CHAPTER 6
Sex- and Gender-Specific Cardiovascular Diagnosis and Treatment

CWHHA ATLAS ON THE EPIDEMIOLOGY, DIAGNOSIS AND MANAGEMENT OF CARDIOVASCULAR DISEASES IN WOMEN

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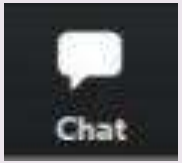
WELCOME & HOUSEKEEPING



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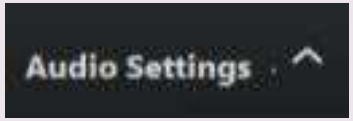

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DISCLOSURE STATEMENT

We do not have an affiliation (financial or otherwise) with a commercial organization that may have a direct or indirect connection to the content of this presentation.

Learning Objectives

At the end of this webinar, you will be able to:

- Discuss the diagnosis for CAD, stroke, valvular heart disease, and heart failure.
- Explain pharmacologic and non-pharmacologic treatment strategies for CAD, stroke, valvular heart disease, and heart failure.
- Describe the benefits and barriers to self-management and cardiovascular rehabilitation/secondary prevention programs.

Canadian Women's Heart Health Alliance (CWHHA)

LAUNCHED IN 2018

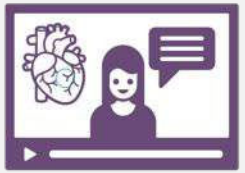
Over 130 members!

Mission: Disseminate education and best practices re: Women's cardiovascular (CV) health among **healthcare providers and women with lived experience.**

Goal: Eliminate knowledge gaps in specific CV issues and develop new practice considerations in care for women, thereby improving the health of Canadian women.

CWHHA WORKING GROUPS

Advocacy



Training and Education

Knowledge Translation and Mobilization

Health Systems and Policy

Sex and Gender Definitions

SEX

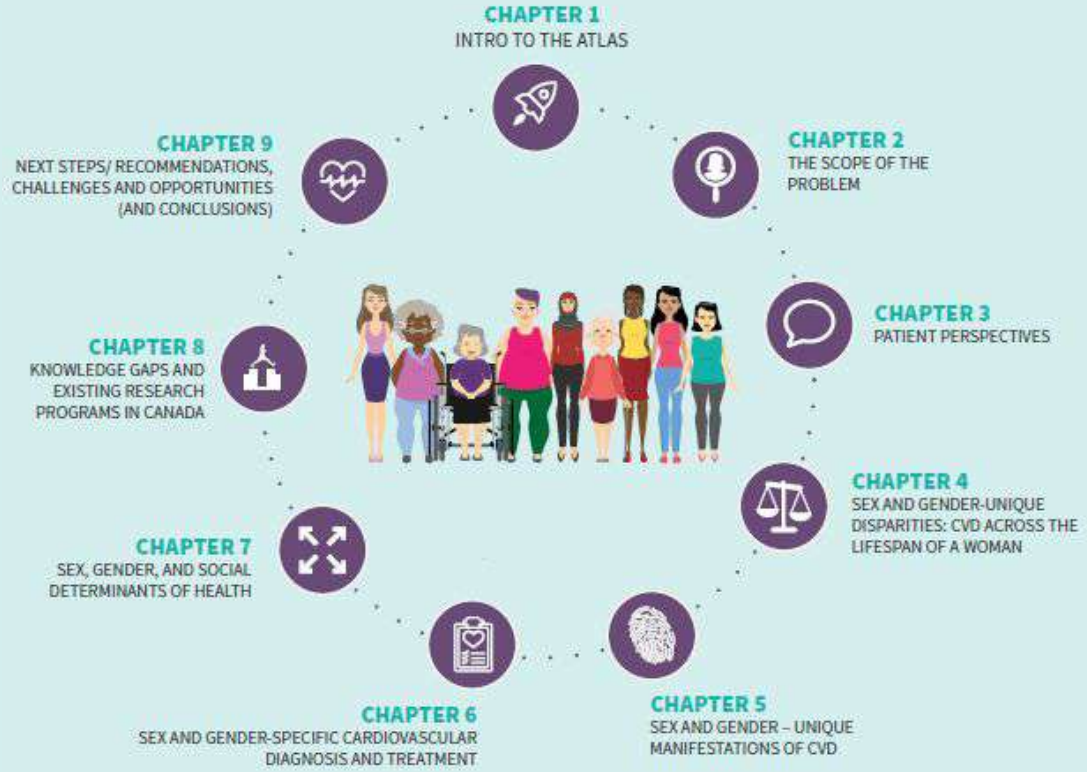
- Biology – chromosomes at birth (female/male)
- Encompasses hormones, genes, anatomy, physiology, etc.

GENDER

- Socially influenced determination (man/woman)
- Is culturally specific and temporal

CANADIAN WOMEN'S HEART HEALTH ALLIANCE ATLAS

Epidemiology, Diagnosis, and Management of Cardiovascular Diseases in Women



- 9 unique "chapters"
- CJC Open
- Editor: Dr. M. Graham
- 1st: published April 2020
- Annual chapter updates
- "Living document"

Norris CM ….. Mulvagh SL. CJC Open 2020

CATHERINE'S STORY

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REVIEW | ARTICLES IN PRESS

The Canadian Women's Heart Health Alliance Atlas on the Epidemiology, Diagnosis, and Management of Cardiovascular Disease in Women-Chapter 6: Sex- And Gender-Specific Diagnosis and Treatment

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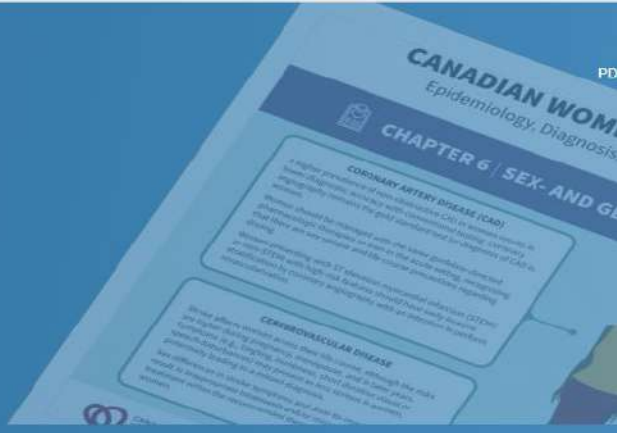
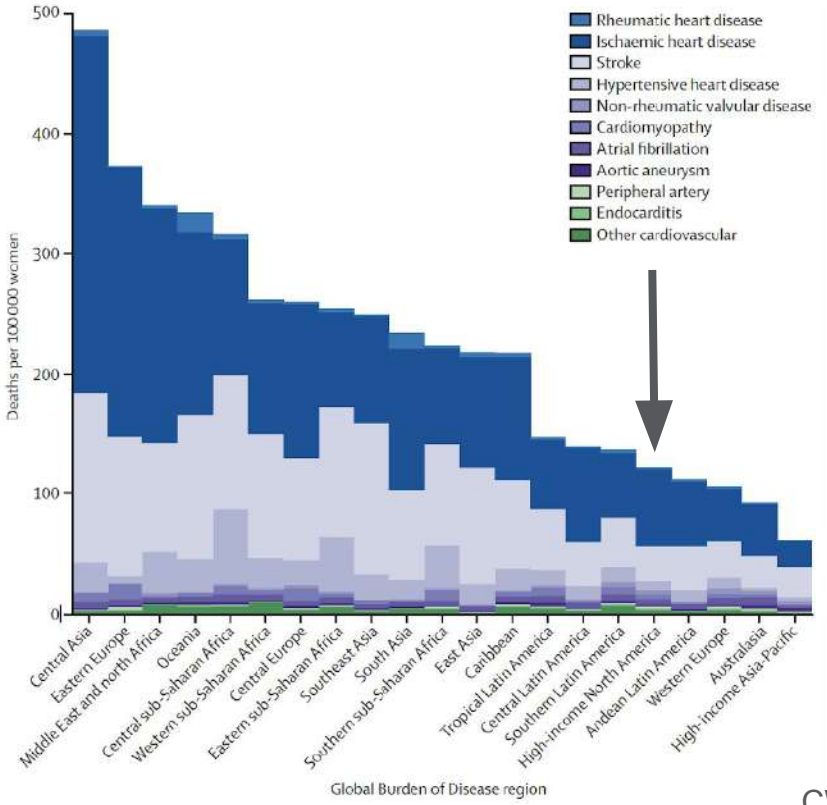


Abstract

This chapter summarizes the sex- and gender-specific diagnosis and treatment of acute/unstable presentations and non-acute/stable presentations of cardiovascular disease in women. Guidelines, scientific statements, systematic reviews/meta-analyses, and primary research studies related to diagnosis and treatment of coronary artery disease (CAD), cerebrovascular disease (stroke), valvular heart disease (VHD), and heart failure in women were reviewed. The evidence is summarized as a narrative and, when available, sex- and gender-specific practice and research recommendations are provided. Acute coronary syndrome (ACS) presentations and emergency department delays are different in women compared to men. Coronary angiography remains the gold standard test for diagnosis of obstructive CAD. Other diagnostic imaging modalities for ischemic heart disease detection (e.g., positron emission tomography, echocardiography, single-photon emission computed tomography, cardiovascular magnetic resonance, coronary computed tomography angiography [CCTA]) have been shown to be useful in women, with their selection dependent upon the goal of the individualized assessment, and testing resources available. Non-contrast computed tomography (CT) and CT angiography are used to diagnose stroke in women. Although there appears to be sex-specific differences in the efficacy of standard treatments for diverse presentations of ACS, many cardiovascular drugs and interventions tested in clinical trials were not powered to detect sex-specific differences and knowledge gaps remain. Similarly, although knowledge is evolving about sex-specific

Age-Standardized CVD Deaths per 100,000 Women Across Global Burden of Disease Regions in 2019



Vogel et al, 2021, Lancet, 397: 2385-2438.

CANADIAN WOMEN'S HEART HEALTH ALLIANCE ATLAS

Epidemiology, Diagnosis, and Management of Cardiovascular Disease in Women

CHAPTER 6 | SEX- AND GENDER-SPECIFIC DIAGNOSIS AND TREATMENT

CORONARY ARTERY DISEASE (CAD)

A higher prevalence of non-obstructive CAD in women results in lower diagnostic accuracy with conventional testing. Coronary angiography remains the gold standard test for diagnosis of CAD in women.

Women should be managed with the same guideline-directed pharmacologic therapies as men in the acute setting, recognizing that there are sex-unique and life-course precautions regarding dosing.

Women presenting with ST elevation myocardial infarction (STEMI) or non-STEMI with high-risk features should have early invasive stratification by coronary angiography with an intention to perform revascularization.

CEREBROVASCULAR DISEASE

Stroke affects women across their life course, although the risks are higher during pregnancy, menopause, and in later years. Symptoms (e.g., tingling, numbness, short duration visual or speech disturbances) may present as less serious in women, potentially leading to a missed diagnosis.

Sex differences in stroke symptoms and door-to-imaging times result in inappropriate treatments and/or missed opportunities for treatment within the recommended therapeutic time window for women.

VALVULAR HEART DISEASE

Current guidelines for the diagnosis and management of patients with valvular heart disease (VHD) have limited sex-specific recommendations, despite numerous sex-specific evaluations and outcomes having been reported.

HEART FAILURE

Women are less likely than men to receive certain heart failure medications, such as angiotensin-converting enzyme inhibitors.

Treatment of heart failure with preserved ejection fraction (HFpEF) includes treatment of comorbid conditions, with a need for more clinical trials stratified by sex.

CARDIOVASCULAR REHABILITATION

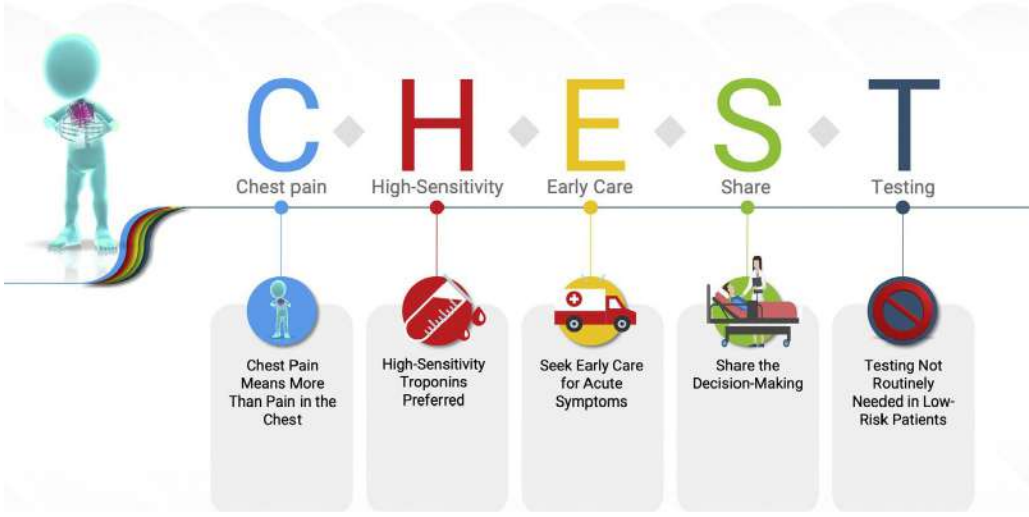
All women should be referred for cardiovascular rehabilitation/secondary prevention (CR/SP) after an acute cardiovascular event. However, women are less likely than men to be referred to or participate in CP/SP programs.

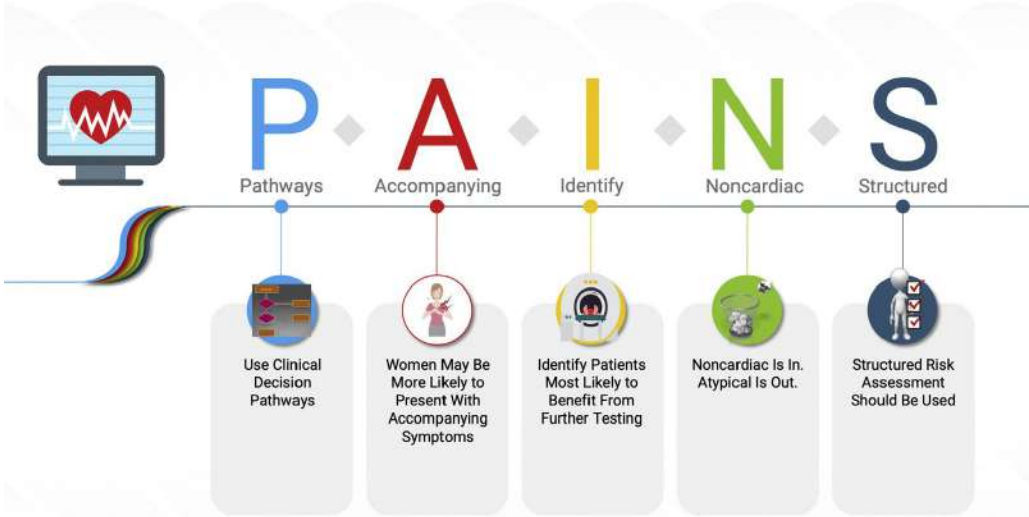
Women's reduced participation in CR/SP programs is due to an array of demographic, socioeconomic, medical, and societal challenges faced by women.

Evaluation and Diagnosis of Acute Chest Pain

Cardiac
Possibly Cardiac
Noncardiac

Anginal Equivalents
Atypical





Gulati et al, 2021, JACC, 78(22).

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KEY MESSAGE # 1

Women who present with acute chest pain are at risk for underdiagnosis, and potential cardiac causes should always be considered.

- Obtain a history that emphasizes accompanying symptoms that are more common in women with ACS.
- A focused cardiovascular exam is needed.
- An ECG should be obtained and reviewed within 10 minutes of arrival to ED.
- cTn should be measured as soon as possible after presentation. Consider sex-specific hs cTn.

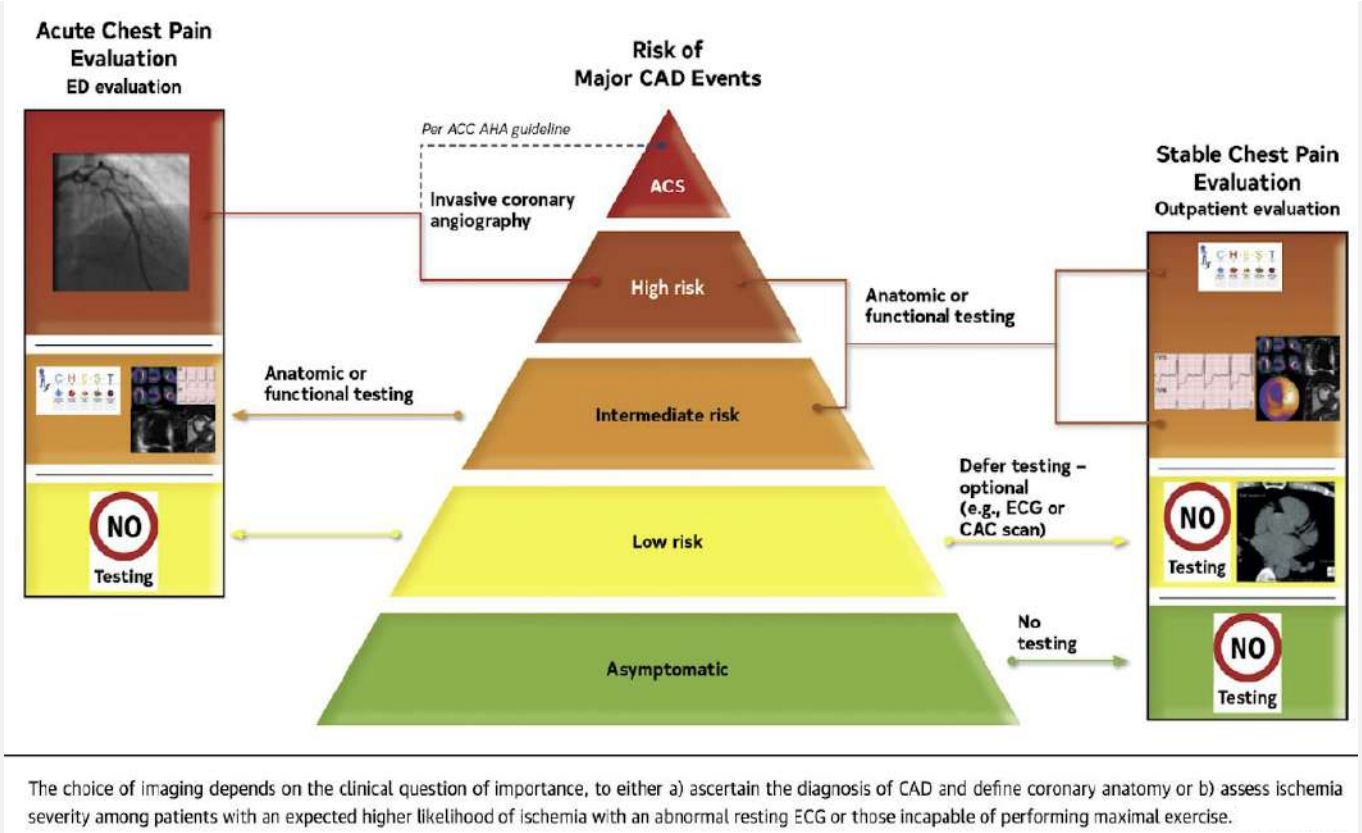
Gulati et al, 2021, JACC, 78(22).

Recommendations for Acute Chest Pain

1. If initial ECG is nondiagnostic, serial ECGs to detect potential ischemic changes should be performed.
2. If initial ECG is consistent with an ACS, then treat according to STEMI and NSTE-ACS guidelines.
3. If there is an intermediate-to-high clinical suspicion for ACS when initial ECG is nondiagnostic, serial ECGs V7 to V9 can assist to rule out posterior MI.

Gulati et al, 2021, JACC, 78(22).

Other Cardiac Testing Considerations



The choice of imaging depends on the clinical question of importance, to either a) ascertain the diagnosis of CAD and define coronary anatomy or b) assess ischemia severity among patients with an expected higher likelihood of ischemia with an abnormal resting ECG or those incapable of performing maximal exercise.

Gulati et al, 2021, JACC, 78(22).

KEY MESSAGE # 2

Coronary angiography is the gold standard test for diagnosis of obstructive CAD.

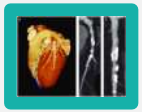
Additional Noninvasive Diagnostic Testing:

Exercise ECG
Able to achieve ≥ 5 METs

Stress Nuclear
(e.g., PET or SPECT)

Echocardiography
(e.g., transthoracic, stress)

Cardiovascular Magnetic Resonance Imaging (CMR)



Coronary Computed Tomography Angiography (CCTA)

Should follow a clinical decision pathway.

KEY MESSAGE # 3

Various non-invasive imaging strategies are used for stable or non-acute presentations of chest pain.

Exercise treadmill testing is rapid, inexpensive, and is the most common non-invasive test for low risk women who can exercise.

IMPROVED DIAGNOSTIC AND PROGNOSTIC EVALUATION

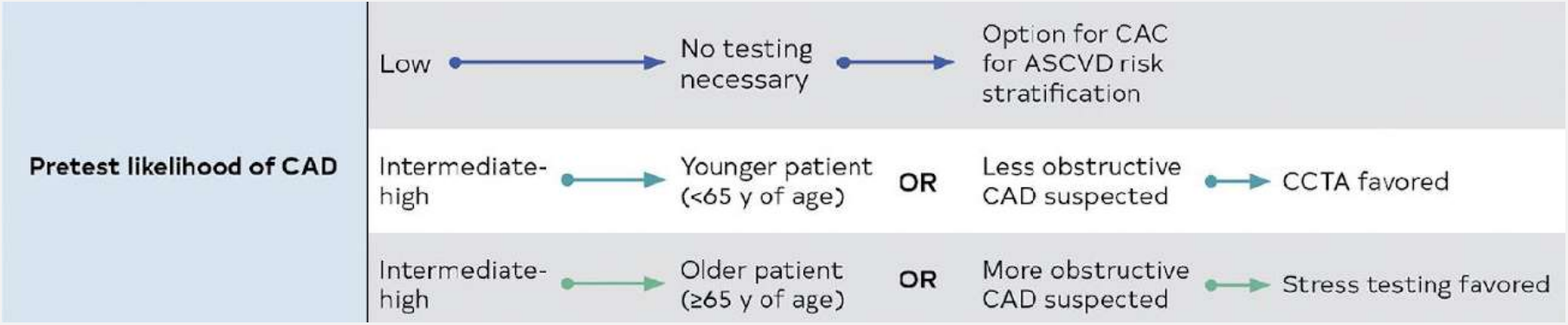
- Integrate multiple parameters (e.g., exercise time, changes in ST-segment, presence of angina)
- Additional risk correlates are heart rate and blood pressure response and recovery

CONTRAINDICATIONS

- Abnormal ST changes on resting ECG
- Some rhythm disturbances
- Unable to achieve ≥ 5 METs
- Severe symptomatic aortic stenosis
- Uncontrolled heart rate or HTN

Gulati et al, 2021, JACC, 78(22).

What is the Correct Diagnostic Test?



Gulati et al, 2021, JACC, 78(22).

KEY MESSAGE # 4

Recommendations for the Pharmacologic Management of Women with Stable CAD.

Strong Recommendation
Conditional Recommendation
High Quality Evidence
Moderate Quality Evidence

- ASA 81MG DAILY OR CLOPIDOGREL 75MG DAILY
- DUAL ANTIPLATELET THERAPY SHOULD NOT BE USED ROUTINELY
- STATINS AS PER DYSLIPIDEMIA GUIDELINES
- ACE-I OR ARB
- BETA-BLOCKERS IF LVEF < 40%
- CALCIUM CHANNEL BLOCKERS

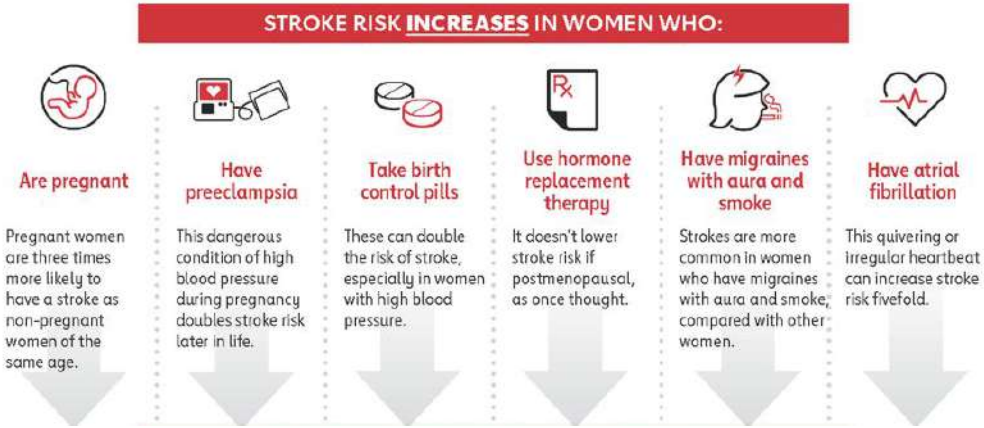
Recommendations for Non-Pharmacologic Management of Women with Stable CAD

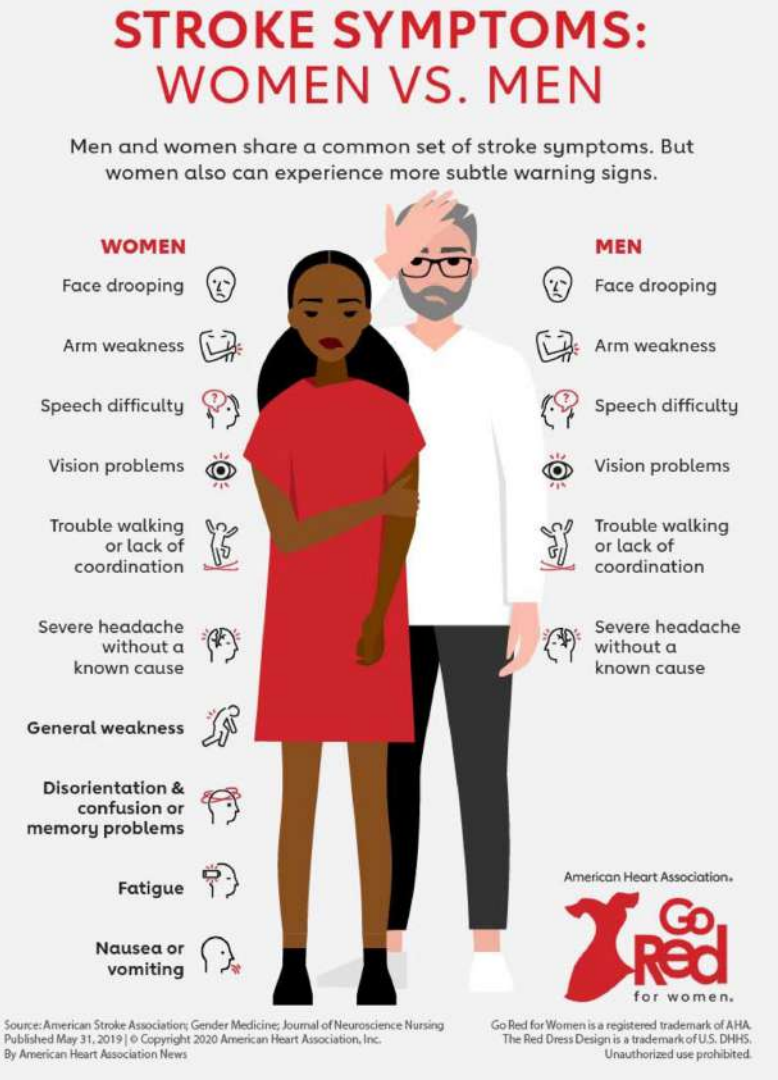
Coronary artery bypass graft (CABG) surgery is considered the gold standard for revascularization for multivessel CAD with diabetes that is not amenable to PCI.

*The ISCHEMIA trial failed to show that routine invasive therapy reduced MACE compared to optimal medical therapy (23% females).

Hillis et al, 2011, Circulation, 124: 2610-2642.
Teo et al, 2014, CJC, 30: 1482-1491.
Reynolds et al, 2021, Circulation, 144: 1024-1038.

Cerebrovascular Disease (Stroke)





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KEY MESSAGE # 5

Stroke affects women across their life course. Risks are highest during pregnancy, menopause and in later years.

Recognize nontraditional symptoms of tingling, numbness, visual/speech disturbances.

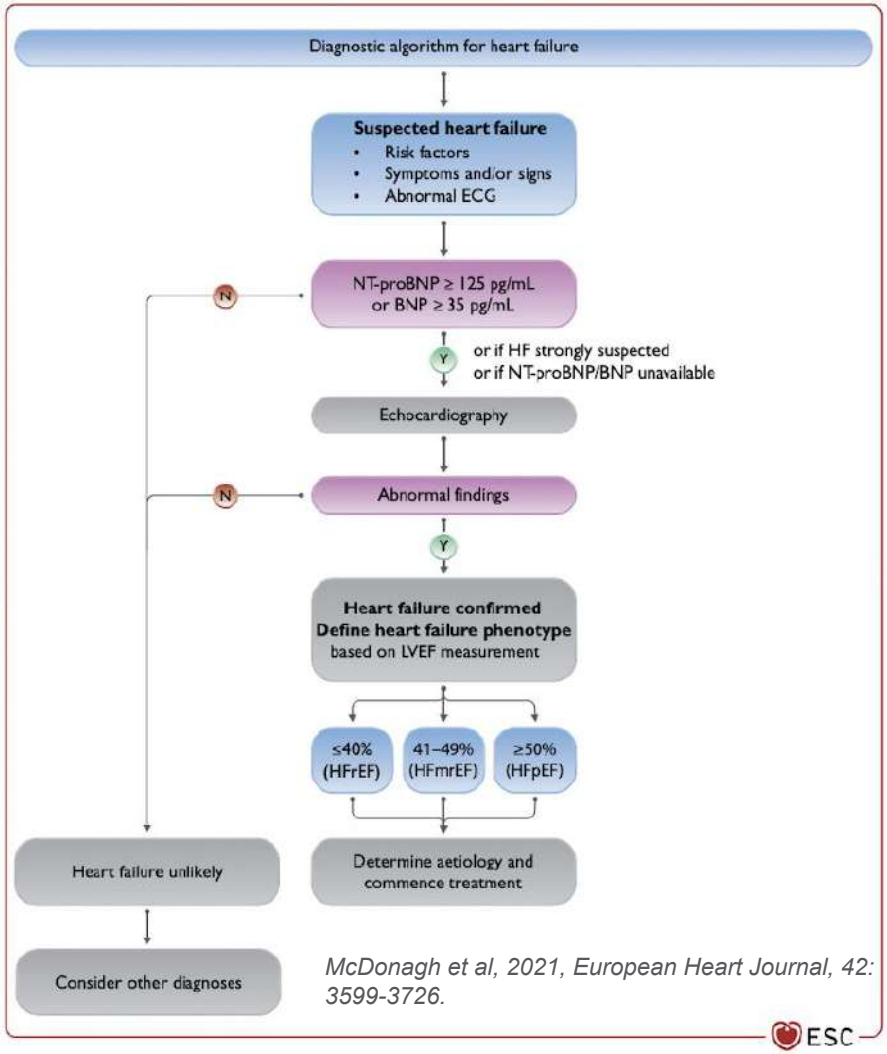
Heart Failure

- **Second cause of hospitalization, third cause of death in women**
- **Symptoms**
  - Shortness of breath, fatigue, swelling
- **Underlying mechanisms**
  - Heart is too stiff (HFpEF) - more frequent in women (55%)
  - Heart is too weak (HFrEF) (29% women)
- **Causes**
  - Previous heart attacks (ischemic)
  - Toxic: alcohol, illicit drugs, chemotherapy
  - Valvular heart disease
  - Genetic
  - Cardiomyopathies

Diagnostic Algorithm for Heart Failure

NT-proBNP sex-specific cutoffs are not recommended.

NT-proBNP differs by sex, increases with age, and varies by HF phenotype.



McDonagh et al, 2021, European Heart Journal, 42: 3599-3726.

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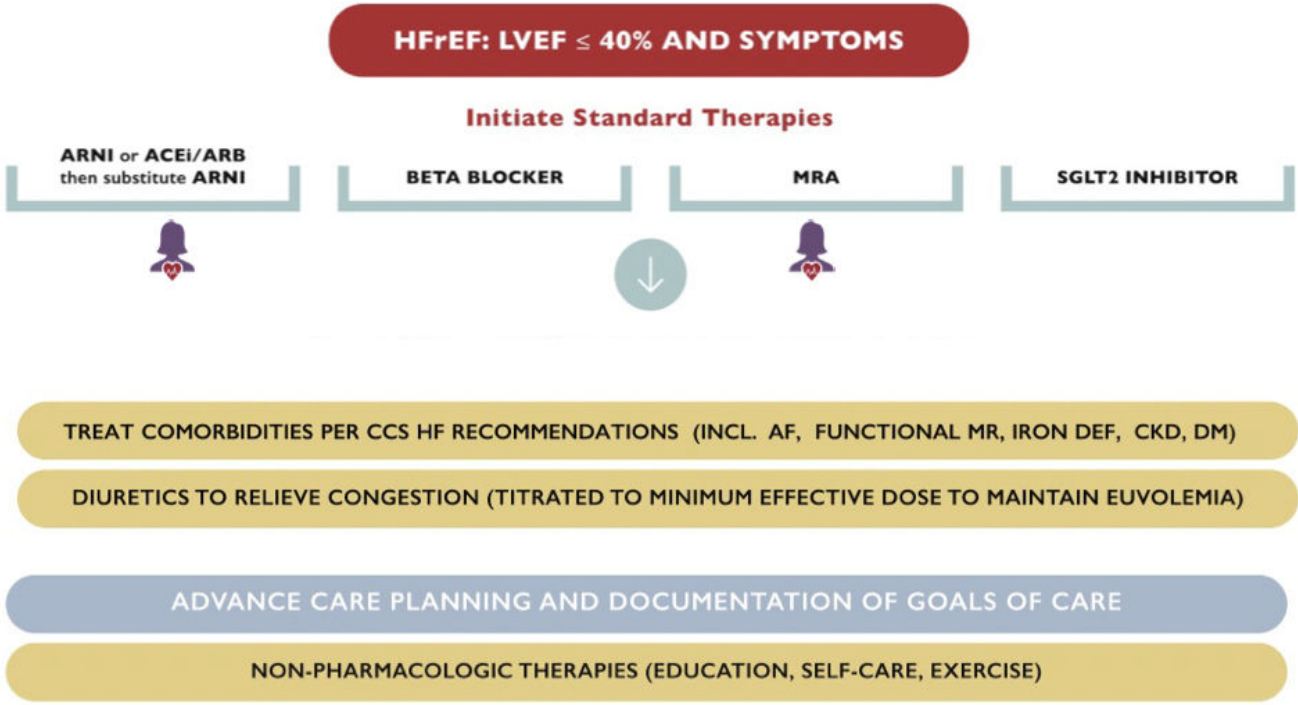


McDonald et al, 2021, CJC, 37: 531-546.

KEY MESSAGE # 6

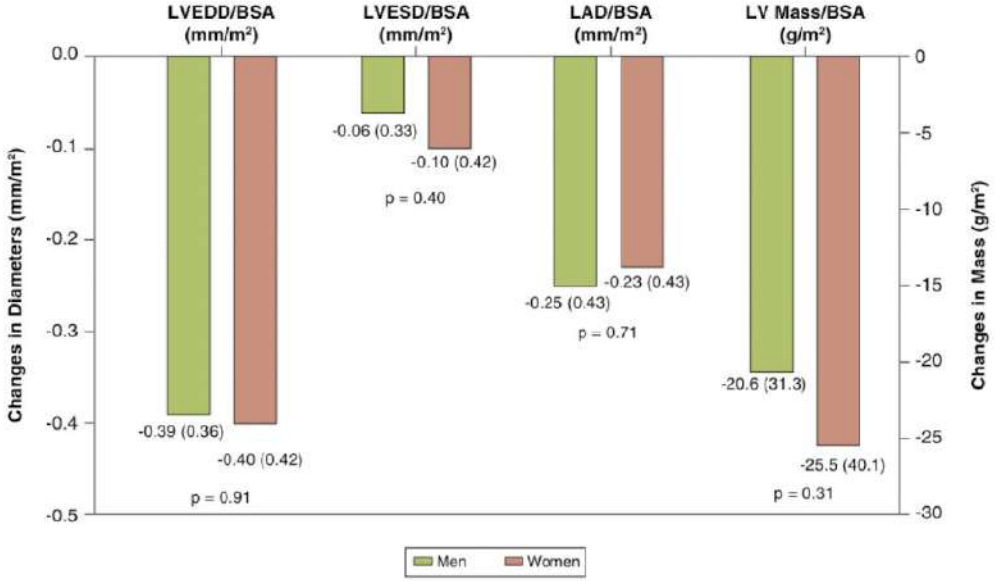
Women with heart failure report lower quality of life than men.

Women less frequently receive ACE-Is and MRAs compared to men.

Women are underrepresented in clinical trials and current guidelines are lacking in sex-specific recommendations.

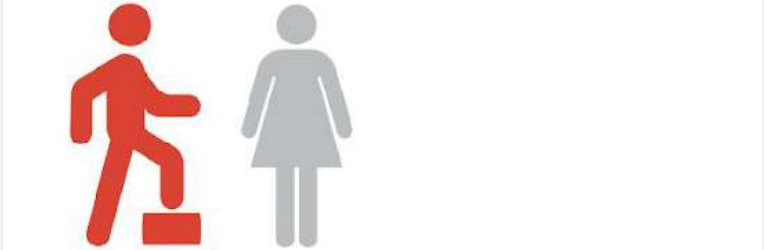
Valvular Heart Disease

FIGURE 2 Reverse Remodeling After Mitral Regurgitation Surgery Compared in Men and Women



Changes in left ventricular and left atrial dimensions and/or mass indexed to body surface area observed after mitral regurgitation surgery in men **(green bars)** and women **(pink bars)**. Note the similar reverse remodeling in both sexes. BSA = body surface area; LAD = left atrial diameter; LV = left ventricle; LVEDD = left ventricular end-diastolic diameter; LVESD = left ventricular end-systolic diameter. Data are presented by mean (SD). *Mantovani et al, 2016, JACC: Cardiovascular Imaging, 9(4): 388-396.*

Cardiovascular Rehabilitation/Secondary Prevention



Women are 50% less likely than men to participate in cardiac rehabilitation.

Heart & Stroke 2018 Heart Report, 2018.

"A Woman Survivor's Perspective—With a cardiac diagnosis, there is Loss. Fear. Denial. Anger. There is deep to the core existential uncertainty and angst. One is shaken with the reality of one's mortality. The physical healing and recovery is a task on one level. However, this must be accompanied by the emotional and spiritual re-piecing together of one's 'new life'.

The challenge of a cardiac rehab program is to include not just exercise and educational components, but also to provide emotional, psychological and social supports to help heal the fragile and traumatized psyche, in order to give the woman her life—with hope, balance, and perspective—back."

—M. Hardy, Woman With Lived Experience, Canadian Women's Heart Health Alliance (personal communication, June 16, 2019)

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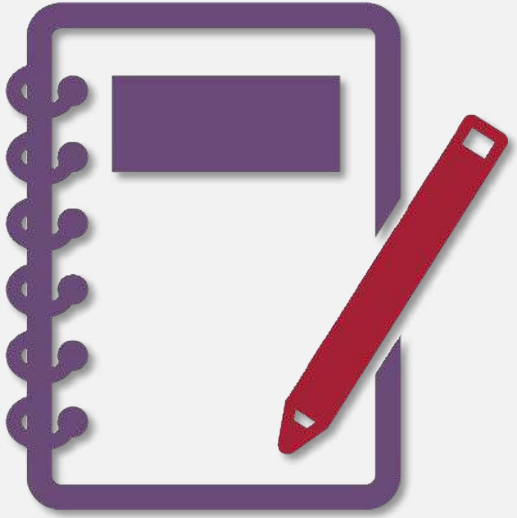
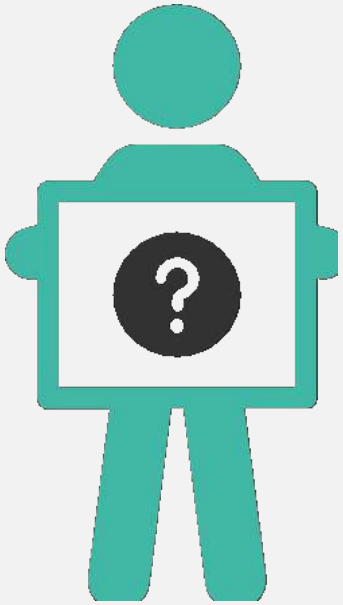
In Summary

- CVD is the leading cause of death in women.
- Since 2017, CV mortality has increased in Canada.
- Younger women are having heart attacks and more women have non-obstructive CAD.
- Stroke affects women across the life course.
- Current guidelines (e.g., valvular heart disease, heart failure) have limited sex-specific recommendations.
- All women should be referred for CV rehabilitation/secondary prevention.



Q&A



WE WANT TO HEAR FROM YOU.

Questions, Comments...

THANK YOU!

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