, using data from largely male sample participants, who are known to have heart chamber dimensions and stroke volume that differ from those of women, even indexed for body size, CVD risk profiles, and VHD clinical presentations.[39,40] This in turn perpetuates sex-based disparities in the diagnosis of VHD in women, contributing to later referrals to surgical and percutaneous interventions at more symptomatic stages of the disease and placing female patients at risk of poorer prognosis.[38] Older women, especially those with concomitant pulmonary hypertension, are at a higher risk of mortality in the setting of aortic valve disease. As well, women are less likely to receive mitral valve repair than replacement and report significantly worse functional status and quality of life metrics after surgery for ischemic mitral regurgitation, which may be due to a mismatch between their ventricular size and the degree of mitral regurgitation.[38] Although mitral valve transcatheter-edge-to-edge repair was shown to improve clinical outcomes irrespective of sex relative to guideline-directed medical therapy alone, reduction in heart failure hospitalizations was less pronounced in women than in men ($P = 0.002$).[38] There are no sex differences in outcomes in patients who undergo surgical or percutaneous intervention for tricuspid regurgitation,[38] although the data with newer percutaneous tricuspid valve devices are still emerging. Importantly, VHD has implications during pregnancy, and should be intervened upon after discussion with the multidisciplinary heart valve team at centres with experience.[38]

Current sex-specific guidelines according to region

In the contemporary era, patient management with a goal to achieve optimal outcomes is driven by published guidelines of experts within a specialty, most often with the administrative support of professional associations. A sufficient evidence base of objectively graded data is required in the development of guidelines. A paucity of evidence-based CV data in female individuals and women has resulted in a paucity of CV guidelines for the management of CVD in women. Herein we examine the situation in Canada, the United States, and globally.

Canada. Guidelines and position statements for CV care are developed by and available through the CCS (www.ccs.ca). These evidence-based guidelines represent the consensus of a multidisciplinary panel of "experts" who are charged with the mandate of formulating disease-specific recommendations. Currently, these recommendations have been assumed to be applicable to male and female patients.

A CCS-endorsed document addressing ischemic heart disease in women was published in 2000, as a result of a CCS-initiated consensus conference.[41] Subsequently, in 2018, an initiative was undertaken by the CCS to determine the feasibility and outcomes of a structured process for incorporating sex and gender factors into the clinical practice guideline (CPG) addressing the management of ST-segment elevation myocardial infarction. A CVD sex and gender "champion" was appointed to this CPG development

committee. To determine whether CPG recommendations should be influenced by sex, the identified research comprising the evidence base were systematically assessed to determine: (1) the male-female distribution of the study population; (2) the adequacy of sex-specific representation using the participation/prevalence ratio; and (3) whether data were disaggregated by sex.

It was concluded that although implementation of a systematic process for critically appraising sex-specific evidence for CPGs was straightforward and feasible, the inadequate enrollment of female subjects, and/or lack of analysis and reporting of results according to sex, hindered a comprehensive sex-specific assessment of the quality of evidence and strength of recommendations required for a CPG. Going forward, it would be imperative that results be stratified according to sex for clinicians to have the ability to provide sex-specific care.[42] Additionally, gender-specific analyses should similarly become available. Thus, at the current time, there are no existing sex- and/or gender-specific Canadian guidelines for the management of ACS.

In recognition that lipid levels are affected by hormonal changes throughout a woman's life span and that a role for sex- and gender-specific management of hyperlipidemia exists, the 2021 CCS guidelines on the management of dyslipidemia for the prevention of CVD in adults recommends counselling patients who have had pregnancy-related complications on the increased lifetime risk of atherosclerotic CVD, and reinforcement of healthy lifestyle behaviours.[43] Use of CV age, as opposed to 10-year risk calculators, is recommended in clinical decision-making with regard to lipid-lowering pharmacotherapy in this population.

A more comprehensive approach to managing the pregnant patient with CVD has recently been published as the 2021 CCS clinical practice update on cardiovascular management of the pregnant patient.[44] This document addresses sex-specific CVD risk factors and comorbidities, and introduces the concept of "cardio-obstetrics," as well as including management guidance on the pregnant patient with congenital heart disease to improve pregnancy outcomes in women with heart disease. Specialized care in multidisciplinary cardio-obstetric programs is recommended for all women with suspected CVD who are of childbearing age, including preconception counselling, antenatal and postpartum cardiac surveillance, maternal and fetal risk stratification, optimization of cardiac lesions, safety review of medications in pregnancy, and labour and delivery planning. The document highlights "red flags" that should trigger prompt assessment and describes the approach to some of the cardiac emergencies that the care provider might encounter in a pregnant woman.

United States. The American Heart Association (AHA) released the initial women-specific scientific statement on the prevention of CVD in 1999,[45] and then intermittently has released updated "evidence-based," or "effectiveness-based" guidelines in 2004,[46] 2007,[47] and 2011,[48] culminating in the most recent updated review (2020)[49] and additional scientific statement (2021).[50] These documents uniformly underscore that: women have unique risk factors for CVD (such as polycystic ovary syndrome and pregnancy-associated conditions including gestational hypertension, gestational diabetes, preterm delivery, small for gestational age delivery, pregnancy loss, and placental abruption, that increase future risk of CVD); women also have different manifestations of CVD, and studies have shown sex differences in their response to risk factors and treatments; knowledge of unique risk factors in women as well as ameliorating the treatment gap is critical in lowering CVD risk in women. Also emphasized is that black, Asian, and Hispanic women are more likely than white women to experience adverse pregnancy outcomes and the reasons for these disparities need to be addressed and researched.

Although initially much within these recommendations did not differ according to sex, the application of recommended preventive therapies was often underused in women. Nonetheless, sex-specific risk factors were identified within these documents and their release paralleled a dramatic reduction in mortality due to CVD in the United States over the ensuing decade.[51] However, despite the increased awareness of CVD as the leading cause of death in American women, guideline-directed preventive therapies remain underused in women compared with men in primary and secondary prevention.[52-58]

In the United States, the endorsed risk assessment tool for primary prevention by the AHA and the American College of Cardiology (ACC) is the Atherosclerotic Cardiovascular Disease (ASCVD) risk score.[59,60] None of the risk factors within the ASCVD risk score are sex-specific, and risk for women is heavily influenced by age. The 2019 ACC/AHA primary prevention of CVD guideline allows refinement of ASCVD risk using risk enhancers, many of which are sex-specific or sex-predominant for women, including preeclampsia, polycystic ovarian syndrome, early menarche, premature ovarian insufficiency, premature menopause, autoimmune diseases, and a history of breast cancer.[59]

Beyond guidelines for the prevention of CVD, there are other guidelines that mention women within sections labelled "special populations," including the recent AHA/ACC HF guideline, which mentioned the increased risk of HFpEF in women, pointing out the sex differences in specific biomarkers in HF, and mentioned sex-specific risk factors for HF in addition to nontraditional risk factors that increase risk of HF in women.[61] All of these documents consistently report that the level of evidence was not available at the time of writing to provide sex-based guidelines for the treatment of heart events in women. Of note, there are no women-focused statements/guidelines on HF, arrhythmias, and/or valve diseases. More recent guidelines, such as the 2021 AHA/ACC multisociety guidelines for the evaluation and diagnosis of chest pain,[62] were unique in that they deliberately embedded women-specific recommendations within the guidelines rather than considering them as a special population, and were the first to give recommendations for the evaluation of ischemia with no obstructive arteries, which disproportionately affects women.

Global. Similar to Canada, there are no specific documents dedicated to CV guidelines in women outside of the United States, largely because of a lack of adequate evidence base. Within the 2016 European guidelines for CVD prevention,[63] a few recommendations tailored specifically for women are provided, including: advising against CVD risk assessment in women

younger than 50 years with no risk factors (with the proviso that it might be beneficial to assess CVD risk in women before prescribing combined oral contraception); recommending the screening of women older than 50 years, or postmenopause, in the same manner men are screened (ie, for those at increased risk of CVD because of family history of CVD or hyperlipidemia, or who present with major risk factors); and, including pre-eclampsia as a sex-specific CVD risk factor to be considered. These recommendations were on the basis of evidence from 8 risk estimation systems (Framingham,[64] **S**ystematic **CO**ronary **R**isk **E**valuation [SCORE], [65] ASSIGN-SCORE,[66] QRISK1 and QRISK2,[67,68] **Pro**spective **Ca**rdiovascular **M**ünster (PROCAM) cardiovascular epidemiology study,[69] Pooled Cohort Studies Equations,[70] CUORE,[71] Globorisk[72]). The percentage of women included ranged from 32% to 64% (median 52%, mean 49%), and several sex-specific cut points for CVD risk factors were recommended, including waist circumference (sex- and race/ethnicity-dependent),[73-76] high-density lipoprotein cholesterol (> 1.2 mmol/L indicates lower risk in women, whereas for men the value is > 1.0 mmol/L) and alcohol consumption (limits: 1 glass per day for women, and 2 glasses per day for men). The QRISK3 scoring system included under-recognized risk factors such as race/ethnicity, chronic kidney disease, migraine, atypical antipsychotics, corticosteroid use, systemic lupus erythematosus (SLE), mental illness, erectile dysfunction, and HIV/AIDS in its algorithm.[77]

More recently, Vogel et al. published the results of *The Lancet* Women and Cardiovascular Disease Commission, with the goal of reducing the global burden of CVD in women by 2030.[78] This comprehensive global review of CVD in women convened by leading authorities throughout the world, including representation from Canada, identified consistent themes across virtually all CVD states that women remain under-represented in clinical trials, registries, and pathological studies, and, on the basis of significant gaps in evidence specific to women's CVD, an ongoing reliance on male-pattern diagnostic and treatment criteria results in delayed, deferred, and/or under-researched treatments and outcomes for women. It is important to note that in addition to traditional risk factors (eg, hypertension, diabetes, and dyslipidemia) and sex-specific risk factors for CVD (eg, hypertensive disorders of pregnancy), *The Lancet* Women and Cardiovascular Disease Commission includes a third category of "under-recognized" risk factors, such as depression and anxiety, abuse and intimate partner violence, and socioeconomic deprivation, to achieve a comprehensive assessment of a woman's CV risk.

The challenge of access to care

Beyond the general challenges in access to health care that Canada is acutely experiencing, driven by limitations in human and technologic resources, administrative inefficiencies, geographic disparities, and inadequate systems and policies promoting efficient care delivery, women continue to experience disproportionate disparities when they present for assessment of CV risk, cardiac symptoms, or established CVD due to sex-unique physiologic characteristics and gender-specific social dynamics. A glaring example of sex-unique disparity in access to care is that surrounding individuals who experience pregnancy complications (eg, hypertensive disorders of pregnancy, gestational diabetes, and preterm delivery), also known as "adverse pregnancy outcomes," which are well established sex-specific risk factors for developing CVD later in life. However, their incorporation into clinical patient evaluation schemes is not yet established, because only 50%-60% of interdisciplinary health care providers are fully aware of these future health risks.[79,80] The peripartum period represents an opportunity to identify these higher-risk women, promote awareness, and perform a comprehensive CV risk assessment. Yet, in one report, less than half of such women identified to be at increased CV risk were referred for further evaluation.[81]

Barriers to access interfere with postpartum patient compliance and need to be addressed to improve logistics, integration, and quality of care. A national health systems strategy for incorporating postpartum CV care into existing prevention care models has been proposed, involving primary care physician risk assessment and mitigation recommendations, inclusive of personalized medical management and lifestyle interventions.[82] This approach would also allow for concomitant care of women's partners and children, who might be at increased risk of developing CV risk factors.[83] Provincial and national systems are needed to streamline access to primary care and preventative care resources.

Vulnerable populations and CV health: The need for health systems policy change

Vulnerable populations include racialized and indigenous minorities, elderly, socioeconomically disadvantaged, rural or remote inhabitants, and those who experience disabilities, face mental health challenges, or belong to the LGBTQ2S+ community.[84-86] As detailed in chapters 2 and 7 of this Atlas series, these factors and other social determinants of health intersect in a complex fashion to play a prominent role in determining health outcomes.[74,85] These marginalized groups are susceptible to disproportionately worse CV outcomes and increased mortality. Women are more likely to experience social disadvantage, an independent risk factor for CVD,[87] manifested as disproportionate challenges in access to prevention, diagnoses, treatment, and management of CV health conditions. Indigenous women face additional challenges of colonization and related historical/intergenerational trauma contributing to increasing burdens of CV health conditions,[85] and 53% higher CV mortality rates than nonindigenous women; yet, they are under-represented in research.[88] Indeed, despite the growing population of all racialized groups (comprising 26.5% of the population in the 2021 Canadian census)[89] and their recognized excess CVD morbidity and mortality, they are under-represented in research studies profoundly affecting the validity and generalizability of results data.[90-93] A recent systematic review reported that across several countries, including Canada, many minority and racialized groups are faced with structural and systemic barriers to health care (eg, lower income, limited insurance coverage, discrimination and ethnic biases, and delayed treatment), which contribute to health disparities and substandard care among the most disadvantaged social groups.[94] Cardiac patients from racialized and minority groups continue to report experiences of discrimination, lack of culturally and linguistically appropriate resources, and delayed diagnosis or treatment that consequently

Table 1. Recommendations to improve CV research, care, and outcomes for vulnerable populations

1. Standardize the inclusive collection of indigenous, race/ethnicity-based identity, gender diverse and sex-disaggregated health care data, including ability and mental health status, in all Canadian communities across all locations and socioeconomic categories.
2. Require the inclusion of sex/gender and racialization considerations in research protocol methodology, results analysis, and discussion, for all levels of research, including registries.
3. Ensure an intersectional analysis in qualitative and quantitative studies to explore the combined effects of various intersecting factors, such as gender, race, ethnicity, socioeconomic status, and disability on the CV health of vulnerable populations.
4. Develop and implement sex/race/ethnicity-specific risk prediction tools and management algorithms for CV care including ability, and mental health factors.
5. Implement contextually, culturally, and linguistically appropriate CVD awareness, education (health literacy), and primary and secondary prevention programs for health care professionals to access and utilize.
6. Form a racism/ethnicity institute to support research on the effects of racism on CV health.
7. Ensure ethics and review boards, research sponsors and funding bodies and institutions practice inclusivity, equity, diversity, and accessibility principles to allow validity and generalizability of study results.
8. Develop policies and procedures for accountability and audit of all the recommendations noted above.

CV, cardiovascular; CVD, cardiovascular disease.

influences their clinical care as well as their capacity to self-care.[95,96]

Emerging research also highlights the intersection of gender roles and expectations with cultural norms, employment, and immigration status of racialized and indigenous populations, influencing their risk for CVD (eg, higher levels of sedentary time and lower levels of physical activity).[97] Women living in rural and remote locations experience greater burdens of CV health challenges, which are further exaggerated for women living on First Nations reserves due to lack of access to health care services and practitioners; this also results in logistical challenges to participating in research.[85] Women experiencing disabilities receive less CVD preventive screening and are less likely to be included in CVD research, leading to an increased disease burden and higher risk for adverse cardiac events among individuals with disabilities.[98] Women with mental health challenges are more likely to die of CVD than men with mental health challenges.[99] There is limited information regarding CVD risk, diagnosis, and treatments in individuals of the LGBTQ2S+ community. Transgender individuals experience greater CVD morbidity, and face unique risk factors from gender-affirming hormone therapy[100,101]; there is a clear need for research to better understand CVD risks, experiences, and treatments among gender-diverse individuals.[102] Resources, including a tool kit, for increasing the participation of marginalized groups in research have been developed, although these are not specific to CVD research.[103,104] Table 1 provides recommended policy action changes to improve CV research, care, and outcomes for vulnerable populations.

What Should Comprehensive CV Care For Women Look Like?

Across the spectrum of CVD prevention, diagnosis, and management, there are specific opportunities that optimize delivery of care for women across the spectrum of their lives and needs. From early adulthood, through menopause, from primary through secondary prevention, and from diagnosis through treatment, women interact with the health care system in primary care, specialized clinics, hospital emergency departments (EDs), in-patient, and rehabilitation settings. In all of these health care delivery settings, an awareness of the unique and/or more common characteristics and presentations of CVD in women must be recognized and incorporated into clinical assessments and management plans. We highlight key features of health care delivery to women through a sex and gender lens, including implementation of CVD risk assessment tools in primary and obstetrical practices, recognition of the need for referral to specialized centres focused on CVD care for women, consideration of CVD diagnosis in women who present to EDs, and the implementation of focused CV rehabilitative care for women.

Sex-specific CV risk assessment tools in primary care

Risk prediction tools are used by clinicians to estimate a patient's risk for CVD, guide the need and intensity of CVD prevention strategies, and to assess their effectiveness. These tools convert data, real or modelled, on the presence and/or severity of risk factors into a summary score to estimate the probability of having a CV event over a period of time (eg, 10 years). It has been recognized that initial risk prediction models, such as the Framingham risk score, underestimate CV risk in women.[105] This might in part be due to the observations that traditional risk factors (smoking, diabetes) have a differential effect in women and men.[106] Moreover, in postmenopausal women, hypertension, smoking, diabetes, and hyperlipidemia confer a greater risk of CVD.[107]

More recently, CVD risk factors that are unique or more common in women have been identified. Some of these "nontraditional" risk factors are hormonally related and vary with physiology over a woman's life span, including pregnancy (eg, preeclampsia, gestational hypertension and/or diabetes, preterm birth), a history of breast cancer, and menopause.[108] Hormonally related vascular changes are likely related to alterations in estrogen, diminished biologically active nitric oxide, and increased angiotensin II receptor activity, causing reduced carotid artery distensibility/vascular compliance, subclinical atherosclerosis, and/or endothelial dysfunction.[109] Additionally, women are more susceptible to autoimmune diseases (eg, inflammatory arthritis, SLE) and the associated inflammation contributes to plaque formation/rupture and thrombosis.[107,110] There might also be an inflammatory role in atopic dermatitis, iron deficiency anemia, depression, and migraines, which are all more common in women.[107] Lipoprotein(a) is a recognized, but poorly understood risk factor in the development of CVD and calcific aortic valve diseases,[111] with evidence of a genetic link.[112] Another emerging risk factor, gender/gendered social roles,

Table 2. Traditional, female-specific, female-predominant, and intersecting factors to consider in the assessment of cardiovascular risk in women

Traditional risk factors	Female-specific risk factors	Female-predominant risk factors	Intersecting risk factors
Hypertension	Early or late menarche	Systemic autoimmune diseases	Age
Diabetes mellitus	Polycystic ovary syndrome	Rheumatoid arthritis	Ethnicity
Obesity	Adverse pregnancy outcomes	Systemic lupus erythematosus	Race
Smoking	Hypertensive disorders of pregnancy (eg, preeclampsia, eclampsia)	History of breast cancer treatments	Gender
Physical inactivity		Migraines	
Unhealthy diet	Gestational diabetes	Depression	
Family history of premature CVD	Preterm delivery		
	Pregnancy loss	Possible risk factors:	
	Increased parity	Atopic dermatitis	
	Infertility and treatments	Iron deficiency anemia	
	Primary ovarian insufficiency	Lipoprotein(a) increased in menopause	
	Premature, or early menopause		

CVD, cardiovascular disease.

has been associated with increased risk of ACS for those ascribing to more traditional feminine roles.[113]

Interestingly, beyond the recognition that certain traditional CVD risk factors have differential (greater) effect in women, it has also been observed that intersecting factors such as age, ethnicity, nutrition, and physical activity might influence risk. For example, eating patterns having high alignment with heart-healthy dietary guidance reduce the absolute risk of CVD events more in women aged 40-79 years than in men of the same age.[114] These findings suggest that the biological mechanisms underlying the association between exercise, diet, and CVD risk might differ in women compared with men.

Table 2 provides a summary of traditional, female-specific, female-predominant, and intersecting risk factors to be considered in the assessment of a woman's overall CVD risk. Women must be assessed for CVD risk beyond the traditional risk factors. It is important to obtain a "cardio-obstetric" history, inclusive of medical, family, and pregnancy history, CVD symptoms, and depression screening. Physical examination should include blood pressure, body mass index, and waist circumference; and laboratory testing should include fasting plasma glucose/lipoprotein levels,[48] with consideration to inflammatory biomarkers (eg, high-sensitivity C-reactive protein). Because of the heterogeneity of the progression of women+ (including transgender men and nonbinary people) through the menopausal transition, it is important for clinicians and the women they partner with in health care to understand and document where they are in the menopausal transition. Although there are staging tools like the **St**ages of **R**eproductive **A**ging **W**orkshop (STRAW + 10), that scale subtle changes in flow and length of menstrual cycles, vasomotor symptoms, sleep disturbances, and mood/cognition changes might contribute to an increased CV risk and overall health concerns. Noninvasive echocardiography, coronary artery calcification scanning using computed tomography, and carotid artery intima-medial thickness assessment might also assist with risk stratification.[115]

Existing CV risk assessment prediction tools are outlined in the *Global* subsection of the *Current sex-specific guidelines according to region* section; these uniformly use traditional risk factors in their scoring algorithms and most do not include sex- and gender-specific, or race- and ethnic-specific variables. The QRISK3 includes some of the nontraditional risk factors (eg, migraine, mental health, SLE) and includes ethnicity.[77] Although the Reynolds Risk Score was initially intended to be used for women, it requires high-sensitivity C-reactive protein for calculation, and has not been widely adopted.[116] A risk scoring tool, which included sex-specific risk factors, was assessed prospectively; however, on a limited test population it did not perform better than the traditional risk assessment tools described previously, and more evidence is needed.[8] Although certain risk calculators (eg, Pooled Cohort Equation used in the ACC/AHA ASCVD risk calculator)[117] include racial variables, these have been limited to Caucasian or black races and do not include ethnicity; thus the effect of inclusion of race- and ethnic-specific analyses is unknown and must be considered to ensure future risk prediction models perform well across various ethnic populations. Other CVD risk factors known to be more impactful in women have also been unaccounted for in CVD risk prediction tools, including autoimmune disorders (rheumatoid arthritis, SLE) and depression.

Health care for women is often driven primarily by their reproductive needs; in the Canadian health care setting, this is primarily accessed through family practice services, presenting an opportunity for these encounters to include assessment of CV risk, although this is not frequently done.[118] In other health care models, such as in the United States, services to women are primarily offered through specialized obstetrics and gynecology practices, and unfortunately awareness by the health care providers is most often limited to "bikini medicine,"[119] (ie, solely addressing the reproductive issues in isolation of their influence or association with CV risks). These encounters by women seeking reproductive care are excellent opportunities to engage patients in awareness of their CV risks and management through appropriate lifestyle and treatment as indicated.

Specialized care centres/centres of excellence

Specialized patient care provided by heart centres for women (HCW) improve diagnostic accuracy, quality of life, and CV risk factor management for women with ischemia with no obstructive arteries and MINOCA.[120,121] Interestingly, the decline in CVD mortality first seen in men in 1979, was not comparably seen in women until 2012.[122] This time frame coincides with accelerated public advocacy to increase patient and physician awareness of CVD in women, to

Table 3. Heart centres for women in Canada

Centre/program name Date established	Description	Location
Women's Cardiovascular Health Initiative 1991	A comprehensive assessment and lifestyle program for women with existing or potential heart problems with a unique focus on cardiac rehabilitation for women. The program is affiliated with the University of Toronto, and reports actively training health care professionals.	Toronto, Ontario
Women's Heart Health Clinic 2009	Two programs: 1 at BC Women's Hospital and the other at VGH covering the full scope of women's heart health services. A cardiologist from VGH provides cardiac care and an NP provides clinical and prevention services. The focus of the NP clinic is to reduce risk and provide lifestyle coaching, whereas the focus at VGH is on diagnostics and therapeutics.	Vancouver, British Columbia
Women's Healthy Heart Initiative 2009	Nurse-led collaborative heart disease prevention clinic for women providing patient-centred care and treatment focused on decreasing modifiable heart disease risk factors through healthy lifestyle: improving nutrition and increasing physical activity to lower women's cholesterol and blood pressure levels, achieving weight loss, and avoiding diabetes.	Montreal, Quebec
CWHHC 2012	Programs include: an outpatient Women's Heart Health Clinic specializing in spontaneous coronary artery dissection, postpartum risk assessment, unexplained chest pain, and MINOCA; an evidence-based peer support program (Women@Heart); an outpatient primary prevention program (CardioPrevent) for high-risk postpartum women; clinical and research fellowships in women's cardiovascular health. CWHHC is the convening body for the Canadian Women's Heart Health Alliance and Canadian Women's Heart Health Summit	Ottawa, Ontario
The Maritime Heart Center Women's Heart Health Clinic 2017	Multidisciplinary, specialized outpatient cardiac clinic designed for the assessment and care of women with a history of heart disease, and/or major risk factors for heart disease.	Halifax, Nova Scotia
Cardio F, le Centre hospitalier de l'Université de Montréal 2021	A multidisciplinary approach to clinical care, including care in cardiac disease in women, cardio-obstetrics, and neurovascular conditions in women. Also dedicated to teaching, knowledge translation, clinical research, and innovation related to women's cardiovascular health.	Montreal, Quebec

CWHHC, Canadian Women's Heart Health Centre; MINOCA, myocardial infarction with nonobstructive coronary arteries; NP, nurse practitioner; VGH, Vancouver General Hospital.

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advance research and education, and with the emergence of specialized and focused CVD care for women.[123] A current estimate of the number of comprehensive HCW programs is challenging, because there is no centralized registration or credentialing, but search engines suggest that there are at least 60 in the United States,[124] 6 in Canada (Vancouver, Toronto, Ottawa, Montreal, Halifax),[125] and a handful throughout the rest of the world (Italy and Singapore).[126] To obtain a more granular assessment of Canadian facilities that offer CV care with a sex and gender focus, the CWHHA recently conducted a nationwide survey of academic and community clinical practices. Table 3 provides a list of HCW where woman-focused CV comprehensive and/or preventive care is provided in Canada; note that these are all located in the more densely populated, larger urban cities.

HCW can drive the implementation of therapeutic advancements and multidisciplinary care (eh, cardiogenetics, cardio-obstetrics, cardio-oncology, cardiorheumatology), while also facilitating the design, implementation, and recruitment for research studies that can improve the representation of women and the translation of knowledge into clinical practice. However, outcomes data suggest that not all women have benefited equally from a reduction in CVD mortality; those in under-represented minority or socioeconomically disadvantaged groups continue to have poorer outcomes.[74] Clearly specialized HCW are needed to provide focused specialty care, but with the primary care "gatekeeper" model of care in Canada, community access for primordial and primary prevention, and initial assessments are essential, with appropriate referrals of higher-level acuity cases to specialized HCW. Advocacy and education are key to promoting community-based CV care for women, especially for racial/ethnic, younger, and/or socioeconomically disadvantaged individuals who might face barriers to access.

Emergency access to CVD care

Perhaps the most glaring example of disparities in access to care for women occur in our EDs. Women diagnosed with ST-elevation myocardial infarction not only take longer to recognize symptoms and seek medical attention, but experience greater delays in door-to-electrocardiogram and door-to-device times.[127] The latter delay is predictive of mortality in men and women,[128] and might explain persistent differences in mortality after ST-elevation myocardial infarction in women. It has been identified that Canadian women who present to EDs with CV health-related concerns report feeling "misunderstood, misinterpreted, misdiagnosed, and mistreated."[129] The causes of missed diagnosis of ACS in women are multifactorial, including variation in presentation symptomatology, differences in terminology used to describe pain (ie, chest tightness or pressure instead of chest pain) and gender nuances in the communication style used by women. Women continue to experience suboptimal treatment delays, the degree of which might vary according to different institutional cardiac catheterization activation protocols. One reported action item for EDs to work toward equitable CV care is the establishment of sex- and gender-specific diagnostic protocols that acknowledge and familiarize with variations in symptomology, terminology, and female-specific risk factors.[130]

The application of protocolized chest pain algorithms in the ED improves the diagnosis of ACS, mitigates treatment delays in both sexes,[131] and leads to reductions in the delay of acute care delivery and resultant mortality gaps observed in women.[132] Such algorithms have been established in most provinces, but there has been no inclusion of sex-specific considerations in their development of standards of care. Improving symptom awareness among women, educating health care professionals on sex-specific clinical presentations, and implementing this information into algorithms are requisite cornerstones to assure access to acute care for women experiencing ACS.[133]

Because there is presently no consensus on what constitutes a female-specific ED protocol, a Canada-wide survey was undertaken to identify the current journey of a women arriving in the ED with chest pain and determine if any Canadian EDs are using female-specific CV protocols. The survey was sent to 450 health care sites between September 2021 and January 2022 and responses were requested by February 2022. Of the 282 respondents, only 1 site noted the integration of female-specific troponin threshold in their routine use. No formal female-specific chest pain protocols were identified.[130]

In 2021, to address this disparity, a point of care emergency clinical summary entitled "Chest Pain in Women in the ER: Focus on Acute Coronary Syndrome" was developed by members of the Knowledge Translation Working Group of the CWHHA. This summary is posted on the British Columbia Emergency Medicine Network Web site (https://www.bcemergencynetwork.ca/clinical_resource/chest-pain-in-women-in-the-er-focus-on-acute-coronary-syndrome) and the Canadian Women's Heart Health Centre Web site (https://www.cwhha.ca/chest-pain-in-the-er). A more detailed and unique algorithm inclusive of symptoms, intersectional risk factors, and management of chest pain in women who present to the ED with chest pain is currently being developed by a Knowledge Translation Working Group Alliance subcommittee.

Access to CV rehabilitation and psychosocial care

Cardiac rehabilitation. In 2022, the first-ever women-focused cardiac rehabilitation (CR) guidelines were released by the International Council of Cardiovascular Prevention and Rehabilitation,[134] and supported by Canadian representation. To close the gap in sex- and gender-biased referral practices, these guidelines state that programs be widely implemented throughout Canada enabling automatic referral in partnership with providers, and be inclusive of enrollment forms and suggested scripts that motivate women to attend.[135] With more women enrolling, there is an opportunity for programs around the world to implement women-focused aspects into their programming to meet the needs of female patients. Customizing program offerings to meet the needs and preferences of women can lead to greater engagement,[136] because it addresses many of their top barriers such as distance, transportation, family responsibilities, and discomfort during exercise.[134] It also leads to improved functional and psychosocial outcomes, however, more research is necessary. The new guidelines provide many suggestions on how this can feasibly be achieved, and provide implementation tools to support programs in their efforts.

Globally, women-only or women-focused programming is currently offered in 110 programs in 38 of 111 countries with CR programs.[137] It appears that only larger programs with many resources are able to offer tailored programming. However, half of the available women-only programs offered around the world are in the Eastern Mediterranean region.[134] As an international leader in women-focused CR, Canada is poised to not only more broadly implement this model of CR in every Canadian province and territory, but also to lead reciprocal collaborations with experts across the globe to facilitate the implementation of women-focused guideline recommendations.

Currently, many efforts are under way in Canada, including: publication of a national CR directory; a national survey of CR programs to identify their needs to augment women-focused program availability; training for CR program staff on sex and gender issues; and cocreation of open access resources to implement women-focused CR programming (eg, education, exercise, psychosocial support).[138]

Beyond women-focused CR programs, a need for specific CR programs for SCAD patients has been recognized, because of the unique demographic population (primarily young women with few traditional CVD risk factors) and the associated enhanced psychological support needed. The role of general CR for SCAD survivors has been evaluated in multiple studies and has been shown to be overall safe and effective.[139-142] Of the studies that evaluated CR for SCAD survivors, there was no reported association between CR participation and recurrent SCAD, MACE, or death.[139-142] Most of the CR programs endorsed conservative exercise prescription characterized by low- to moderate-intensity aerobic exercise with heart rate restrictions (ranging from 50% to 90% of maximum heart rate) and strict blood pressure control,[139,141-143] whereas several other programs allowed patients to progress to higher-intensity exercise.[141,143] The only study that evaluated a SCAD-specific program, reported that exercise prescription, using moderate aerobic exercise (target heart rate 50%-90% and target blood pressure < 130 mm Hg) along with free-weight progressive training (weight limit < 20 pounds) achieved a balance between safety and efficacy.[139] Beyond exercise training, program components that addressed stress reduction, peer support, and behavioural therapy, appeared effective in decreasing some of the high psychosocial burden experienced by SCAD survivors.[139] The high psychosocial burden in this population is well established and might directly affect recovery. Despite a recent study by Saw et al.,[2] who reported a low rate of recurrence at 3-year follow-up, the concern around suffering a repeat event continues to be a legitimate and ongoing contributor to high levels of stress and anxiety for these patients.[144] Psychosocial interventions such as stress management,[141,143,145] peer support,[139,145] mental health counselling,[139,145] mindfulness classes,[139,145] and cognitive behavioural therapy[145] show promise in enhancing health-related quality of life. This is evidenced by documented improvements in depression scores,[139,141] self- reported anxiety levels,[139,143] and perceived stress[139,141] after participation in CR. In addition to these interventions, survivors report wanting SCAD-specific education.[144] Although these studies have limitations, including small sizes, it appears that enhanced

Table 4. Recommendations for improving women's access, enrollment, and outcomes in CR

1. Systematic approaches to CR referral including the use of automatic CR referral at time of acute care discharge in conjunction with care provider and peer liaison endorsement.
2. Alternative programming options (home-based, virtual, women-only) should be available to all women to reduce barriers, with consistent optimization of psychosocial and mental health support, and new strategies to build peer/social support opportunities for women.
3. Standardized triage assessment and algorithms need to be developed and tested to support patient allocation to program models, taking into consideration factors specific to women's identified barriers, needs, and preferences (eg, session timing availability, safety, psychosocial well-being, structured support).
4. More evidence is needed that focuses on implementing women's preferred forms of exercise, as well as exercise prescription optimization and its relation to outcomes, which appear to differ from men's. This research must include specific populations and diagnoses not traditionally represented in CR programs (eg, heart failure with preserved ejection fraction, ischemia with nonobstructive coronary arteries, stress cardiomyopathy, peri/postpartum cardiomyopathy, SCAD).
5. Rigourous research and funding that prioritizes the systematic inclusion of women in all CR and secondary prevention research, sex-based analysis and understanding of sex-related anatomy and physiology, expanded understanding of gender roles, behaviours, and influences on CR patients and programming.
6. The COVID-19 pandemic has presented unique challenges to the health care system and CR care provision; research is needed to evaluate the use of digital health technology, eHealth, mobile health, artificial intelligence, and remote monitoring/supervision, which can offer potential options to overcome barriers to women's participation and CR completion.
7. Continued advocacy (government/charitable foundations, funding agencies) and investment in education/awareness campaigns targeting the general public and health care providers related to CR referral and capacity-building (including integration of women-focused aspects). This should also include advocacy to ensure women's safety in exercising outdoors.
8. Development of women-focused CR programs, especially for certain CVD entities that are not infrequent, and that are unique to, or more common in women (eg, SCAD).

CR, cardiac rehabilitation; CVD, cardiovascular disease; SCAD, spontaneous coronary artery dissection.

psychosocial support is essential for SCAD survivors, yet the precise delivery of such interventions is unknown and requires further research. In the interim, CR that consists of tailored exercise prescriptions along with SCAD-specific program components, including enhanced psychosocial support appears beneficial in this population. Table 4 provides recommended actions for improving women's access, enrollment, and outcomes in CR.

Psychosocial care. There is a clear need for improved mental health screening and research in women with CVD, because they are most at risk, and least studied, compared with men. Women are disproportionately affected by symptoms of depression and anxiety acutely during, and when recovering from, a cardiac event.[146] A systematic review of 20 longitudinal studies indicated that more women than men report depression during hospitalization with coronary heart disease (36% vs 23%), and this trend continued over 2 years (23% vs 20%).[147] Similarly, after a CVD diagnosis, Bouchard et al. report that anxiety is much higher in women compared with men during hospitalization, immediately postdischarge, and up to 12 months postevent.[148] The effects of depression and anxiety on women's CV health can be hazardous. A systematic review and meta-analysis including > 225,000 women from 56 studies showed that psychological distress (defined broadly as anger, hostility, anxiety, depression, social isolation, type A behaviour pattern, type D personality, and post-traumatic stress disorder) was associated with a 21% increased risk of major adverse CV events among women with ischemic heart disease.[149]

Mental health screening is recommended, but not consistently performed, during hospitalization for an acute cardiac event. It is also recommended that screening continue at regular intervals throughout the recovery period. Several validated screening tools are available to researchers and clinicians, many of which are available in a wide variety of languages and are easy and quick to use, with minimal patient, researcher, or clinician burden (eg, Patient Health Questionnaire-9,[150] Hospital Anxiety and Depression Scale,[151] Generalized Anxiety Disorder Assessment-7,[152] Cardiac Anxiety Questionnaire[153]). CR provides opportunities to track women's mental health symptoms, but because women are less likely to participate in these programs, their symptoms might not be systematically identified, monitored, or addressed. There is burgeoning evidence that indicates that clinical and behavioural interventions might be beneficial for the treatment of depression and anxiety in patients with CVD, but women comprise a minority in these investigations (approximately 25% in studies within the most recent meta-analysis).[154]

What can accelerate these needed changes?

Education and training. Despite increasing awareness of sex- and gender-based differences in medicine, there remains a profound lack of formal sex- and gender-specific integrated curricula in North American medical schools. Although medical students recognize the importance of sex- and gender-specific medical education, less than half report that their medical curriculum provides appropriate training for clinical management of these issues.[155] A recent sex and gender based medicine faculty survey administered to 44 medical schools across the United States and Canada showed that 70% of responders had no formal curriculum.[155] Within medical residency programs, limited training opportunities for CVD risk and prevention in women exist, although more than 90% of residents agreed this was a very important women's health topic.[156] There are similar gaps within cardiology residency training programs. Less than one-third of practicing cardiologists reported cardio-obstetrics didactic training during their residency programs, along with very limited exposure to pregnant patients. This is striking because 76% of surveyed cardiologists lack access to dedicated cardio-obstetrics teams.[157] Moreover, there is no specific education regarding women's

heart health in nursing curricula in Canadian nursing schools, which is most concerning, because nurse contact is often the first, and sometimes, only health care provider interface for many Canadians, especially those in rural environments.

These gaps clearly need to be met with the development of a core CVD component, ideally within a comprehensive women's health curriculum, at the undergraduate and postgraduate levels for all health care providers. Considerations should be made for curricular collaboration among different specialties such as obstetrics/gynecology, family medicine, internal medicine, and cardiology. Joint core competency assessments, postgraduate faculty development, and continuing medical education courses are recommended. Efforts are being made in this direction; recently, the Institute of Gender and Health within the Canadian Institutes of Health Research, has partnered with the University of Toronto's Collaborative Graduate Program in Women's Health to improve sex and gender competency in medicine, but their focus has been solely on postgraduate education.[158] The Training and Education Working Group of the CWHHA has developed a series of educational modules, accredited by the CCS, which are available for integration into existing health care provider curricula.[159]

Advocacy, population education, and campaigns. Although campaigns in the United States have been associated with raising women's awareness of their leading cause of death, this increased awareness has generally been limited to women from higher socioeconomic backgrounds and those who identify as Caucasian.[160,161] Some women reported feeling empowered to take responsibility for their health as a result of perusing campaign materials, whereas others noted tensions in health equity within cultural and historical contexts.[162,163] Unfortunately, women from racial, ethnic and socioeconomic backgrounds who are most at risk for CVD have been reported to be systematically excluded in social media campaigns, which include donation and merchandise sale intents.[164,165] Further, the benefits of lifestyle changes within most women's means were minimized to support paternalistic institutional practices for affluent, heteronormative women.[166,167] It is perhaps not surprising then, that American surveys of CVD awareness in women showed an initial improvement in 2007, but then a decrement in 2012.[160]

The CWHHA has emphasized inclusivity in all educational materials, and to reach diverse ethnic populations, has translated all "key message" infographics into > 15 languages, including: Arabic, simplified Chinese, traditional Chinese, Creole, French, Hindi, Inuktitut, Portuguese, Punjabi, Russian, Spanish, Swahili, Tagalog, Vietnamese, American sign language, and Quebec sign language. To engage the public in conversations on social media on women's heart health risk reduction, it is imperative that in the design and implementation of these awareness and information campaigns the following considerations be made:

1. Women's racial, ethnic, and other cultural identities and norms in risk identification and reduction;
2. Women's access to services when presenting options for medical care; and
3. Diversity in gender identities and roles in health maintenance.

Research. Those of female gender and women remain underrepresented in research and there has been a lack of sex- and gender-based analysis in research studies, which hinders our understanding of the underlying mechanisms of CVD in women. This has led to significant knowledge gaps in terms of the epidemiology, pathophysiology, presentation, diagnosis, drug metabolism, treatment effects, and other outcomes in women's CVD. Addressing these gaps in knowledge requires a multifaceted approach, including integrating sex and gender considerations into all aspects of research design, execution, and reporting. Specific recommendations to facilitate improvements include:

- Improving the education of trainees by: emphasizing the importance of sex and gender considerations in CVD research; providing training on sex and gender concepts and methods; encouraging the use of sex and gender analysis tools; facilitating collaboration with sex and gender CVD experts; and, fostering a culture of inclusivity, diversity, equity, and accessibility to encourage trainees to maintain this culture in their future career.
- Enhancing recognition among faculty, scientists, and researchers of the critical role that sex and gender play in shaping CVD health outcomes and leading to more accurate and comprehensive results.
- Ensuring funding agencies continue to develop and enforce guidelines and policies requiring researchers to consider and incorporate sex and gender factors in their research design, analysis, and reporting.
- Adding sex- and gender-reporting guidelines and requirements to scientific journal, learned societies, and scientific conference submissions.
- Ongoing advocacy on the part of patients, families, public, health providers, researchers, and others for the incorporation of sex and gender considerations in CVD research.

How does Canada compare globally in women's heart health research and funding?

In the context of increasing rates of premature CVD in Canadian women,[168] it is essential that we examine Canada's evolving contributions to women's heart health in a global context. A comprehensive search was conducted from 2002 to 2022 by a library information sciences expert using PubMed, Scopus, and EMBASE databases with the intent to provide a high-level overview of how Canada compares globally in relation to publications (documents) and funding agencies targeting women's CV health and research (see Supplemental Appendix S1 for detailed search and search terms). The total number of documents was identified according to country/region and funding sponsor (Table 5), respectively indexed to country/region size according to population (using 2020 National Census Data) and to economic wealth by gross domestic product (GDP; using 2020 World Bank Data). Canada ranked first in terms of the total number of documents produced (9.7 per 1 million population), followed by the United States and Australia, respectively, at 7.9 and 7.7 documents per 1 million population (Fig. 2B). Canada also ranked first in terms of the total number of documents (229)

Table 5. Comparison of women's cardiovascular disease-related documents, funding agencies, and GDP across regions

Region or country	Documents, n	Funding agencies, n	Countries, n	Population 2020 (millions)	GDP (trillion USD$)	Documents per 1 million population	Documents per USD$ 1 trillion GDP	Funding agencies per USD$ trillion GDP, n
Canada	367	11	1	38	1.6	9.7	229.5	6.9
United States	2598	80	1	331.4	20.9	7.8	124.3	3.8
Australia	197	5	1	25.7	1.3	7.7	151.5	3.8
United Kingdom	398	13	1	67.1	2.7	5.9	147.4	4.8
Europe	1973	32	36	447	15.3	4.4	129	2.1
Asia/Middle East	1094	14	37	4191	35.5	0.3	30.8	0.4
Latin America	137	5	13	409	4.7	0.3	29.1	1.1
Africa	106	0	21	1300	2.4	0.1	44.2	0
Undefined	506							
Total	7376	160						

GDP, gross domestic product.

Source: National Census, where applicable, and World Bank data. Several countries are presented and we chose to combine countries/regions to facilitate comparison with all European Union nations including the Republic of Ireland and the United Kingdom made up of Northern Ireland, Scotland, Wales, and England. The total number of funding agencies but not dollars were obtained.

per 1 trillion GDP, whereas the United States (124.3) ranked fifth in comparison (Fig. 2C). Although Canada ranks fifth with regard to the total number of funding agencies relative to other countries/regions, it is first with respect to funding agencies per 1 trillion GDP (Table 5). Considering population size and funding structures, Canada remains competitive in the global landscape despite the limited total funding directed specifically to women's CVD research. Multinational collaborations are key to optimize the limited global research dollars in smaller countries and opportunities for a global effect on CVD in women. The trajectory of progress made in Canada compared with other countries and continents varies depending on the specific initiative. On the basis of our search, we created an illustration to provide a quick snapshot of the progress for various topics across continents using a "stoplight of action" with red meaning little or no progress;

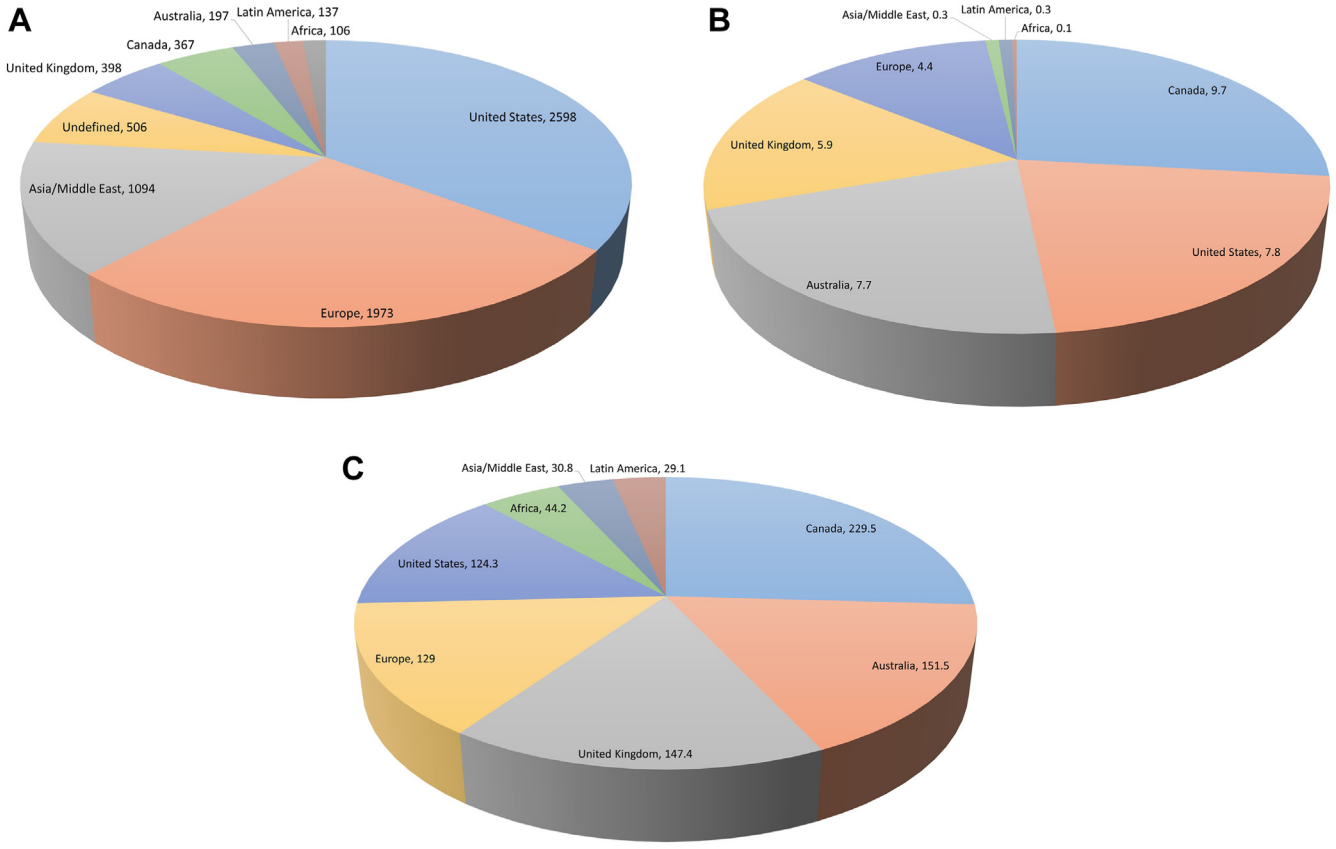

Figure 2. (**A**) Country rankings in terms of total number of women's cardiovascular health publications (documents). (**B**) Country rankings in terms of women's cardiovascular health publications (documents) per 1 million population. (**C**) Country rankings in terms of women's cardiovascular health publications (documents) per 1 trillion gross domestic product.

Country / Region & Area of Focus	Canada	USA	Europe	Australia & New Zealand	Asia	Africa	South America
Training & Knowledge Gaps	Green	Green	Green	Green	Yellow	Yellow	Yellow
Research	Yellow to Green	Yellow to Green	Yellow to Green	Yellow	Yellow	Yellow	Yellow
Funding: Grants & Scholarships	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Academia: Education & Leadership	Yellow	Green	Yellow	Yellow	Yellow to Red	Red	Red
Journal Publications & Conferences	Yellow to Green	Yellow to Green	Yellow to Green	Yellow to Green	Yellow	Yellow	Yellow
Guidelines	Red to Yellow	Yellow to Green	Yellow to Green	Red to Yellow	Red to Yellow	Red to Yellow	Red to Yellow
Health Policy & Advocacy	Yellow to Green	Yellow to Green	Yellow to Green	Yellow to Green	Yellow to Green	Yellow to Green	Yellow to Green
Patient Partners & Considerations	Yellow to Green	Yellow to Green	Yellow to Green	Yellow to Green	Yellow to Green	Yellow to Green	Yellow to Green

Figure 3. Stoplight of action in the various areas of women's cardiovascular health.

yellow, beginning progress; and green, significant progress (Fig. 3).

Historically, the United States has led several prominent initiatives addressing CVD in women. The **W**omen's **I**schemia **S**yndrome **E**valuation (WISE) study,[169] sponsored by the National Institutes of Health along with the AHA Go Red campaign, have made important contributions to our understanding of women's heart health. There are established women's heart health programs across the United States that help with the delivery of patient care to women, but also serve to train the next generation of health care providers interested in delivering specialized care to women.[126] However, in the private payer system, there is also a financial incentive to market these programs to affluent socioeconomic sectors, that might not appropriately address the disparities in CVD care for women.

As described briefly, an international female-led effort, including Canadian representation, to reduce the worldwide CVD burden in women by 2030 was recently established with formation of *The Lancet* Women and Cardiovascular Disease Commission.[78] A global report and call to action was authored by 17 women experts from 11 countries and published in *The Lancet* coincident with inaugural presentation at the 70th Annual Scientific Session of the ACC in 2022. *The Lancet* Women and Cardiovascular Disease Commission outlines 10 recommendations to reduce inequities in the prevention, diagnosis and treatment of CVD in women with the goal to reduce the CVD burden by 35% and to reduce premature deaths by one-third by 2030 (Table 6). This is to be achieved through targeted education of health care providers and patients for early detection and prevention of women's heart disease, implementation of and improved access to women's heart health programs, especially for underdeveloped regions, and prioritization of sex-specific research for women's heart disease.

Canada has recently become a leader in women's CV health. Since the establishment of the CWHHA in 2018,

Table 6. Recommendations for reducing CVD risk and for disease management strategies in women from *The Lancet* Women and Cardiovascular Disease Commission

1. Direct funding for real-time and accurate data collection on prevalence and outcomes of CVD in women globally
2. Develop educational programs on CVD in women for physicians, scientists, allied health care providers, and communities
3. Prioritize sex-specific research focused on identifying the pathophysiology and natural history of CVD
4. Develop strategies to improve enrollment and retention of women in cardiovascular clinical trials
5. Prioritize funding in global health organizations for CVD health programs in women from socioeconomically deprived regions
6. Educate health care providers and patients regarding early detection and prevention of CVD in young women
7. Establish policy-based initiatives and medical and community outreach CVD risk factor programs in settings frequented by women
8. Research is needed to identify the effect of sex-specific, psychosocial, and socioeconomic risk factors on CVD in women, and evaluate intervention strategies
9. Scale up healthy heart programs in highly populated and progressively industrialized regions
10. Embrace public-private partnerships to develop broad scale programs to save lives in women with CVD

CVD, cardiovascular disease.

Table 7. Recommended actions to address remaining gaps in cardiovascular care for women in Canada

- Recognize and understand that there are sex-specific, and sex-"more common" cardiovascular risk factors and manifestations of CVD
- Include multidisciplinary, collaborative didactic, and clinical practice training specifically addressing sex and gender within core curricula at the undergraduate and postgraduate levels, and continuous medical education, for all health care providers
- Implement CVD risk prediction tools that include sex-, gender-, race-, and ethnicity-specific components
- Develop a national health systems strategy for incorporating postpartum cardiovascular care into existing prevention care models
- Continue advocacy campaigns to increase awareness of CVD in women, but ensure that they use inclusive and culturally sensitive materials to reach marginalized individuals in vulnerable communities
- Use sex-specific algorithms, including sex-specific thresholds for high-sensitivity troponin analysis to diagnose ACS in women who present with acute chest pain symptoms
- Refer automatically, and encourage enrollment and participation in CR by women who have experienced ACS or HF; establish and utilize women-focused CR programs; provide peer support opportunities
- Perform mental health screening during hospitalization for an acute cardiac event and provide appropriate treatment and resources
- Utilize resources of specialized heart centres for women for higher-level acuity cases, where available, and broaden their availability
- Require the inclusion of sex, gender, and racialization considerations in research protocol methodology, results analysis, and discussion, for all levels of research, including registries
- Increase the representation of female patients and female investigators in CVD clinical trials
- Develop Canadian CVD guidelines with sex- and gender-specific recommendations, whenever possible

ACS, acute coronary syndromes; CR, cardiac rehabilitation; CVD, cardiovascular disease; HF, heart failure.

there has been a concerted effort toward advocacy and care of women's heart health through partnerships between health care providers, allied health, and people with lived experience with CVD. Within the CWHHA governance, 4 working groups were established, each co-led by a health care provider and a lived experience partner, in the following domains: knowledge translation and mobilization, health systems and policy, training and education, and advocacy, and have worked together to enhance our understanding of women's heart health and improve research and patient care. The full extent of these initiatives are available at www.cwhha.ca. Perhaps the most formidable achievements include the Wear Red Canada advocacy campaign and this Women's Heart Health Atlas. The current document is the last of 9 intended chapters, each having been focused on particular aspects of women's CV health and disease, including epidemiology, pathophysiology, diagnosis, treatment, research, and advocacy, all through the lens of sex and gender influences on CV health and disease.[74,85,108,129,170-172] The publication of each "chapter" has been accompanied by an educational webinar, intended for professional and lay audiences, as well at TwitterChat tutorials. This is a first-of-a-kind women's heart health atlas in the world, and Canada's diverse population provides a unique intersectional perspective. This series of publications has created a foundation that places Canada on the world stage, providing a forum for many of the experts on women's heart health to accelerate their research activities and to disseminate their knowledge of CVD care for women.

Summary of Recommendations

Proposed solutions to resolve the remaining gaps in CV care for women are interconnected, yet can be categorized into 4 broad areas: education, clinical care, research, and awareness advocacy. Specific recommendations and action items in each of these areas are detailed in Table 7. The inclusion of evidence-based sex and gender content in the learning objectives and core curricula of undergraduate, postgraduate, continuing education, and practical health care training is required to assure a health care workforce that can recognize, diagnose, and treat CVD in women. Inclusion of sex and gender in the assessment, prevention, diagnosis, and management of CVD and CVD risk factors will improve CVD outcomes for women. Sex- and gender-based analyses and greater inclusion of women in CV clinical trials will build an evidence base to create guidelines that can be disseminated broadly in the health care domain. The maintenance and intensification of advocacy efforts using principles of inclusivity and cultural sensitivity is essential to continue to amplify awareness of CVD as a leading threat to quality life for women in Canada. These specific recommended actions in the research, education, awareness, and clinical care are required to resolve gaps in CVD care for women in Canada to achieve the ultimate goal of improved CV outcomes.

Conclusions

In this concluding chapter of the CWHHA Atlas series on the epidemiology, diagnosis, and management of CVD in women, we have provided a summary addressing the current status and challenges in the presentation, diagnosis, treatment, and prognosis of CVD in women. We have defined comprehensive CV care for women and emphasized its foundation in appropriate training, education, awareness, and research. We conclude with recommended solutions to address persisting knowledge gaps and disparities in CV care for women in Canada by detailing specific actions to be taken in the domains of education, clinical care, research, and advocacy.

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Heart Health Centre at the University of Ottawa Heart Institute.

Ethics Statement

The research reported has adhered to the relevant ethical guidelines.

Patient Consent

The authors confirm that patient consent is not applicable to this article because no patient data were used in this review.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2023.12.001.