

Women's Heart Health: An Evidence Review

October 2008



Women's
BC WOMEN'S HOSPITAL
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This report was prepared for the Provincial Women's Heart Health Steering Committee (British Columbia, Canada), and the Provincial Health Services Authority (PHSA) Population and Public Health Program.

Acknowledgements to the PHSA Population and Public Health Program for their financial support, and to Pfizer Canada Inc., who provided an unrestricted educational grant to support this project.

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Foreword

The Provincial Health Services Authority (PHSA) has commissioned three papers to examine women's health in the areas of heart disease, diabetes and respiratory disease. The other two papers, "Type 2 Diabetes and Women's Health in British Columbia: A Review of the Evidence", and "Women's Respiratory Health: An Evidence Review", can be found at www.phsa.ca/PopulationHealth.

This work has been undertaken as a follow-up to an earlier 2007 PHSA report, "Life Expectancy as a Measure of Population Health", showing that the health of BC women is not improving as quickly as the health of women in many other jurisdictions as measured by the rate of gain in life expectancy. The main reasons for this were found to be relatively high mortality rates from diabetes, heart disease and respiratory disease.

These three papers, through a gender-based analysis, examine the possible explanations for these increased disease-specific mortality rates.

All three papers reach the conclusion that the health of BC women could be improved through addressing women's fundamental living and working conditions, particularly for "at risk" populations—the poor, single mothers, recent immigrants, aboriginal women and women of other ethnicities, maturing women, women with mental illness and/or addiction, and others who are marginalized or excluded from society.

More specific policy considerations were not included in the mandate for these three papers. In other work being conducted in PHSA, however, the following policy options are being analyzed in the BC context:

1. improved food security and income security
2. universal access to affordable child care
3. improved access to safe, affordable housing
4. improvements to the public education system
5. improvements to the built environment
6. improved access to effective preventive and curative health services.

Gender-based considerations of these policy areas will be important to offer insights as to specific action that will improve women's health.

John Millar
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Executive Summary:

This literature review and synthesis was developed to inform the activities of the British Columbia Provincial Women's Heart Health Steering Committee. The Committee is concerned with assessing heart health issues for women, particularly with respect to British Columbia, and aims to develop appropriate programmatic responses, research agenda and concomitant academic and clinical structures to serve British Columbia's women. This review builds upon previous preliminary data that the Committee has considered about BC women's cardiovascular health, knowledge and practices. This evidence review presents an in-depth and nuanced analysis of the current international literature relating to women's heart health. 350 articles were collected pertaining to women's heart health. This material was reviewed for sex, gender and diversity specific information and analysis and then narratively synthesized within three broad sub-categories: health promotion and prevention, diagnosis and treatment and policy issues.

This evidence review is responding to the burden of cardiovascular disease for women in Canada. Cardiovascular disease is a leading cause of death in Canadian women. Approximately 40% of all deaths in Canada are currently related to cardiovascular disease [1]. Compared to men, the onset of cardiovascular disease (CVD) in women is somewhat later, by approximately 10 years, and women are less likely to seek care, be investigated and treated with as wide a range of interventions as are men.

Preventing heart disease and promoting heart health for women requires improving a variety of risk factors, which operate at multiple levels. Pre-disposing risk factors, such as intrauterine environment and family history, are pre-programmed either in utero or during development. Clinical risk factors include those which can be measured and enhance women's risk of developing disease at certain levels, such as: sleep duration, migraine, lipid levels, and levels of C-reactive protein (CRP). Lastly, individual-level factors include those which can be influenced by individual behavior such as diet, obesity, smoking status, psychosocial factors and health literacy. Some of these factors have been shown to have a different effect on women's heart health, when compared to men. In particular, women with a family history of CVD are at a greater risk compared to men; women experience more dramatic changes in lipid profiles with age and experience greater health risks from smoking.

Yet affecting individual-level behaviours is complex, as opportunities for engaging in healthy behaviours are shaped by social, economic, and historical circumstances. However, the literature has not always captured this, focusing primarily on studying differences in single risk factors between women and men, or between sub-populations of women. Yet, prevention can not be fully understood from the individual level. The most comprehensive individual-level intervention reviewed which has attempted to access the multi-factorial nature of disease and its prevention is the WISEWOMAN programs in the United States. This intervention included diet, physical activity and smoking cessation programming, as well as social and cultural supports, and was carried out with various sub-populations of low-income, uninsured women across the US. While this program has had variable success in reducing women's risk, the authors have indicated that future programs need to more effectively account for social and environmental factors and organizational issues which affect women's access to and sustainability of programs.

Risk factors often overlap and intersect in women's lives and are further shaped by social, economic and historical processes which enhance or hinder opportunities for women's cardiovascular health. For example, sex and gender biased research and the historical framing of heart disease as a man's disease has contributed to the lack of general awareness regarding women's heart disease. Some evidence

also indicates that women tend to value others health above their own, what has been referred to as an “otherness orientation.” These social and historical processes have shaped women’s health literacy and access to preventive care.

Moreover, women are not a homogenous group and therefore not all women’s heart health can be understood in the same way. Different sub-populations of women have been shown to experience different risk, and therefore have unique needs in regards to heart health promotion and disease prevention. In particular, non-white ethnic minority, low-income, and rural dwelling women are among those who have greater risk and encounter more barriers to preventive health. For example, lack of access to health care, healthy food options, exercise facilities and social support networks are significant social, economic and environmental barriers.

There are also diagnosis and treatment issues affecting the management and outcomes of cardiovascular disease for women. The literature reveals that in comparison to men, women delay in seeking treatment, and present with different symptoms. For example, women are more likely to present with non-specific chest pain and atypical symptoms than men. There are also gender differences in diagnostic testing; evidence indicates that women are less likely to be referred for invasive testing. Sex differences exist in the effects of pharmacological treatments, including evidence that women experience more contraindications to ASA use. Women have also been found to be less likely to enroll in cardiac rehabilitation, have lower adherence and higher drop-out rates, and have poorer functional recovery and more depression than men after coronary artery bypass surgery (CABG).

Policy issues have the potential to influence women’s heart health at all levels and in a variety of ways. For example, broad social and economic policies can affect risk factors directly and indirectly, can address (or not) the determinants of health and affect a range of environmental characteristics. Health system policies can affect resource allocation, models of care, and impact professional education. Research funding agency policies can affect quality of evidence, the inclusion of women and sub groups, and the funding, monitoring and publication of useful analyses.

Therefore, policy has the capacity to impact systemic, institutional and community level and individual level issues. Systemic level issues include environmental and cultural barriers to healthy living, socioeconomic factors and inequality, and enhanced research policies and practices which incorporate a gender and diversity lens. Institutional and community level issues include: community programs, and health care systems and organizations which affect access and quality of care for women. Lastly, individual level issues include: policies and programs addressing risk-reduction and health behaviours, creating tailored and multi-component programs for women, improving health literacy, creating interventions for diverse populations, and improving provider communication and support.

Considerations for Action:

This synthesis reveals that women’s heart disease is a multi factorial problem and heart health promotion for women is a challenge on individual, clinical and policy levels. Evidence in all aspects of sex, gender and women’s heart health is still emergent, but continuously evolving. Actions at the policy and program levels can be taken, however, such as initiatives in heart health promotion and prevention of disease. Specific attention can be paid to improvement in outcomes for sub-populations at risk, and, in some cases, attention can be paid to tailoring programs and practices to the needs of particular groups of women. Overall, it is

important to pursue multifactoral programs and policies, reflecting the multifactoral nature of women's heart health and disease. In all cases, it is critical to evaluate the effectiveness of all such activities in order to contribute to the emergent knowledge about how best to address women's heart health.

Based on this review, there are a number of key messages and areas where action should be considered. They are as follows:

1. Heart health promotion and prevention of disease

The greatest health benefits and most cost effective solutions come from changes at the prevention level. In particular, the most important risk factors to be addressed include: smoking, physical activity, healthy diet and weight management. Yet, because of the complex nature of women's health, change at the individual level requires change at the policy level to address gender and diversity based differences in risk, and access to health and health care.

2. Sub-populations at risk

The review reveals that there are identifiable sub populations of Canadian and BC women who face increased risk for heart disease, such as older women, low income women, Aboriginal women, South Asian women, and women with a mental illness or addiction. For example, the inverse gradient of CVD and socioeconomic status (SES) is particularly pertinent for women, and particular groups of women who are more likely to live in poverty. These sub-populations of women, therefore, stand the most to benefit from research, programs and policies which address barriers and seek to improve their heart health.

3. Tailoring of programs and practices

Evidence from this review reveals that there is not a proven universal intervention which can be applied to all women. Instead, programs need to be tailored to women and sub-populations of women. Evidence from this review suggests a number of factors which are important to consider when tailoring, including: changes in women's health through the life-course, addressing health literacy, improving social support and addressing psychosocial factors, and developing women-centred approaches to diet, physical activity and smoking interventions.

For secondary prevention, the greatest strides for improving women's heart health can be made in the form of eliminating gender biases in diagnosis, testing and care. Improved clinical practices that reflect the integration of sex, gender and a range of diversity issues and social determinants into diagnosis and treatment are key to improving women's treatment and care. Research, policy and program development of cardiovascular screening, diagnostic and treatment for women, needs to account for these factors in order to provide effective secondary prevention and treatment options for women.

4. Comprehensive programs

More comprehensive and multi-component research studies, policies and programs are required in order to adequately address the complex nature of women's heart health. As shown by the evidence reviewed, the prevention/promotion literature has focused largely on individual change while the treatment literature has focused on intervention effectiveness. Multi-factoral programs and policies are needed which address the broad social, economic and environmental barriers, research policies and practices, health care systems and organizations, as well as the individual level health behaviours.

Overview of Cardiovascular Disease

Currently, heart disease and stroke are the leading causes of death for women in the higher income countries, including Canada [2]. Although typically seen as a “Western disease” or “disease of affluence,” trends indicate that the burden of cardiovascular disease (CVD) will shift to low and middle income countries, exacerbating global health inequalities [3, 4]. Indeed, by 2020, it is predicted that heart disease and stroke will be the leading cause of death for women in low income countries, as well [5].

There is also inequity in the distribution of heart disease within higher income countries, such as Canada. A number of studies have observed an inverse gradient between measures of socioeconomic status (as measured by income and education) and CVD risk [6-10]. In particular, older persons, Aboriginal people and women have demonstrated greater social disadvantage and more CVD risk factors [11, 12].

Differences between countries and sub-populations tend to reflect differences in risk profiles, such as smoking, obesity and diet. For example, the global male smoking rates have peaked and are in slow decline, whereas female rates are set to double by 2025 and continue to escalate throughout the 21st Century [13]. Within Canada, smoking-related deaths for men have been decreasing, yet increasing for women reflecting historical gendered trends [14]. Obesity is another major health risk for women in Canada. Women in Canada are less physically active than men, and the prevalence of both overweight and obese women has increased by 7% since 1985 [15]. As well, 31% of all deaths from CVD are related to a low consumption of fruits and vegetables [16]. In addition to any changes in risk profiles and health-related behaviours, CVD can be expected to increase with aging populations.

Women have specific sex and gender-based issues related to cardiovascular disease, and exhibit different patterns and presentation of cardiovascular risk factors and diseases [17]. For women, heart disease tends to develop approximately 10 years later in life, compared to men. Stroke accounts for a higher proportion of deaths among women than men, particularly for older women. Women also: report different symptoms, and have different access and issues related to management, treatments and diagnostic services [17]. As well, there are additional factors women encounter based on: geography, socioeconomic status and race/ethnicity.

Methods

In order to identify some of the key issues related to women's heart health, we carried out a thorough literature search of the following databases: Embase, PubMed, Academic Search Premier, Cochrane Reviews, Elsevier, Ovid, and Contemporary Women's Issues. During the search, we utilized a variety of keywords, including: heart health, heart disease, CVD (all kinds including: coronary, cerebral, vascular), sex, women, gender, ethnicity, obesity, hypertension, diabetes, smoking, ethnicity, age, race, SES, psychosocial and stress. Our literature search returned 350 relevant articles, of which 149 were related to health promotion and prevention, 133 related to diagnosis and treatment and 53 related to policy issues. The remaining 15 articles were collected for background information on women's heart health. These articles were then reviewed and analyzed for information on sex, gender, and diversity issues associated with women's heart health. This body of literature has been narratively synthesized in three main sections: promotion and prevention, diagnosis and treatment, and policy issues.

Sex, Gender and Diversity Analysis

In the process of review and synthesis, a sex, gender and diversity analysis was applied to the material. Sex and gender analysis (SGBA):

“is an approach to research and evaluation which systematically inquires about biological (sex-based) and sociocultural (gender-based) differences between women and men, boys and girls, without presuming the nature of any differences that may exist” [18].

SGBA is a tool that promotes consideration of a range of issues related to both the research process and the application of knowledge in program or policy development. Using such an approach helps to improve our understanding of sex and gender as determinants of health, of their interaction with other determinants, and the effectiveness of how we design and implement sex- and gender-sensitive policies and programs [19].

Sex and gender are both fluid concepts that are influenced by cultural and temporal factors. Individuals are affected by a range of biological factors such as genetics, physiological characteristics, physical characteristics, and hormones, as well as a range of social characteristics and factors such as gender identity, gender relations and institutional gender. In addition, both gender and sex intersect with cultural definitions, traditions, expectations and assumptions unique to particular groups. Hence, developing sophisticated understandings (and measures) of sex and gender in research and knowledge uptake is key to reflecting on how all factors affect women's health [20]. In the context of CVD or heart health, all of these factors interact to produce patterns and issues of concern to health program planning, policy development and treatment practices.

Applying this lens of analysis to the literature review enables us to critically examine how women's heart health has been studied, identify the important sex and gender specific factors and issues of concern to women and women's health advocates, and identify important gaps and future considerations for research, programs and policies.

The results of our evidence review are reported in three discrete sections: health promotion and prevention, diagnosis and treatment, and policy issues. While our synthesis reveals that the overall policy and program framework surrounding women's health and women's heart health affects everything from research to programming to treatment and health systems, very few articles in the prevention and treatment literature reflect this broader perspective. Indeed, one of the limitations of the prevention and treatment literatures is their narrow focus.

Despite the clear gradient on many risk factors pertaining to heart health and the increasing importance of including sex, gender and diversity into all considerations regarding women's heart health, there is little recognition of or integration of these perspectives into the research topics, designs and discussions presented here. Having said this, we do report on some interventions directed at particular groups of women who may be considered “higher risk” for heart disease, or who are in particular sub-groups (such as [21-29]).

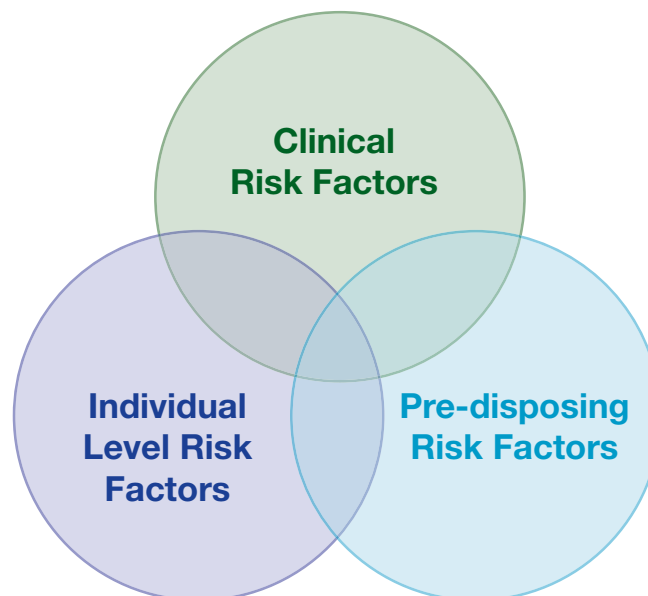
1) Health Promotion and Prevention

Preventing CVD and promoting women's heart health is an important objective, considering the severity and scope of heart disease for women in Canada and the world. Primary prevention is one of the top priorities of any cardiovascular health strategy, because many risk factors, such as smoking status, diet, and physical activity, are potentially modifiable [30]. Successful prevention strategies are needed that can enable women to create and sustain healthful behaviors which protect them from illness and mortality from heart diseases.

Yet, primary prevention can be difficult because many women, particularly when they are younger or are not yet experiencing poor health, may not perceive some health behaviour changes as necessary. As well, relatively less is known about women's cardiovascular health because most research studies in the past included only men. Interventions aimed at risk reduction, and particularly ones targeting at-risk groups, have generally been unsuccessful in resulting in behavior changes [28]. Various sex, gender and diversity issues pose significant challenges to diverse women's heart health.

Researchers recognize that while no risk factors, other than hormonal status, affect only women or only men, certain risk factors have a greater impact on women [31, 32]. These include: HDL, triglyceride levels, depression, diabetes, smoking, family history and inflammation [32, 33]. Further, risk factors may have either, or both, sex and gender implications. Women have unique cardiac risk profile related to sex-specific factors such as: pregnancy, menopause and the use of exogenous hormones [34]. As well, there are social or gendered experiences which influence women's heart health.

Figure 1: Factors Influencing Preventive Health



The following discussion is divided according to three broad categories of risk factors: pre-disposing, clinical, and individual level factors. Pre-disposing risk factors refer to ways in which women's heart health is pre-programmed either in-utero or during development. Clinical risk factors describe physiological conditions which, at certain levels, are associated with an increased risk of CVD morbidity or mortality and can be clinically assessed or measured. Lastly, individual level risk factors include those factors that can be modified through behavioural or structural change. Yet, as will be demonstrated, environmental factors as well as women's experiences of gender, diversity and other social factors impact and structure women's capacity to modify and improve these risk factors. In addition, exposures to risk factors can be a result of social, economic, political and/or cultural mechanisms [5, 35].

Risk Factors

a) Pre-disposing Risk Factors

i) Intrauterine and childhood environment

Programmed structural and metabolism changes may occur when human fetuses are adapting to a limited nutritional supply which may cause future diseases, such as hypertension, coronary heart disease (CHD) and non-insulin diabetes [36, 37]. While most studies looking at programming by birth weight have included only men, there are emerging studies including women. For example, women born weighing less than 2500g had an 11-fold risk of dying from CHD compared with women born weighing more than 2500g [34]. Forsen et al. (2004) found an association between tempo of weight gain and future risk of CHD that was different for girls and boys. Girls who later developed CHD were: short at birth, thin but caught up in height during infancy, and began to gain weight rapidly around four years of age [38]. In contrast, boys who later developed CHD were thin at birth, remained thin during infancy, and began to gain weight rapidly at age one.

It has been argued that persons who experience impaired growth in utero may continue to experience adverse environments contributing to the development of CHD. Yet, various studies reviewed by Osmond and Barker (2000) revealed that individual and structural level factors do not affect the association between intrauterine or childhood development and CHD, although, influences in later life do compound the effects of the intrauterine environment [36]. Similarly, Lawlor et al. (2004) found an association between trunk length¹ and CHD that was independent of smoking, socioeconomic position (SEP) in childhood or adulthood, birth weight and other confounders [39].

ii) Family history

Genetic factors may predispose or protect individuals from CVD through actions on vascular adaptation [34]. One review found that women with a family history of CVD² have a significantly greater cardiac risk than men [31]. It has been shown that women with a positive family history of CVD have heightened stress responsivity in comparison with men, which may contribute to future risk of cardiovascular diseases [40]. Similarly, Patel et al. (2007) observed an increased composite risk factor burden in a diverse, urban sample of women with a family history of myocardial infarction (FHMI) which was not seen in men [41]. Further, FHMI

¹ Affluent social circumstances, high energy diets at age 2, and breast feeding were all found to be associated with longer leg length, and hence, lower risk of future CHD.

² "Family history" is defined as a major CVD event of a first degree relative, occurring before age 50 in men and age 55 in women.

was independently associated with coronary artery calcification in women but not in men. Yet, in this and other [42] studies, women with a family history of heart disease did not engage in more health promoting behaviours or exhibit a greater awareness of risk. Unhealthy behaviours may be passed on from family members, and could also be the product of a lack of knowledge or cultural norms [42].

b) Clinical Risk Factors

i) Sleep duration

Both too little (5 hours or less) and too much (9 hours or more) sleep has been shown to increase risk of coronary events for women, even after adjusting for other CHD risk factors [43]. Less than 5 hours of sleep per night has also been associated with a significantly increased risk of hypertension in women and men between the ages of 32 and 59 years [44]. Inadequate sleep may result in decreased glucose tolerance, and an increased exposure to raised 24-hour blood pressure and heart rate, elevated sympathetic nervous system activity, and increased salt retention leading to the development of hypertension. Over-sleep may be a symptom of early cardiac issues, depression or anxiety.

ii) Migraine

The evidence examining the link between migraine and heart disease is mixed. Kurth et al. (2006) found that any history of migraine increased risk of major CVD over ten years, but migraine with aura was associated with a higher risk of major CVD, myocardial infarction, ischemic stroke, death due to ischemic CVD, and coronary revascularization and angina [45]. Migraine may increase prothrombotic factors and the release of vasoactive neuropeptides during migraine attacks may stimulate inflammatory responses. Furthermore, migraine with aura has been linked with a worse CVD risk profile, via: elevated cholesterol levels, higher blood pressure (BP), higher likelihood of hypertension and increased Framingham risk score for CHD. In contrast, Cook and co-authors found that the health providers with migraines who participated in their study were not at a greater risk of developing CHD, MI or angina after adjusting for other risk factors [46].

iii) Hypertension and lipid disorders

Women's lipid profiles change as they age. High density lipoprotein cholesterol (HDL-C) levels are reported to correlate closely and inversely with risk of CHD. A review by Meagher (2004) provides ample evidence of a reduction in cardiovascular events in both men and women when low density lipoprotein cholesterol (LDL-C) levels are lowered [47]. While HDL-C levels are higher, and LDL-C levels lower, in women than men from young adulthood and beyond, most studies have described a decrease in HDL and increase in LDL and triglyceride levels following menopause [31, 47-49].

Hypertension is another prevalent risk factor for CHD, especially in elderly women [31]. While rates are similar for young and middle-aged women and men, hypertension increases more for women than men with age [50]. Multiple factors may contribute to the prevalence of hypertension in older women including: autonomic, environmental and genetic mechanisms, and hemodynamic and metabolic factors [50]. Yet, hypertension can be improved by changes in diet and physical activity [51].

Women also have a greater risk of hypertension and CVD during pregnancy. Specifically, women have an increased risk of CVD morbidity following pre-eclampsia. By the third trimester of pregnancy, women have a

lipid profile that would be considered atherogenic in non-pregnant women [34]. While this returns to normal levels post-partum, some researchers have suggested that each pregnancy may reset ovarian functions and reduce overall estrogen exposure, increasing women's long-term risk of CVD [34].

iv) Levels of C-Reactive Protein (CRP)

CRP is an indicator of tissue damage or inflammation, and has been identified as an independent risk factor for cardiovascular events [31, 47]. An elevated CRP level (greater than 3.0 mg/L) was associated with a 1.45 increased risk of CHD in a group of older women, regardless of other risk factors [52]. In Meagher's review (2004), CRP was identified as the strongest predictor of CVD, when compared with other markers of inflammation as well as homocysteine and lipoprotein levels. However, CRP level also correlates with other risk factors, and therefore may lose predictive value after adjustment [47].

c) Individual Level Risk Factors

i) Diet and nutrition

Numerous authors discuss the importance of dietary modifications for reducing CVD risk (including: [16, 51, 53-55]). Evidence shows that women and men following a Mediterranean style diet (a diet generally low in saturated and high in monounsaturated (e.g. olive oil) fats) exhibited much lower risk of CVD and mortality [21, 56, 57]. Following a low-fat plant based diet incorporating mostly vegetables, legumes and whole grains, has also been shown to produce greater cholesterol-lowering outcomes than a more typical US low-fat diet. Polyunsaturated fat has been proposed to reduce risk of CHD through its positive effects on: blood lipids, insulin sensitivity, inhibition of thrombosis and threshold for ventricular fibrillation [58]. For example, Oh and co-authors (2005) found an inverse association between intake of polyunsaturated fats and CHD risk that was strongest among women whose BMI was greater than 25, or who were younger than 65 years old [58]. In addition, trans-fat intake was associated with an increased risk of CHD, particularly for younger women. Trans-fats can contribute to an increased risk of CHD by adversely influencing blood lipids, including: concentrations of low and high density lipoprotein cholesterol, triglycerides, lipoprotein(a), low density lipoprotein particle size, endothelial function, insulin resistance and thrombosis.

Other foods that should be avoided include simple, processed starchy foods, since these: raise blood glucose levels quickly and induce higher insulin levels, increase serum triglyceride levels, and are associated with CVD. In contrast, whole grains and foods with high fiber content are preventive of heart disease. Dietary fiber may: increase the excretion of cholesterol, increase satiety and insulin sensitivity, or lower plasminogen activator inhibitor type 1 and factor VII coagulation activity [59].

Both fish and omega-3 fatty acid consumption have been associated with decreased CHD risk for women, particularly death from CHD [60]. Omega-3 fatty acids may reduce CHD risk and mortality through: the reduction of serum triglycerides, platelet aggregability, and antithrombotic and antiarrhythmic effects [60]. In addition, vitamin C supplements³ [61], soy protein⁴ [62] and low-fat dairy products, calcium and vitamin D [63] have been shown to improve women's prevention of CVD.

3 Women who used supplements observed a 28% lower risk of nonfatal MI and fatal CHD than non-users.

4 Women with the highest soy protein intake had a 75% lower risk of total CHD and 86% lower risk of nonfatal MI than those in the lowest intake quartile, independent of established CVD risk factors and other dietary factors. Soy food intake improves serum lipid and lipoprotein profile.

Moderate alcohol consumption has been linked with a lower risk of CHD for women. Tolstrup and co-authors (2006) report that Danish women who drank alcohol on at least one day a week had a lower risk of CHD than women who drank alcohol less than one day a week [64]. According to a review by Rimm et al. (2000), over 70 epidemiologic studies have demonstrated an association between moderate alcohol consumption and lower risk of CHD in healthy women and men; and may also be beneficial for people with adult-onset diabetes or previous CVD [65]. This is partially explained by its effects on clotting factors and serum lipids.

Studies examining the relationship between coffee intake and cardiovascular risk for women have produced mixed results. While Lopez-Garcia et al. (2006) did not find any association with cardiovascular risk for total caffeine intake, decaffeinated coffee or tea for women or men [66], Andersen et al. (2006) found a protective effect with an intake of 1-3 cups of coffee per day for postmenopausal women [67]. Dietary antioxidants in coffee may prevent inflammation, reducing the risk of cardiovascular and inflammatory diseases.

ii) Levels of physical activity

Moderate activity for approximately 30 minutes per day has been associated with reductions in CVD morbidity and mortality for women and men [68-70]. Physical activity impedes the formation of atherosclerotic plaques that can lead to an MI, improves endothelial function, reduces inflammatory and immune responses and provides antithrombotic effects [71]. Regular physical activity also decreases various cardiac risk factors, including: obesity, insulin resistance, dyslipidemia, and hypertension. For example, higher cardio-respiratory fitness has been linked with improved CVD risk profile and lower rates of non-fatal CVD events in both women and men [72] and lower levels of CRP in women [73].

According to one literature review [74] and one prospective study [75], even low intensity activities, such as walking, result in reduced CVD risk and mortality for women. These findings carry important implications for the development of women-focused prevention strategies, since not all women are interested in or capable of engaging in moderate and vigorous activities.

iii) Obesity

Linked to diet and physical activity, obesity is another important risk factor for CVD. Yet there is some disagreement over whether body mass index (BMI) can serve as an accurate measure of obesity, and CVD risk. While increased measures of BMI have been associated with a worse prognosis for women and men with CVD [76, 77], evidence from one review suggests that waist circumference is more predictive of CHD than BMI [31]. Similarly, Behan and Mbizo (2007) observed a correlation between waist circumference and several biomarkers in women for diabetes and CVD, including: triglycerides, CRP, cholesterol/HDL, non-HDL, LDL and glucose; and inversely with HDL but not A1c or WBC [78]. They identified a trend of increasing glucose, LDL and CRP with increasing waist circumference. Kip and colleagues (2004) found that the metabolic syndrome, but not BMI, was predictive of future CVD risks for women [79]. A minority (24%) of obese women in their study did not have metabolic syndrome or diabetes, and a similar parallel minority (28%) of women with a normal BMI had metabolic syndrome or diabetes. Measurements of BMI may not quantify the amount or ratio of subcutaneous to visceral fat.

iv) Smoking status

Smoking may be a stronger risk factor for MI in women than in men, has been linked with early menopause, has an unfavorable effect on plasma lipoproteins [31] and has been associated with higher measures of BMI, and possibly the development of central adiposity in young people [80]. Because of the anti-estrogenic effect of smoking, women may be at an even greater risk for disease than men. More than half of MI's in middle-aged women are due to smoking [81]. Relative risk is approximately 50% higher in female smokers compared with male smokers for MI and all cause mortality, and smoking as little as 3-5 mg. of tobacco per day or not inhaling is still shown to significantly increase women and men's risk of developing MI [82]. Smoking may also compound diabetic risk factors for CVD. It has been shown that diabetic women who smoke 15 or more cigarettes a day have a 84% greater risk of developing stroke compared with diabetic women who have never smoked [83]. Even passive smoking has been shown to increase women's risk of CVD. A systematic review by Kaur (2004) reveals that exposure to SHS increases women's risk of dying from heart disease [84].

These findings are problematic, in consideration of the fact that young women's smoking rates are more often equal to or surpassing boys, contrary to past trends [85], and women are more often exposed to secondhand smoke [86]. Yet, quitting smoking for more than 2-3 years for women and men [31], and 10 years for a diabetic woman [83], was found to decrease the risk of developing CHD similar to that of a non-smoker. This potential for improvement to women's CVD risk profile makes smoking cessation a particularly important goal. In addition, gender sensitive policies are needed to reduce women's exposure to SHS.

v) Psychosocial factors

Evidence on the effects of psychosocial factors and gender on heart disease are mixed. Some studies have found that psychosocial factors are less pertinent for women than men in determining patterns of heart disease. A prospective cohort study in London with civil service employees (Whitehall II Study) demonstrated that psychological distress increased men's, but not women's, risk of CHD [87]. As well, Lee et al. (2002) did not find that job strain was related with an increase in the incidence of CHD for the women (all nurses) who participated in their study [88]. Yet, these authors suggest that these observed differences may be the effect of sampling, study design or gender biases in measuring psychosocial factors.

Other studies have demonstrated that psychosocial factors are associated with greater CVD risk for women, as well as men. High levels of phobic anxiety have been shown to increase women's risk for fatal CHD, particularly from sudden cardiac death [89]. In a review by Brezinka and colleagues (1996), psychosocial risk factors identified for women were: troubling emotions and lack of social support, low social class, education and the double load of work and family [90]. Similarly, education, unemployment and low job control have been associated with more risk factors and an increased risk of CHD for both women and men [10, 31, 91]. In a study by Danhauer and colleagues (2004), greater psychosocial distress was shown to negatively influence healthy eating behaviours for both women and men [92].

Some evidence reveals links between mental illness and increased risk for cardiovascular disease in women and men, yet the study did not examine sex or gender differences [93]. One study which does discuss gender differences found that cardiovascular health decreased in persons with depression and mental health issues [94]. Furthermore, the authors found that mental health issues were more commonly reported by women, compared to men. Furthermore, greater smoking rates have been documented among persons with mental illness. A literature review by Johnson et al (2006) reveals that smoking among people with mental

illness is approximately double that of the general population, and even greater for persons with alcohol and drug dependencies [95]. These higher rates of smoking result in greater rates of morbidity and mortality from cardiovascular diseases. Furthermore, there are specific dependence and cessation issues for persons with mental illness and addictions which impede cardiovascular health, and must be considered when tailoring cessation programs.

vi) Health literacy

Multiple authors have found that women do not tend to view heart disease as a threat to their health, in that they regard it as a man's disease, often perceiving breast cancer as a greater health risk [96-100]. Indeed, until the late 1980s, heart disease was regarded as primarily affecting men, and few clinical trials included women [101]. The FDA failed to report on sex differences, leading to the development of biased guidelines and policies. This sex biased history is clearly part of the reason why women underestimate their risk for heart disease, and are less likely to recognize signs and symptoms [101].

The relationship between health knowledge and healthy behaviour is not entirely clear. In some studies, women with: more social support, fewer perceived barriers to CHD risk modification, higher CHD knowledge levels, and more education [96], and no smoking history or family history of CHD [42], have demonstrated more healthy behaviours. Similarly, Mosca et al. (2006) found that women who were exposed to information about heart disease and perceived themselves as being at risk were more likely to engage in preventive health behaviors [100]. In contrast, a study by Biswas and co-authors (2002) revealed that even though diabetes, smoking and hypertension are the greatest risk factors, women with these were not worried about susceptibility to heart disease [102]. Only when women presented with four or more risk factors, were more than half of them worried about susceptibility to CVD. Yet, the authors also recognize that 'worry,' which they measured, may not be associated with proactive behaviours, and may actually inhibit healthy behaviours.

Complicating the pathway between knowledge or perception and action are gendered roles and responsibilities. Women often have an "otherness orientation," in which they place the health needs of others above their own. High levels (nine hours or more/week) of care-giving for ill spouses has been associated with greater risk for CHD in women [103]. In a study by Mosca et al. (2006), 56% of women who were caring for the health of family members stated that the other person's health was more important to them than their own [100]. Women were also more likely to increase their child's physical activity levels than their own.

Some of the literature also discusses issues around the awareness of health care providers, and ways in which they can play a lead role in improving women's knowledge of CVD and engagement in risk reduction behaviours [54, 101, 104, 105]. Health professionals often underestimate women's CVD risk [101]. In one study, one-third of internists and half of OB/Gyns did not know that tobacco use was the leading cause of MI in women [105]. Improving women, men, and health care provider's knowledge of women's CVD risk is a key goal for preventive health.

Diversity/ Intersection of Risk Factors

In practice, pre-disposing, clinical, and individual level factors intersect with social-structural issues to affect and determine women's heart health. The following discussion will describe and examine the literature on issues of prevention and health promotion for women with diverse characteristics, demonstrating some of these complexities.

a) Ethnic/Racial Belonging

A variety of researchers have found that women who belong to an ethnic minority face a greater risk for CVD [106-109]. Some studies have revealed that Black and Native American women have the greatest rate of multiple risk factors, while Asian women are the least likely to have multiple risk factors [106, 110]. In a study by Struthers et al. (2006), 98% of Native American women had at least one cardiac risk factor, especially women who were: older, less educated, less employed, or had diabetes [111]. Other studies have found that Black women report more risk factors, and have the highest rates of CHD morbidity and mortality followed by Hispanic and White women⁵ [29, 34, 112, 113]. Similarly, a systematic review by Nazmi and Victora (2007) found that poverty and non-white race was associated with higher CRP levels [114].

In Canada, Aboriginal people have more carotid atherosclerosis compared with Canadians of European origin, and also have higher: smoking and obesity rates, glucose intolerance and concentrations of fibrinogen and plasminogen activator inhibitor-1 [12]. Aboriginal people also have lower education and employment levels and annual household incomes, and higher rates of risk factors and CVD compared with Europeans. Obesity and abdominal obesity are likely related to Aboriginal person's higher rates of glucose intolerance, and may be due to historical changes in food and activity levels. In turn, higher rates of glucose intolerance and tobacco use by Aboriginals may impact their greater development of thrombosis, fibrinogen and plasminogen activator inhibitor-1.

Anand et al. (2000) also studied CVD history and risk factors in South Asian, European and Chinese populations in Canada⁶ [115]. Within each ethnic group, they found that the degree of carotid atherosclerosis was associated with a higher prevalence of CVD, with highest rates being observed for South Asians. South Asians also had higher: glucose intolerance, total LDL cholesterol, and triglycerides, lower HDL cholesterol and greater abnormalities in novel risk factors, including: higher concentration of fibrinogen, homocysteine and plasminogen activator inhibitor. Increased risk of CVD events could be due to: risk factors affecting plaque rupture, an interaction between prothrombotic factors and atherosclerosis or other factors that have yet to be revealed. Aside from their higher levels of glucose intolerance, Chinese persons had a more favourable risk profile and lower rates of CVD than Europeans.

Multiple studies have found that non-white women also report less awareness of CVD, underestimate their own risk, and report problematic patient-provider relationships [22, 98, 100, 116]. For example, Christian and co-authors (2007) found that Black and Hispanic women's awareness of heart disease and heart attack as the leading cause of death (LCOD) has not matched the improvement observed in White women⁷[116].

b) Geographic Location

Geography overlaps with race/ ethnicity and socioeconomic status, with non-white minorities often living in more socially and economically deprived areas, with fewer health resources or opportunities for healthy living [113]. For example, Mississippi has the highest heart disease death rate and the highest proportion of

5 When comparing women living in economically disadvantaged areas, poor Black women continue to have higher mortality rates than poor White women. Black and Hispanic women have higher average blood pressure, diabetes, smoking rates and are less likely to be physically active.

6 Although they were not specifically studying gender differences, the ethnic differences they report are useful for thinking about prevention of CVD for diverse women.

7 Hispanic women were more likely than White women to suggest there is nothing they can do to prevent heart disease (22% vs. 11% of white women), and reported more confusion related to basic preventive strategies.

rural-dwelling African American women in the U.S. [117]. There are often numerous structural barriers to health for women living in rural areas, including: poverty, access to health care providers, health infrastructure and social isolation. A study by Chikani and colleagues (2005) found that women living in rural areas were at greater risk for CHD (exhibiting more obesity, poorer diet, and higher blood pressure) [118]. Rural, farm-dwelling women in this study were also less likely to be in jobs with high demand and higher decision latitude when compared to non-farm women.

c) Socioeconomic Status

Poverty is a gendered phenomenon. Women often have lower SES and less access to healthcare resources than men, so face a greater risk of heart disease [35]. The rate of women with multiple risk factors tends to increase with age and decrease with higher: education, income, and employment [106]. Smoking, glucose, obesity and CRP are greater among individuals with higher social disadvantage [11, 114]. For example, it has been shown that obese individuals with lower levels of education reported the highest rates of heart disease, particularly women and persons living on a lower income [119].

Lawlor and colleagues (2005) found that adverse socioeconomic status across the life-course increases women's risk of CHD, and this was not entirely explained by adult risk factors such as smoking⁸ [120]. Other findings revealed that participants who belonged to 'manual classes' during childhood remained at an increased risk for CHD, even if they changed class later in life [121]. Low childhood socioeconomic position was also associated with smoking and lower physical activity in adulthood.

Some evidence reveals that women living on a low income are also more likely to live in environments that don't support healthy living [122, 123]. Living in less affluent areas and areas with high crime rates was associated with greater BMI measures and CHD risk. Poorer neighbourhoods generally have more fast food outlets, less full sized grocery stores, less fitness facilities and higher obesity rates. Women living on a low income may have less: education, employment, and access to social networks which may limit their ability to engage in healthy behaviours [124], and have been associated with higher rates of CAD [125] and CHD [120]. Environmental factors that produce chronic stress may also lead to unhealthy behaviours or impede women from attending to their health [126].

Conclusions

As demonstrated by this review of the issues in the promotion of heart health and the prevention of heart disease in women, multiple risk factors overlap and operate at a range of levels. These relationships are complex and clearly influenced by both sex and gender. Further, various diverse characteristics, such as ethnicity, age, social and geographic location, interact with sex and gender to produce, reduce or amplify risk. Therefore, future research, policy and programs relating to the prevention of CVD needs to move beyond linear models and address these complexities by developing multi-component theoretical frameworks and interventions. These possible approaches will require action on multiple levels, from individual to broad social and economic levels, in order to cover and ameliorate the multiple risks discussed here.

⁸ Women with the greatest odds for having CHD (based on measurements of BMI, triglyceride concentrations and waist to hip ratio) had the lowest socioeconomic position during childhood. Participants were almost all white, so findings may not be generalizable.

2) Diagnosis and Treatment

This section details the sex and gender issues associated with the recognition and response to heart health issues and heart disease. Again, diverse characteristics such as ethnicity, age, life stage affect both women and providers in the course of reacting to and treating cardiovascular disease.

Treatment Seeking

There is some evidence that women delay seeking treatment. A study by Nolan (2000) found that 42% of women and men in her sample delayed seeking medical attention for 3 or more hours after the onset of cardiac symptoms [127]. This is particularly important, as thrombolytic therapy must be administered within 4 hours to be effective. Women's increased delay time was associated with: elevated depression, tendency to seek advice from others and the taking of analgesic medicines [127].

Two Scandinavian studies and one Vancouver study sought to understand the reasons for this delayed presentation. Frich et al. (2005) interviewed 20 Norwegian women with family history of coronary heart disease [128]. Aged 15 to 57 years, these women downplayed their own risk, did not seek out cholesterol testing from their care providers and misinterpreted symptoms of coronary heart disease. In an older cohort of Swedish women (36 – 80 years of age) who presented to hospital with incident myocardial infarction, researchers found that these women had difficulty interpreting and understanding their symptoms [129]. They ignored the pain and delayed seeking help, especially calling for an ambulance. They reported that they felt they had to put others needs (spouse, family) before their own.

Ratner et al. (2005) conducted a telephone survey of 3419 people > 40 years of age, in which scenarios were presented for assessment of the likelihood of coronary artery disease and the need to call '911' [130]. Interestingly, neither the gender of the respondent nor that of the affected person in the scenario were associated with the recognition of symptoms of acute myocardial infarction or the likelihood that 911 would be called. Of note, Chinese respondents were the least likely to identify symptoms of acute myocardial infarction and thus were the least likely to call 911. Overall, 78% of respondents correctly identified AMI and 37% called 911.

Presentation

Women are more likely to present with non ST-elevation MI (NSTEMI) compared to men, and two-thirds of women present without recognized prodromal symptoms as their initial presentation of CAD [131]. Women with acute coronary syndromes (ACS) are more likely to present with nonspecific chest pain, which contributes to some of the difficulty in diagnosing heart disease in women.

While both men and women with evidence of ischemia or MI report chest pain with almost equal frequency [132], women are more likely to report atypical symptoms such as mid back pain, nausea, vomiting, dyspnea, palpitations and indigestion [133-136]. In a recent review of 69 studies that examined sex differences in symptoms of ACS, women reported chest pain slightly less frequently than men, but the authors concluded the difference was not large enough to warrant sex-specific public health messages regarding symptoms of ACS [137]. McSweeney et al. (2003) surveyed 515 women post-MI and found

atypical prodromal symptoms such as unusual fatigue, sleep disturbance and shortness of breath, one month prior to the incident MI [138]. Women more commonly present with a higher prevalence of plaque erosion consistent with unstable angina than men [33]. Men and women report differences in pain perception, which may contribute to the difference in symptoms reported by women and men [33].

The prognostic significance of women's atypical presentation was examined in the Women Health Initiative Observational Cohort of 83,622 healthy, post menopausal women aged 50-79 years. Women who developed nonspecific chest pain were significantly more likely to experience a cardiovascular event (11%), compared to women without nonspecific chest pain (9.5%). Specifically, women with nonspecific chest pain were 2x (RR 2.18; 95% CI 1.66-2.86) more likely to present to hospital for angina; 1.6x (RR 1.59; 95% CI 1.10-2.31) more likely to have nonfatal MI; 1.7x (RR 1.67; 95% CI 1.28-2.20) more likely to require coronary revascularization; and 1.8 x (RR 1.75; 95% CI 1.27-2.41) more likely to develop heart failure [139].

Diagnostic Testing

The role of physicians in the gender bias related to the diagnosis and interpretation of coronary heart disease symptoms was investigated by Chiamonte et al. (2006) in which 56 physicians were randomized to assess vignettes describing male/female subjects who were/were not under stress [140]. Neither the sex of the physician nor their attitude towards women affected the assessments. In non-stressful vignettes, there was no difference in the diagnosis or treatment of female and male subjects. However, in scenarios that included stressful situations, women's symptoms were more likely to be ascribed to psychogenic rather than organic causes.

A study in 1999 carried out by Schulman found that when patient actors presented the same story and same history, women were about 40% less likely to be referred for cardiac catheterization than males, and black patients were about 40% less likely than white patients. Black women were 60% less likely to be referred for catheterization. Non-white patients were found to have a two-fold increased risk of not being admitted for acute cardiac ischemia [141]. Further, non-white patients who had acute myocardial infarction had a 4.5 fold increase risk of not being admitted to the hospital.

Mora et al. (2003) evaluated exercise testing in asymptomatic women and found the ECG changes were not predictive in this population, but low fitness (exercise capacity and heart rate recovery) were prognostic of cardiovascular death [142].

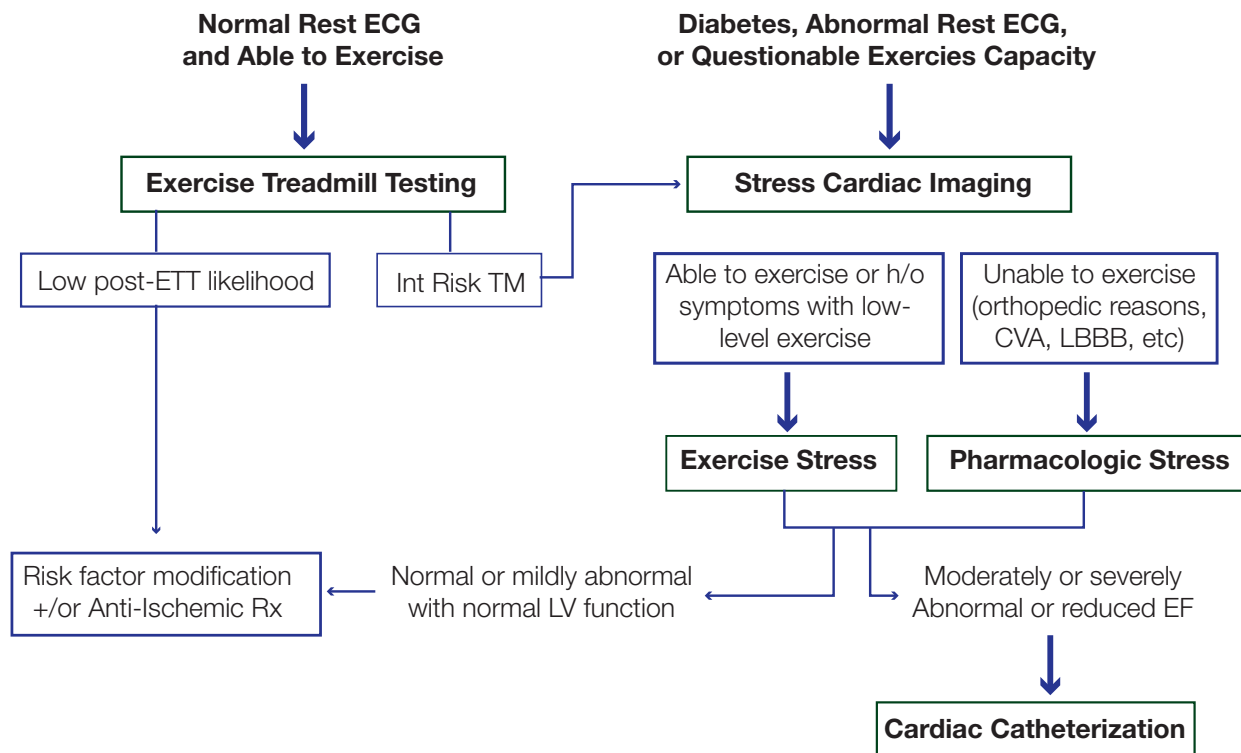
In 2005, the American Heart Association also released its Scientific Statement on the 'Role of Noninvasive Testing the Clinical Evaluation of Women with Suspected Coronary Artery Disease' [143]. While current evidence does not support the use of imaging in low-risk asymptomatic women, evidence is emerging for the use of imaging in asymptomatic women with an intermediate risk score (Framingham Risk Score). In contrast, non-invasive diagnostic studies are recommended for symptomatic women at intermediate risk. Treadmill testing with exercise ECG is the oldest and most common form of non-invasive testing. While this test is not as accurate (lower sensitivity, lower specificity) in women as in men, current guidelines still suggest its use as the initial test of symptomatic women at intermediate risk of CAD. Newer data suggest that the diagnostic and prognostic accuracy of the exercise ECG can be enhanced by including functional capacity and heart rate recovery in the interpretation of the ST-segment response to exercise.

The indications for cardiac imaging in symptomatic cohorts of women are summarized in the figure below. Cardiac imaging is recommended in women with indeterminate or intermediate-risk exercise ECG test, as well as in those women with an intermediate-risk Duke treadmill score. Diabetic women merit special consideration and are recommended for cardiac imaging because of their high risk for cardiovascular death. Cardiac imaging with contemporary techniques of stress echocardiography or gated SPECT myocardial perfusion imaging provides accurate diagnostic and prognostic information in women with suspected CAD.

That 2005 ACC/AHA guidelines algorithm for the non-invasive evaluation of symptomatic women is given below:

Figure 2: 2005 American College of Cardiology (ACC)/ American Heart Association (AHA) Guidelines for Non-invasive Evaluation

Intermediate - High Likelihood Women with Atypical or Typical Chest Pain Symptoms



Risk Stratification

While early detection can be more effective for women than men, some authors have found that the Framingham risk assessment tool may underestimate [33] or overestimate [144, 145] cardiovascular risk in women. Pletcher and Baron (2005) suggest that risk estimation can be improved by using serum CRP levels, coronary artery calcium scanning, or other novel risk factors for women at intermediate risk for CVD [56].

Shai et al. (2004) examined lipid data from 32,826 women in the Nurses Health Study to identify predictors of coronary heart disease [146]. HDL-C ratios were the strongest predictors of CHD while low levels of HDL-C

were a key discriminator of higher coronary heart disease events. Using the same sample, Shai et al. (2005) also confirmed that increased levels of Lp(a) were associated with increased risk of coronary heart disease in women [147].

Ridker et al. (2003) demonstrated that C Reactive Protein (CRP) added additional prognostic information in women with metabolic syndrome [148]. Cushman et al. (2005) evaluated CRP levels in elderly women and men and determined that CRP independently predicted increased risk of coronary heart disease in both sexes [52]. Ballantyne et al. (2004) confirmed the independent predictive value of CRP and also noted that lipoprotein-associated phospholipase A2 independently predicted coronary heart disease, but only in patients with low LDL levels (< 130 mg/dl) [149]. Pai and colleagues (2004) also showed that elevated levels of CRP were associated with increased risk of coronary heart disease in men and women, but only in women were tumor necrosis factor (TNF) and interleukin-6 also associated with increased risk [150].

Zylberstein et al. (2004) confirmed that elevated serum homocysteine levels were independently associated with increased risk of MI, fatal and non-fatal, in women, as was early noted in men [151]. However, despite promising evidence from recent meta-analyses of the benefit of homocysteine reduction on the risk of IHD and stroke [152, 153], 3 large prospective trials failed to demonstrate efficacy of homocysteine lowering (NORVIT, VISP, HOPE-2). The Vitamin Intervention for Stroke Prevention (VISP) examined the use of a vitamin B combination in stroke patients and did not show a reduction in CV events [154]. The Norwegian Vitamin Trial (NORVIT) randomly assigned patients to placebo; vitamin B12 + folic acid; vitamin B6; or vitamin B12 + B6 + folic acid. In patients randomized to receive folic acid, homocysteine levels did decline but there was no reduction in CV events. Indeed, in the patients receiving all three B vitamins, there was some suggestion of harm relative to placebo (HR 1.22; 95% 1.00-1.22) [155]. The Heart Outcomes Prevention Evaluation (HOPE-2) also demonstrated a reduction in homocysteine levels with combination vitamin B use, but no reduction in CV events in diabetic patients with vascular disease [156].

In an NIH evidence report, the role of diabetes as a risk factor for CHD was examined. Several studies have suggested that DM is a stronger risk factor in women than in men [157]. Huxley et al. (2006) completed a meta-analysis of 37 studies to examine the risk of fatal CHD and diabetes in men and women [158]. In this analysis, women with diabetes were at significantly increase risk of fatal CHD compared to men (OR 1.46; 95% CI 1.14-1.88). Juutilainen et al. (2004) also reported that women with diabetes were at increased risk of CHD death or major CHD event compared to men, but this sex effect was modified by the presence of hypertension (p interaction 0.011) and elevated cholesterol (p interaction 0.04) [159]. Wang et al. (2004) evaluated the association between diabetes and CHD in Aboriginal women and men and found that Aboriginal women appear to be especially disadvantaged [160]. The risk of CHD in Aboriginal women with diabetes was 3.7 compared to 1.4 in Aboriginal men. Hunt et al. (2007) found that the presence of metabolic syndrome significantly modified the association between diabetes and sex on the risk of CHD mortality [161]. When diabetes and the metabolic syndrome occur together, the risk of CHD mortality is 14.3 (95% CI 6.62-30.7) in women, compared to 4.21 (95% CI 2.32-7.65) in men. While the NIH evidence summary confirmed a slightly higher adjusted OR for CHD mortality in women than men, the difference was modest and not statistically significant. They also noted that while CHD mortality was slightly higher in women, all-cause mortality was higher in men. There was no evidence of ethnic differences in the impact of diabetes on CHD mortality.

In a study of 1041 patients with stable CAD followed for 9.2 years, there was strong evidence of a sex difference in the effect of the metabolic syndrome on mortality. In women with metabolic syndrome the

relative risk of mortality was 2.2 (95% CI 1.1, 4.3), $p = 0.02$, while in men the presence of the metabolic syndrome was not associated with mortality RR 1.0; 95% CI 0.5-1.9, $p = 0.93$ [162]. In the Women's Ischemic Syndrome Evaluation (WISE) study, women with angiographic evidence of CAD and metabolic syndrome had significantly increased the risk of adverse coronary events (RR 4.93; 95% CI 1.02,23.76, $p < 0.05$), compared to women without metabolic syndrome. Hunt et al. (2007) also demonstrated that when diabetes and the metabolic syndrome occur together, sex is a strong modifier of the joint effect of diabetes and metabolic syndrome on CHD mortality with women experiencing a significantly higher risk than men, RR 14.3; 95% CI 6.62, 30.7 and RR 4.21; 95% CI 2.32, 7.65, respectively [161].

The NIH evidence report by Grady et al. (2003) also confirmed the value of troponins for risk stratification in women [157]. Elevated troponins were associated with an increased risk of death in both women (OR 2.63; 95% CI 1.75-3.95) and men (OR 2.83; 95% CI 1.92-4.17), but in women elevated troponins were also associated with an increased risk of non-fatal MI (OR 1.80; 95% CI 1.28-2.54), but not in men (OR 1.06; 95% CI 0.8 – 1.45).

Interventional Procedures and Outcomes

A comparison of interventional procedures in the US, England and France demonstrated that women were less than half as likely to undergo interventional treatments for coronary artery disease. This difference was consistent across countries despite differences in health systems and patterns of medical practice [163]. A recent study of over 20,000 AMI patients admitted to hospital with ACS in Switzerland found that women were significantly less likely to undergo PCI, both for ST elevation MI and non-ST elevation MI. Even after adjustment for baseline differences women were 30% less likely than men to undergo PCI (OR 0.70; 95% CI 0.64-0.76). [164].

The benefit of an early invasive management strategy was demonstrated in FRISC II and RITA 3, but there was the suggestion of harm for women enrolled in these studies [165]. This is in contrast to TACTICS-TIMI 18 in which the benefit of this strategy was demonstrated in women (RR 0.72; 95% CI 0.47 – 1.11), without any evidence of effect modification by sex (p interaction = 0.60) [165]. In women with elevated troponins, the benefit was even greater (RR 0.47; 95% CI 0.26 – 0.83). Potential reasons for the differences between FRISC II and RITA 3 versus TACTICS-TIMI 18 include the delayed timing of intervention in the invasive arm of FRISC II, a lower risk population in FRISC II and RITA 3, lack of routine GP IIb/IIIa use and higher use of CABG in FRISC II.

a) Percutaneous Coronary Interventions (PCI)

Jacobs et al. (2002) compared outcomes following percutaneous coronary interventions (PCI) in women between 1985/86 and 1993/94 [166]. Despite increases in the number of high risk women undergoing PCI in the latter period, outcomes improved. Combined death/MI/CABG in-hospital decreased from 11.6% to 6.0% and there was no sex difference in the rate of death +/- MI at one year.

A sex-based analysis of data from the TAXUS IV trial of the paclitaxel-eluting stent showed that the benefits of this drug eluting stent, over bare metal stents, was generalizable to women; 30-day major adverse cardiac event rate was 2.1% in women compared to 3.2% in men ($p = 0.48$). Surprisingly, target vessel revascularization was higher in women than in men randomized to the drug eluting stent; 10.8% versus 5.7%

respectively ($p = 0.03$). This sex difference was not observed in patients randomized to bare metal stents where the rates in women (17.5%) and men (17.0%) were comparable ($p = 0.95$) [167]. More recently, a pooled analysis of data from four DES clinical trials of sirolimus eluting stents also demonstrated comparable efficacy in women and men at 30 days and at 1-year [168]. The evidence from clinical trials is also supported by real world data from the NHLBI Dynamic Registry. This Registry collects data on all patients undergoing PCI at 17 clinical centres across the US [169].

In AMI patients undergoing primary PCI, myocardial salvage was greater in women (64%) than in men (50%), $p < .001$. Myocardial salvage is the proportion of the initial perfusion defect that is salvaged by the reperfusion treatment, in this case PCI. Even after adjustment for sex differences in baseline characteristics female sex was an independent predictor of greater myocardial salvage ($p = 0.002$) [170].

In 2005, the American Heart Association published a Scientific Statement on PCI and Adjunctive Pharmacotherapy in Women [171]. Recommendations include the use of drug eluting stents (DES) as the data demonstrate reductions in restenosis, target vessel revascularization and major adverse cardiac events at 1 year with a similar magnitude in women and men. Results also suggest favourable long-term outcomes associated with DES use in women with small vessels (< 2.75 mm). The AHA Statement also recommends the use of an early invasive strategy with adjunctive GP IIb/IIIa antagonist use in women with UA/NSTEMI and high-risk features. The evidence also supports the efficacy of primary PCI over thrombolytic therapy, when access to primary PCI is readily accessible. The use of adjunctive pharmacotherapy based on the ACC/AHA guidelines is summarized in the table below:

Figure 3: ACC/AHA Guidelines on Adjunctive Pharmacotherapy

Antiplatelets	
Aspirin	Women undergoing elective PCI or PCI for ACS should receive aspirin 80-325 mg at least 2 h before procedure. Aspirin should be continued indefinitely on a daily basis for secondary prevention, but exact dose after treatment with DES has not been determined.
Thienopyridines	
Clopidogrel	Women undergoing elective PCI or PCI for ACS should receive 300-600 mg load; clopidogrel, 75 mg, should be continued for at least 2-4 wk after bare metal stent implantation and for several months after drug-eluting stent implantation (3 mo for sirolimus, 6 mo for paclitaxel). Optimal loading dose and pretreatment time for clopidogrel remain unclear. Clopidogrel should be withdrawn for 5-7 d before planned CABG to minimize bleeding complications.
Ticlopidine	Ticlopidine (500 mg load, 250 mg twice daily) can substitute for clopidogrel in clopidogrel-intolerant patients.
GP IIb/IIIa Inhibitors	
	GP IIb/IIIa inhibition reduces ischemic complications in high-risk (troponin-positive, diabetic, older adult) patients including women undergoing elective PCI or PCI for ACS with balloon angioplasty or stenting. GP IIb/IIIa inhibition with abciximab in women with STEMI (without shock) undergoing primary balloon angioplasty or stenting may reduce ischemic complications without increasing risk or major bleeding.
Antithrombin agents	
UFH	During STEMI, UFH treatment benefit is established in women. Observational data support use of empiric UFH during PCI in women to achieve an ACT of 250-300 s. Current guidelines advise weight-adjusted UFH (60- to 70-U/kg IV bolus; 12- to 15-U·kg ⁻¹ ·h ⁻¹ infusion) with target activated clotting time 250-300 s for HemoTec and 300-350 s for HemoChron. Lower doses may be considered in women and older adult patients and when UFH is combined with GP IIb/IIIa inhibitors during PCI; maximum bolus and infusion when UFH is used as adjunct to fibrinolytic therapy is 4000-U bolus and 1000-U/h infusion. No established benefit of long-term UFH after PCI exists.
Low-molecular-weight heparin	Women with UA/NSTEMI treated with LMWH experience more bleeding complications than do men. Combined LMWH and GP IIb/IIIa inhibition appears effective in women with UA/NSTEMI undergoing PCI; however, it is associated with increased bleeding.
Direct thrombin inhibitors	Bivalirudin and provisional GP IIb/IIIa results in similar outcomes compared with UFH with planned GP IIb/IIIa inhibitors during PCI and up to 6 mo after PCI and fewer bleeding complications in women.
This table summarized the findings for women drawn from the literature review. It is not the intention of the writing group to provide formal treatment recommendations; rather, this table should serve as a convenient point of reference. Refer to text for discussion and citations. When recommendations are provided, they are based on previously published ACC/AHA guidelines.	

b) Coronary Artery Bypass Surgery (CABG)

While older studies demonstrated poor outcomes for women following coronary artery bypass surgery (CABG), Humphries et al. (2007) demonstrated a significant improvement in short-term outcomes from 1991 to 2003 in a population-based cohort from BC, Canada, effectively removing the sex difference [172]. In contrast, Bestawros et al. (2005) found higher mortality rates in women post CABG, as well as longer length of stay (10%), and higher overall costs (7%), compared to men [173].

Vaccarino et al. (2003) demonstrated the presence of sex differences in recovery post CABG, with women experiencing decreased physical function at 6-8 weeks post CABG and increased levels of depression, while men did not experience any change in physical function and depression declined [131]. Women also had more hospital re-admission than men, following CABG.

In a study of 229 patients in the north of England discharged from hospital post MI, women had less improvement than men in physical and social functioning. The observed sex difference may have been mediated by lower educational attainment and more women without access to a car, which are both markers for social deprivation. In a Canadian study of patients with coronary artery disease (CAD), Norris et al. (2007) showed that at one year women had worse physical and mental scores, as well as higher depressive symptomology compared to men [174]. The impact of self-rated health was examined by Ruo et al. (2006) among 2675 postmenopausal women with CAD [175]. Women with persistent or new depression were more likely to rate their health as fair/poor. The impact of depression on self-rated health was comparable to the impact of recent angina, MI, angioplasty, heart failure or CABG.

Pharmacological Treatment

Pharmacological interventions may be useful for some women, depending on their risk profile [56]. For example, aspirin or lipid-lowering medications should be reserved for women with 10 year risk of CVD greater than 10%. Other conditions that may be reserved for women with higher risk, include the treatment of hyperlipidemia and dietary supplementation with omega-3 fatty acids or folate. Yet, HRT as well as antioxidant use may be harmful, rather than useful for women's heart health [4, 176].

a) Acetylsalicylic Acid (ASA)

The evidence base of the efficacy of aspirin (ASA) for primary and secondary prevention of cardiovascular events is solid. However, much of this evidence was obtained from studies with few if any women. The Women's Health Study, a randomized controlled trial of low dose aspirin in women, demonstrated a significant reduction in the risk of stroke (RR 0.83; 95% CI 0.69-0.99) but not for MI (RR 1.02; 95% CI 0.84-1.25) [177]. These findings were confirmed in two recent meta-analyses of randomized controlled trials of aspirin for the primary prevention of cardiovascular events. The studies demonstrated that aspirin reduces the risk of MI in men, but not women⁹ [178, 179], and reduces the risk of stroke for women, but not men [178].

In a cross-sectional study using data from the 2000 -2002 Medical Expenditures Panel Survey in the US, aspirin use in patients with coronary heart disease was examined. Women reported more contraindications to ASA use (20.5% versus 12.5%) but even in those without contraindications, ASA use was lower in women (79.8% versus 86.4%). Even after adjustment for age and comorbidities, women were 32% less likely to use ASA than men (OR 0.68; 95% CI 0.48 – 0.97). [180].

⁹ Only in trials that predominantly enrolled men was there evidence of risk reduction (RR 0.62; 95% CI 0.54-0.71); studies with proportionately women demonstrated no risk reduction (RR 0.87; 95% CI 0.71-1.06).

b) Angiotensin Converting Enzyme Inhibitor (ACE-I)/ Angiotensin Receptor Blockers (ARBs)

Using administrative data from the province of Quebec, Keyhan et al. (2007) looked at angiotensin converting enzyme inhibitor (ACE-I) use and survival in men and women with heart failure [181]. They identified all Quebec patients, > 65 years of age, discharged with a diagnosis of heart failure between 1998 and 2003 and compared outcomes of this using and not using an ACE-I. While both men and women benefited from the use of ACE-Is, the benefit was not as great in women (RR 0.80; 95% CI 0.76-0.85) as in men (RR 0.71; 95% CI 0.67- 0.75). This difference was statistically significant (p interaction <.001).

Using the same administrative data set, Hudson et al. (2007) demonstrated sex differences in the effectiveness of angiotensin receptor blockers (ARBs) and ACE-I in this elderly cohort with heart failure [182]. Women using ARBs had significantly better outcomes than women using ACE-I (RR 0.69; 95% CI 0.59-0.80), while in men there was no difference in the effectiveness of ARBs and ACE-I (RR 1.10; 95% CI 0.95-1.30).

In an examination of the data from the Val HEFT Trial of the valsartan (an ARB) in patients with heart failure, Majaholme et al. (2005) noted that valsartan was equally efficacious in women and men [183]. However, in the presence of diabetes and coronary artery disease, women, but not men, were at increased risk of non-fatal cardiac events, with no sex effect on mortality.

c) Statins

HMG-CoA reductase inhibitors (statins) form a class of hypolipidemic drugs used to lower cholesterol levels. Several randomized controlled trials have demonstrated efficacy of statins in women. In women without evidence of CAD, lovastatin reduced the level of LD cholesterol 150 mg/dl on average. And in those with the lowest HDL levels, the benefit was the greatest, with a significant 46% reduction in CAD events in women on lovastatin versus women on placebo [184]. The largest secondary prevention trial was the Heart Protection Study, which enrolled 5082 women (25% of the total cohort) with baseline CAD or a risk equivalent, such as diabetes or prevalent vascular disease. Women on fixed dose statin experienced a 24% reduction in CAD events over a 5.5 year follow-up, a reduction equivalent to that seen in men [185].

Karp et al. (2007) identified sex differences in the effectiveness of statins after myocardial infarction [186]. Using Quebec administrative data, they identified all patients, > 65 years of age, discharged from hospital with a primary diagnosis of myocardial infarction between 1998 and 2003. In patients filling prescriptions for statins, both cardiac-related and all-cause mortality were reduced relative to those who did not fill prescriptions for statins, but the magnitude of the effect was greater in men than women. In a NIH Evidence Report, 20 trials of lipid lowering were evaluated, but only 9 published results by sex [157]. However, in those statin trials that did report sex-specific outcomes, statin use in women was associated with a 26% reduction in CHD mortality; a 36% reduction in non-fatal MI and an overall 21% reduction in CHD events. However, the efficacy in primary prevention is unclear at this time.

d) Evidence-based Medication Use

Practice guidelines based on evidence from randomized clinical trials support the use of ACE-I, ASA, beta-blockers and statins in patients with AMI [187-189]. In a study by Ramsay et al. (2006), the introduction of the National Services Framework in the UK was associated with an increase in the use of evidence-based medications in patients 60-79 years of age with coronary disease [190]. There were no differences in medication use between women and men, except for anti-platelet agents, which were used significantly less frequently in women. Reid et al. (2002) investigated the use of statins in patients with coronary heart disease and also found no sex difference in the prevalence of statin use [191]. In contrast, a study in Ireland among patients with ischemic heart disease who filled a prescription for nitrates, women were significantly less likely than men to use beta blockers, aspirin, and ACE-I, while anxiolytic benzodiazepines were used more frequently among women.

The CRUSADE (Can Rapid Risk Stratification of UA Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines) National Quality Improvement Initiative demonstrated significant sex differences in treatment and outcomes among patients with non-ST elevation MI [192]. Women, who comprised 41% of the study cohort (n= 35,875) were older and had more co-morbidities (hypertension, DM) than men. Despite their higher risk they were less likely to receive acute heparin, ACE-I, glycoprotein IIb/IIIa inhibitors in hospital and less aspirin, ACE-I and statins at discharge. Women were also less likely to undergo cardiac catheterization (adj OR 0.87; 95% CI 0.82-0.92), but among those undergoing catheterization there was no sex difference in the use of PCI, while CABG was significantly lower in women (adj OR 0.59; 95%CI 0.54-0.64).

Cardiac Rehabilitation

Women are less likely to attend rehabilitation programs, have lower adherence and higher dropout rates, even though they experience similar or greater benefits than men who participate in rehabilitation programs [33, 90]. For example, in a longitudinal study of 253 patients discharged following AMI, only 19% received a referral to cardiac rehabilitation and only 15% enrolled. Among those who received information or a referral, 80% enrolled; among those who did not receive information or a referral, 0% enrolled. Income below \$20,000 per year was associated with a lower likelihood of receiving information or a referral [193].

Similarly, Sanderson and Bittner (2005) examined factors associated with cardiac rehabilitation program completion in 228 women between 1996 and 2003 [194]. Both obesity and depression decreased the likelihood of program completion. The odds of being obese in completers compared to non-completers was 0.28 (95% CI 0.10-0.76), while the odds of having a high BDI-II score (depression) in completers compared to non-completers was 0.87 (95% CI 0.81-0.95).

Further, psychosocial stress such as multiple roles and presence of social support influence women's recovery [127]. Marcuccio et al. (2003) found that many women continue to have negative consequences after diagnosis, and that many do not make changes to their health behaviours because of a lack of resources, poor access to health care, lack of social support, and depression or anxiety¹⁰ [104]. Orth-

10 More women in the study reported changing eating habits after diagnosis, yet there were mixed reports regarding changes in activity levels. 42% of the women indicated that they had changed employment since diagnosis, and 36% reported financial concerns related to their disease. 42% of women also reported that their relationships had changed following diagnosis, many indicating that they had to give up primary caregiver duties. Over half of the women reported anxiety and/or depression related to their illness, while 40% reported that their spiritual life had altered. Only 21% of women reported no life changes due to the disease. When asked what advice they could give back, the most common response was the need to "educate yourself and ask questions" (p.27).

Gomer's (2007) review discusses psychosocial risk factors for CVD [195]. They found that women in lower social strata report more depression, hostility and social isolation and higher morbidity and mortality from CHD.

Another study found that when social isolation and depression are combined, women have a worse prognosis and the progression of coronary atherosclerosis is increased [10]. They also cite a study in Stockholm which found that stressful conditions in women's lives and marital stress were more predictive of CVD than stress at work. They identified much less data on adjustment, though they did find that this tends to be more difficult for women than for men (women report more anxiety, sleep problems and depression). Women are also less likely to return to work following a myocardial infarction and/ or bypass surgery, and are typically not counseled on sexual activity following cardiac events

Davidson et al. (2003) reviewed the perceptions and rehabilitative needs of older women with heart disease and found that older women have poorer prognosis, and experience greater disability, depression and anxiety, are at a higher risk of psychosocial distress, have more need for instrumental and social support, have an altered perception of risk, and need rehabilitation programs tailored to their needs [91]. Women often have additional symptoms that may prevent accurate diagnosis, such as arthritis or lung disease. According to this study, women report feeling shame, guilt and denial during a cardiac episode, are more depressed and anxious than men with heart disease and have poorer outcomes. Depression and anxiety can result in slower recovery and poorer compliance with treatment recommendations, and can also contribute to women engaging in more risky health behaviours. Older women are also less likely to have support at home, because they are more likely than men to be widowed [91].

Conclusions

As demonstrated by this review of the diagnosis and treatment of heart disease in women, there are sex and/or gender based differences in and influences on women's diagnosis, presentation, and access to and outcomes of various treatments. Overall, women tend to delay seeking treatment, report more atypical symptoms than men, exhibit sex differences in risk factors and risk stratification, encounter gender biases in diagnosis and treatment, and demonstrate sex-specific responses in the effectiveness of certain pharmacological treatments. Therefore, research, policy and program development of cardiovascular screening, diagnostic and treatment for women, needs to account for these factors in order to provide effective secondary prevention and treatment options for women.

3) Women's Heart Health and Policy Issues

As we have seen, women's heart health is affected by a wide range of factors, including various biological and genetic predispositions, social influences, and access to and quality of health care, in particular women-specific diagnostic, treatment and rehabilitation practices and patterns. Indeed, women's heart disease has a multi-factorial etiology, including individual level factors, social-structural elements, and a range of pre-disposing and clinical factors. Taken together, the preservation of women's heart health, and the reduction and amelioration of women's heart disease therefore require a range of initiatives. Despite this observation, as we have seen, little of the literature reviewed in the prevention and treatment sections reflects this. Rather, much of the prevention and treatment literature does not explicitly link the multi-level factors or attempt to measure their interactive effects and contributions to women's heart health or disease.

In this section, we discuss the broader context of the policy and practice issues connected to women and heart health, including their effects on individual level behaviours, the delivery of care, and the importance of broad social and health policy. Ultimately, there are several levels of practice and policy implications stemming from this review. They are organized into macro, meso and micro levels for ease of discussion.

Policy Issues Affecting Heart Health and Heart Disease in Women

Policy affects women's heart health and women's heart diseases at multiple levels. Policy can contribute to ameliorating negative social structural influences on women's heart health (such as poverty), create a policy environment for women's heart health promotion programming, encourage sex and gender sensitive research related to women's heart health and disease, and reinforce better clinical practices in addressing women's heart health and disease. Policy can also improve women's health for women by facilitating health enhancing behaviours or improving access to gender sensitive care. If and when women experience symptoms of heart disease, policies can directly affect access to and quality of health care, diagnostic, treatment and rehabilitation, professional practices and program funding.

As discussed in section one, there are numerous approaches to risk reduction and prevention of heart disease in women that make up heart health promotion programming. These approaches often focus on factors that manifest as individual level behaviours, such as tobacco reduction or cessation, physical activity, stress reduction and improved diet. These factors refer to individual practices and are often referred to as "lifestyle" factors. However, these behaviours are fundamentally affected by structural factors, such as socioeconomic status, work patterns, care-giving responsibilities, family structures, and the built environment. In addition, these factors are also psychosocial, complicated by co-occurring factors such as depression and exposure to violence and poverty, which are themselves gendered and unevenly distributed across the population. For these reasons, we have avoided the term "lifestyle" factors and rather referred to these as individual level factors.

As we have seen in section two, there are also several issues of concern in the response to women's heart diseases, in identification, diagnosis, treatment and rehabilitation. These issues also reflect policy and practice decisions, such as the existence and nature of women specific programming, or the nature of professional education. Research practices are also subject to policy decisions, such as requiring clinical trial

inclusion or applying sex and gender analysis to all research. Policy frames affect these standards and lead to mandated standards by both professional associations and research funding agencies.

Further, there are policy making issues that apply to addressing the risks and responses to both women's heart health and heart disease. In general, policy making follows a "policy cycle" or policy process within government [196]. These elements include identification of the issue, collecting data and evidence, consultations with key stakeholders and developing options, decision making, implementation and assessing effects.¹¹ In Canada, the federal policy requiring the use of Gender Based Analysis (GBA) in all policy making in the federal government is an added layer of particular importance to women's health.

All of these processes are affected by the quality of available evidence, or the strength of the surveillance system for women's health, which, in Canada is not comprehensive or consistent [196]. This is due to a wide range of factors including lack of systematic data collection and structures, lack of agreement on key indicators and measures and lack of sensitivity to diverse characteristics of the population. In addition, a range of factors affects the interactions between policy makers and researchers, including the receptor capacity among policy makers, as well as their degree of involvement of with research processes and the relevance of research programs and results¹² [197].

Ideally, policy making relies on forecasting, making predictions about the evolutions of population characteristics and risk, and projecting future trends. Forecasting can also be a basis for economic assessments of costs to individuals and state systems. In practice, however, health authorities or local organizational units have assumed decision making power in many jurisdictions and can create and enact health policy. In the UK, for example, McDonald (2002) reports on a case study of a primary care trust revealing that several assumptions about decision making such as assuming knowledge among local medical personnel and assuming that good practices are learned and applied do not necessarily pan out [198]. While regionalization is often seen to bring services "closer to the patient," McDonald concludes that in essence, it brings "decision making closer to local practitioners, who appear to focus on those aspects of care that are relevant to their own immediate environment" (2002, p.134). She concludes that rational models of decision making, especially encouraged for enhancing population health, are not easy to embrace or enact at the local level.

Fiscal realities, especially of government budgets, are often a final arbiter of policy choice. The Heart and Stroke foundation of Canada (2000) estimates the total annual cost to Canada of CVD is \$20 billion. Birnbaum et al. (2003) offer a conservative estimate that the lifetime medical cost for US women with CVD was \$423,000 (in 2002 dollars) [199]. While overall economic assessments are often based on costing exercises for various conditions, diseases or trends, these exercises are often blind to the effects of gender and diversity in their calculations [200]. In particular, costing exercises often concentrate on state level costs, while ignoring individual level costs, or third party costs. In Canada, efforts to estimate annual direct and indirect costs to all parties are few, but have been made on specific topics such as domestic violence [201].

Undoubtedly, costs are gendered. While few studies report direct health care costs on men and women separately, two studies in both Germany and Sweden report that the costs for women are higher than for men [202]. Studies limited to direct health care costs of CVD are limited, however. With respect to costing

11 These processes are affected by political decisions, ideological approaches to understanding health and health care and budgetary considerations.

12 In general, analysts agree that policy making models range across a spectrum of possibilities, including rational models, to incrementalist approaches (that include a range of values, interests, and locations) to process-oriented approaches that rely on networks, to more idiosyncratic approaches that defy tidy labels.

the effects of cardiovascular disease, Nicholson (2003) argues that while 'working days lost' is an important measure for both women and men, "a more relevant cost analysis would also include wider economic burden of women's absence or incapacity, taking into account their pivotal social and caring roles" [203, p. 47]. Taking these measures into account, the cost of women's CVD is likely higher than men's. The development of a comprehensive costing approach for women's cardiovascular disease in Canada is an important step in creating a policy response.

Despite the multiple levels of policy, the multifactorial nature of women's heart health and disease and the range of possible policy making processes, modeling and evidence uptake practices, the following discussion highlights some of the policy and practice issues that are amenable to policy discussion and decision making that would have an effect on women's heart health.

a) Systemic Issues - MACRO

Systemic issues such as social, health and economic policies, or environmental factors such as the built environment affect women's heart health. In addition, less obvious but equally pertinent policies affect how research is funded, carried out and whether or not women's health research is a priority. Similarly, politics, ideology and fiscal issues affect priority setting in government, affecting not only broad policies but also funding of women's health programs and their evaluation.

i) Socioeconomic factors and inequality

Wisdom et al. (2005) point out that social and economic circumstances play a key role in determining health status, particularly for women [204]. They argue that such factors are mediated by government policies. While this observation is linked to health outcomes, an analysis of the history of health promotion activities in Canada and worldwide, however, reveals that both individual and societal level factors affect health [205]. Although health promotion practice over the past 20 years has seen variable emphases on either or both of these aspects, current research indicates that social and economic factors interact with individual characteristics to create health [205].

Nonetheless, health care policies and programs need to address social and financial barriers that impede the adoption of heart-healthy behaviors. For example, in jurisdictions where the status of women is low and where income inequality is high, the health of women and children is worse [204]. Further, these factors (status and inequality) are directly influenced by policy. In their study of the effect of state level policies on women's health in the US, Wisdom et al. (2005) identified and assessed the strength of key policies and estimated their effects on women's health including heart disease. They found that low SES is the primary indicator of heart disease mortality in women, and a larger risk for women than for men [204].

A range of countries other than the US have determined the effects of socioeconomic factors on health outcomes, and/or the interaction of women's health status and social policy. Indeed, the link between sexism and the actual treatment of heart disease in women has been drawn and calls made for more "systematic gender-based decision making combined with medical oversight and review of individual clinical cases" [206]. In Canada, access to quality care for women, social and economic policy shifts, a measure of the status of women, and heart health outcomes would need to be rigorously assessed over time in order to ascertain exactly how policy interacts with women's heart health in the Canadian context.

ii) Environmental and cultural barriers

Both cultural and environmental issues are relevant to women's heart health. Eyler et al. (2002), report that focus groups of high risk women identify factors that prevent them from engaging in physical activity, such as social support, cultural barriers, family care-giving demands, physical barriers and policy issues such as cost, lack of child care or personal safety. Various levels of environmental issues present barriers to women's heart health. For example, weather, limited daylight, lack of sidewalks, traffic and distance were some of the key barriers reported by a diverse group of women [207]. Many of the minority women in the study indicated that there was little encouragement for physical activity among girls and women in their ethnocultural groups (i.e. African American, Latina), that acceptable eating patterns and body size were also different for them (i.e. African American and American Indian) and that family responsibilities weighed more heavily on them than White women (African American, American Indian and Latina).

In a study by Jilcott and colleagues (2006), community level and environmental level factors were associated with women's health behaviours [27]. For example, participants reported the following barriers: lack of restaurants with healthy food choices (41%), lack of farmers markets or fresh produce (50%), not enough affordable exercise facilities (52%), or women appropriate physical activity programs (42%), heavy traffic (47%), and speeding drivers (53%). Overall, women expressed little awareness of affordable exercise venues or nutrition classes. These findings are consistent with other studies. In the Eyler study, the main suggestions involved the provision of child care, sliding fee scales for programs, financial incentives for participation and increased safety for women in parks and community centres (2002, 127).

King (2003) argues for the need for large, multi-level environmental and policy level public health approaches to increase women's physical activity [208]. For example, she suggests that for women this could mean increasing access to facilities in addition to environmental programs such as: posting signs to encourage stair use at work and targeting PA-based commuting behaviours. She also claims that individual changes are required; for example, encouraging physicians to discuss and support patients to increase regular physical activity. According to King, behavioural strategies such as goal-setting and monitoring can also be effective for increasing women's PA. In sum, she makes the case for linking individual level with population-wide strategies, and also linking physical activity messaging with other community and population based goals

There is a clear need for more multi-level analyses and interventions addressing community barriers, including strategies such as: efforts to identify and establish safe and convenient walking venues, affordable gyms, culturally appropriate PA programs, and identifying and supporting restaurants with healthy options. At the same time, the relationship between these types of factors and women's ethnocultural influences, individual psychosocial issues, health behaviour and empowerment needs more study with more advanced theory and methods, in order to identify the mix of factors that ultimately affect women's health behaviours.

iii) Enhanced research policies and practices

Women and elderly patients are continuing to be severely underrepresented in clinical trials, according to a US analysis of 600 studies between 1966 and 2000 [209]. Ghada Mikhail, a UK cardiologist reports that women account for only 30% of participants in studies and trials in cardiology [210]. There is also a low rate of reporting sex-specific data; for example a comprehensive review of the literature on the burden of CVD in women and men surfaced only 33 studies [107]. These deficiencies and omissions create serious scientific and clinical issues in that elderly females constitute the largest growing segment of heart patients and yet research evidence is not being built to create appropriate prevention and treatment. Indeed, Azad

and Nishtar (2005) call for a global strategy to include and report on, sex and gender issues in cardiovascular research [211].

As noted in our review of both prevention and treatment literatures, there is a need for the introduction of sex, gender and diversity lenses to all pillars of research. More and more researchers and research funding bodies are calling for clear inclusion of both sex and gender related factors in health research. Both gender and sex are required considerations in heart health research and practice [212]. Documents and manuals are beginning to appear to instruct researchers [20], policy makers [19], and peer reviewers [18], on how to integrate these concepts into health research and policy making. Effective usage is imperative, however, as Aulakh and Anand (2007) warn that while the performance of sex and gender analysis is common in randomized control trials on cardiovascular disease, many of these analyses were improperly conducted, resulting in misleading conclusions for clinicians [213].

Theoretical orientations and conceptual frameworks are also in need of improvement in order to fully address women's heart health. The multifactoral nature of women's heart health and disease demands that we take into account all features and contexts of women's bodies and lives in addressing heart health, in both research and practice. There is also a need for more research and interventions for diverse and minority groups. Hence, continued training and more effective measure development is urgently required to bring these concepts forward in a meaningful way.

b) Institutional and Community Level Issues– MESO

Communities and institutions also frequently make policy that affects women's heart health and the responses to women's heart disease. Specifically, health care institutions such as health centres, health authorities or hospitals can overtly recognize women as a group needing specific heart health promotion or intervention programming, and make funding and training available to practitioners to create sustainable successful programs. Similarly, communities can design opportunities and instill practices that enhance social support, increase women's empowerment and offer culturally appropriate health promotion to women.

i) Community programs

In a review of community level risk reduction interventions Fleury et al. (2000) assert that the differences between men and women in incidence and prevalence of heart disease may reflect the social and contextual influences that affect women more negatively [214]. One way of alleviating this range of influences is to design community based programs to address heart disease or heart health promotion in women. The key feature of community based models is that they do not only address individual behaviour but rather create a context for support, empowerment and encouragement of healthier behaviours, by including decision making and participatory models that are relevant to the participants.

In a review of some major US community based models, Fleury et al. (2000) report that while there is no consistent treatment effect and many variable results for women, they can identify some important issues and indicators for future programming. Dobbins and Beyers in a systematic review of 13 community based heart health projects also conclude that such programs are not effective at reducing heart health outcomes at the population level, but may be effective with high risk groups and should be targeted so [215]. For example, an emphasis on long term change, higher emphasis on creating adaptations for women who are low SES, better fit between the program and the cultural systems that the women are part of, and finally, the

need for empowerment at the individual and community level is required [214]. The latter may demand social action and community development strategies that involve increased decision making by women.

Well known and well funded interventions aimed at risk reduction in general, and particularly at high risk groups, have had mixed results and have generally been unsuccessful in producing specific positive behavioral changes. But in general, minority women have poorer prevention, treatment and outcomes, indicating a need for more research and interventions specifically aimed at ethnocultural and low SES women.

ii) Health care systems and organizations

Malarcher et al. (2001) describes the US commitment, funded by the CDC, to provide funding for comprehensive state-wide heart health promotion and heart disease prevention programs that are population based [216]. These efforts include policy and environmental strategies, as well as education, awareness and health promotion efforts specifically aimed at reducing disparities in treatment and risk. Women are a priority population in these programs and are the focus of several major demonstration studies aimed at understanding risk reduction for women, specifically sub-populations of women. The CDC links these efforts to national organizations as well. Malarcher et al. (2001) point out that the surveillance of geographic and temporal trends among a variety of diverse groups and the testing of various interventions is the responsibility of the national prevention agency. Such national efforts with full funding, and research program underpinnings, are critical examples of comprehensive approaches to improving the heart health of all women.

In the WISEWOMAN intervention, aimed at mid life disadvantaged women, the projects faced challenges of fully integrating the clinical, environmental, community and health behaviour elements which were designed to reach beyond a focus on individuals. For example, some of the perceived barriers to integrating a preventive care program within community health centres included: competing demands on health centre resources, difficulties hiring staff for new programs, and administrative burdens associated with data collection and reporting [217].

c) Individual Issues -MICRO

Policies and programs directly affect individuals. In the realm of women's heart health, there are numerous policies and programs that are aimed at changing individual behaviours and/or lowering individual risks, or influencing individuals' treatment and recovery processes. Similarly, policies and programs are also aimed at affecting the practices and behaviours of individual practitioners in medical systems, health care agencies and community organizations. This section assesses some clinical approaches and evaluated programs aimed at women.

i) Policies and programs addressing risk reduction and health behaviours in women

There are clear priorities for prevention and risk reduction regarding women and heart disease. Based on the Framingham Risk Group, the American Heart Association published evidence based guidelines in 2004 for management of risk among women [218]. The chief priorities are, in order of importance, smoking cessation, physical activity, heart healthy diet and weight management. Smoking is the main preventable CVD risk for

women. This risk is compounded for women who use contraceptive pills, and is a more important risk factor for middle aged women compared to men [219].

Women are affected by general level comprehensive tobacco control policies such as advertising bans, tax and price policies and restrictions on smoking in various public and private locations. However, there is evidence to suggest that gender and diversity affect the responses to these broad policies and women, especially low income women, who are less positively affected by tobacco policies than the rest of the population [220, 221]. Programs addressing prevention, cessation or tobacco reduction are also increasingly being tailored for various sub-populations, such as low income women, and Aboriginal youth, as population wide tobacco use rates are decreasing in Canada, but rates among some sub-populations of girls and women are not.

Similarly, policies and programs aimed at other risk factors, such as physical activity, show that there are differential effects based on sex, gender and diversity characteristics. [207, 208, 222]. The AHA suggests that women engage in 30 minutes of moderate intensity physical activity per day [98]. Hence, efforts are being made to investigate more appropriate and effective policies and programs by tailoring these efforts to the needs of women and diverse groups. For example, even lower activity intensities, such as walking for a longer duration provides comparable benefits (including reduced mortality) to more intense forms of physical activity [71, 74, 75]. This is important because walking is both physiologically beneficial and also accessible and appealing form of activity for many women. Other authors have found that community based lifestyle modification programs [223] and motivational interviewing [71] can be effective for increasing women's physical activity..

ii) Tailored programming for women

There is a need for women-specific and multi-component programs. Fleury et al. (2000) specifically suggests that strategies that have been successful in some segments of the population are not necessarily appropriate for women, or all groups of women, particularly women with few social and economic resources.

Specifically, Sherman (2007) discusses the importance of incorporating new preventive guidelines for women [224]. This includes establishing 3 levels of risk for women: high-risk, at-risk, and optimal-risk; encouraging counseling, nicotine replacement and pharmacotherapy in conjunction with behavioral or formal smoking cessation program; prescribing higher doses of physical activity for women trying to lose weight (60-90 minutes daily); and decreasing saturated fat intake from 10-7%. As well, these authors discourage the use of: folic acid, antioxidants or hormone therapy by women.

Some recommendations that Krummel et al. (2001) provide based on their review, include: examining the root causes of tobacco use and dependence, finding better and more gender-sensitive measures of physical activity, developing diet interventions focusing on women's needs, integrating social support and stress reduction in programs, and utilizing multi-component risk reduction interventions [53].

Gettleman and Winkleby (2000) carried out focus groups with low income women to find out how to best structure programs and interventions [22]. Results from the focus groups showed that women preferred: programs that addressed multiple risk factors (especially smoking, lack of exercise, and dietary factors), emphasize staying healthy for themselves, teach specific skills about how to adopt heart-healthy behaviors, and offer them choices in effecting personal changes. For health information, women preferred visual formats, and expressed desire to develop knowledge to help them separate health 'myths' from health

'facts' in order to reduce their misconceptions about CVD. They also expressed that health care policies and programs need to address social and financial barriers that impede the adoption of heart-healthy behaviors.

For tailored programming, there are both biological and social (sex and gender) issues to consider in creating effective interventions. For example, with respect to tobacco cessation, there is consensus that there is a range of biological influences that mediate tobacco cessation (hormones, menstrual cycle, nicotine tolerance, sensitivity and withdrawal, menopause, depression, pregnancy, postpartum, etc) [225, 226]. Women smoke for different reasons and assign different meanings to smoking [227]. Women also use smoking for coping [228], have a harder time quitting and require more social support in quitting [225]. Hence, woman-specific intervention trials are recommended to address these barriers [229]. Indeed, the entire range of bio-psycho-social factors that affects women's tobacco cessation and reduction requires more research and program development [225].

For physical activity programming, there are suggestions for a deeper understanding and consideration of gender when designing physical activity policy and programming. In an analysis of Australian health promotion and policy initiatives on active living, Fullagar (2003) argues for a wider, feminist understanding of activity, leisure and movement that more accurately reflects women's subjective experience of their bodies and physicality. In short, active living approaches need to better relate to the "meaning, context and construction of women's active leisure" [222p. 48] rather than classifying women as a particularly inactive group "requiring regulation, discipline and management" [222p.49]. This would translate into a broader set of suggestions for and measures of women's activity, a wider view of physicality, and more freedom and mastery of the body for women. Current initiatives, reliant upon mechanistic body movement, measurement, gyms and aesthetics, are seen to produce forms of stress, guilt and time pressures, perhaps adding to the burden of women.

iii) Multicomponent programming

There is evidence to suggest that when individual level programs are devised, that they involve multiple components, reflective of the multifactoral nature of the heart disease risk. For example, interventions specifically targeting women report that participants who were more successful at decreasing or staying at an optimal level of high fat food intake had lower levels of psychosocial distress. In the case of multiple risk reduction in postmenopausal women, it has been shown that women can make comprehensive lifestyle changes in programs using social-cognitive strategies and peer support.

Interventions that aim for: healthy diet, physical activity, smoking cessation and weight maintenance are the safest, most effective and cost-efficient programs for women [56]. One literature review found that while CVD interventions are limited for women, program components that were most effective included: personalized advice on diet and PA behaviors and smoking cessation, multiple staff contacts with skill building, daily self-monitoring and multi-component strategies [53]. Other authors have found that with multi-component interventions, women demonstrate an increase in physical activity and consumption of fruits and vegetables [21, 25]. Women with lower levels of psychological stress and worry [92] and with social networks and support [230] also demonstrate improved health behaviours when participating in programs and interventions.

A key example of an evaluated multi level intervention program is the Well-Integrated Screening and Evaluation for Women Across the Nation (WISEWOMAN) program in the US, which addresses heart health promotion and heart disease prevention among mid-life underserved women. The program combined risk

factor screening with a multi-component intervention focused on improving women's diet and physical activity, and smoking cessation. It addresses both environmental and individual level factors in the context of a clinic based setting. It is aimed at multiple behavioural changes and involved linking individuals to community resources, community guides and supportive environments. It also encouraged women to become involved in advocacy efforts to make environmental and policy changes.

This intervention involved linking clinical settings with community resources as a way to improve and support patient's health behaviours. This involved creating a resource with environmental and community level based recommendations, so these could be implemented by community health advisors. As well, there were group sessions and activities designed to encourage patients to adopt healthy behaviors.

Research on the program highlight the interrelationships between the levels of approaches to policy and practice on both heart health promotion as well as responding to heart diseases in women. Phase I compared the effectiveness of minimal and enhanced lifestyle interventions for reducing women's risk for heart disease [27]. This program measured baseline attributes, clinical indicators and health behaviours related to physical activity, nutrition, and then randomized women into two streams of intervention, Enhanced Intervention (EI) and Minimum Intervention (MI). The enhanced intervention included: counseling, group sessions, ongoing support and resources related to healthy eating and physical activity. In contrast, the minimum intervention included a one-time mailing of a resource to women outlining healthy diet and physical activity practices [27].

At the end of the program, blood pressure was higher among the MI participants. MI participants also reported less cholesterol lowering medication usage. Both groups had high body fat levels (41%) and smoking rates (25%). In terms of health behaviours, women in both groups were more confident about beginning to learn about and use physical activity resources than nutrition and diet related resources. Both groups reported confidence in becoming involved in advocacy efforts for community changes (such as letter writing), but less likely to be involved in making direct community improvements (such as speaking at a council meeting).

Some of the challenges they identify include: overcoming clinical prevention's focus on individual knowledge, attitudes and behaviours, limited time of health providers, and developing locally tailored community and public health resource materials. Some suggestions they provide, include: addressing community barriers, identifying and establishing safe and convenient exercise facilities and culturally appropriate activity programs.

In Phase II, adapted interventions designed to target financially vulnerable women and develop culturally and locally appropriate nutrition and physical activity interventions were implemented with varying rates of success with women at high risk, including: incarcerated women. [26], Alaskan Native women [109], and Hispanic women [231].

[24]. Although the programs have helped women increase their activity and improve nutrition, the authors state that it is not clear why enhanced interventions have been less effective in influencing physiological measures (lipids, BP, anthropometric measures). They suggest that some barriers to this may be related to: provider's lack of faith in women's ability to change behaviours, as well as social isolation, unsafe neighbourhoods, and lack of access to healthful foods. They argue that more environmental and societal approaches are needed.

Yancey (2004) discusses the usefulness of WISEWOMAN, claiming that more environmental level interventions are needed since most (including WISEWOMAN) have targeted individuals [232]. For example, nearly three quarters of the women screened through the program were overweight. This is related to the predominance of obesogenic environments (described as the promotion of inexpensive, energy dense but nutrient deficient foods, and labour saving devices and under-investment in mass transit). More environmental and structural level interventions are required, and there is a need to strengthen linkages among public health agencies, community-based organizations and academic institutions. Yancey also recommends: changes to organizational practices and policies so that PA and healthy food choices are incorporated into workplace routines. In communities, recommended strategies and policies include: improving areas for safe walking, building coalitions to bring farmers markets to less affluent neighbourhoods, educating legislators about public policies that can encourage healthy lifestyle behaviors, and promoting nutritional labeling.

Viadro et al. (2004) compared the process and outcomes of three WISEWOMAN programs [233]. They state that a successful program requires: adequate and appropriate planning, buy in, training, professional support and outreach. Challenges they mention, include: integrating clinical and lifestyles interventions, reaching beyond a focus on individuals, acquiring necessary resources, and implementing interventions within already stretched healthcare environments. Yet, overall the programs were deemed successful in reaching underserved women, developing a more comprehensive women's health model, strengthening linkages to primary healthcare, and addressing women's roles as primary caregivers.

Location of women specific programming also matters. Research on the WISEWOMAN program found that integrating WISEWOMAN's services with the culturally appropriate care and support services offered by community health centers may improve the program's ability to reduce CVD burden among underserved women [217]. Some of the perceived barriers to integration that they identified included: competing demands on health centre resources, difficulties hiring staff for new programs; and administrative burdens associated with data collection and reporting. They conclude that integration strategies need to be tailored to the resources, skills and capacities available within health centers, and additional research should be conducted to identify how best to achieve integration within specific institutional and community contexts. In its most current phase (III), the WISEWOMAN program is aiming to address some of these issues encountered in the previous phases, by tailoring interventions to women's degree of risk and level of motivation, and improving access to community resources [234].

iv) Improving health literacy

Champney and Wenger (2005) report that only 43% of US women were aware that heart disease was the leading cause of death for women, mistakenly assuming that breast cancer posed the greatest risk [235]. For younger women with heart disease, the risk of death is highest, and higher than men. A British cardiologist reinforces the lack of awareness in both women and their practitioners of the serious risk of CVD to women, adding that women tend to postpone their risk reduction efforts given that heart disease usually emerges 10 years later for them, compared to men [210]. Miller and Kollauf (2002) analysed public information on heart disease in women between 1957 and 2000 and identified clear omissions of women specific heart health information until the late 1980s [236]. Prior to this, public information had focused on men and how women could take care of men's heart health. After the 1990, more information focused on educating women and care providers about the heart health issues specific to women, reflecting increasing research and education focused on women.

v) Creating interventions for diverse populations

In the Canadian context, Anand and colleagues (2001) claim that the most effective interventions and programs for Aboriginal peoples will be those that focus on tobacco cessation and obesity because these would have the greatest impact on reducing risk for CVD by improving problems with: glucose intolerance, raised blood pressure and abnormal lipids [12]. They also mention the potential utility for community based programs. Because Aboriginal health is also a product of Aboriginal people's economic, cultural, historical and political context, it is important to include Aboriginal people in program development and seek government funds for these programs.

Mensah et al. (2002) provide some recommendations for reducing health disparities among racial/ethnic minorities of women [108]. These include: improving the quality of data available regarding racial and ethnic differences, promoting research that examines interactions between SES and coronary heart disease in women, addressing women's access to specialty care, improving cultural sensitivity of care, and building on successful strategies for primary and secondary care of minority women.

vi) Importance of provider communication and support

Champney and Wenger (2005) suggest that routine aggressive screening by practitioners is required to address and evaluate CVD risk in all women [235]. However, in general, there are multiple barriers that clinicians face in following practice guidelines such as lack of time, familiarity or agreement with guidelines, low self efficacy and absence of both gender specific materials and systemic support for prevention [237]. Nurses, as well as doctors can play a significant role in prevention and treatment of women's cardiovascular disease.

Some suggestions to improve patient-provider communication, include: better dissemination to providers of the guidelines at rounds, use of local opinion leaders to influence lack of agreement, endorsement of guidelines by American College of OB/GYN (so not perceived as just for cardiologists), more continuing medical education to address self-efficacy, provide physicians with information on successful outcomes, audit and provide feedback to physicians, address external barriers, and improve access to care and cost barriers [238].

Jilcott et al. (2004) explored counselor attitudes and beliefs during the WISEWOMAN program [239]. They found that counselors were often skeptical about their patient's motivation to make behavioural changes. Yet, at follow up, the counselors involved in an enhanced intervention reported greater self-efficacy for counseling and spent more time counseling their patients than counselors who were in a minimum intervention.¹³ These counselors were also more likely to report improving their own health behaviours. When time is limited, even minimal interactions can be effective and time efficient [71].

¹³ MI involved distributing print materials, and sometimes, a limited amount of counseling. In contrast, EI involved more thorough counseling, utilizing goal setting strategies and follow-up techniques.

Conclusions

Several policy meetings and conferences have occurred in the past decade and made recommendations to address the important issues of heart disease and women. Three key examples are presented below:

In a 2000 International conference on women, heart diseases and stroke, a Declaration was released that took a broad view of responding to women worldwide. It made several recommendations

- *First, address women's poverty reduction and gender inequity as the top priorities for reducing the global burden of women's heart diseases and stroke.*
- *Second, develop women's leadership in participatory decision making in health policy formulation*
- *Third, modify research infrastructure to support gender sensitive research and to involve women directly in research processes*
- *Fourth, improve surveillance of women's health outcomes using gender sensitive indicators*
- *Fifth, institute gender based analysis into all policy processes*
- *Sixth, address the social determinants of the risk factors of women's heart health, such as tobacco use, diet and physical activity, and*
- *Seventh, create an "info-structure" to disseminate research, surveillance, monitoring and evaluation to policy makers, service providers and the public [17].*

In a 2002 conference on women and heart disease a diverse groups of US experts drafted recommendations based on evidence reviews. Four key issues were identified.

- *First, enhance the provision of preventive interventions, particularly tobacco cessation, to women by primary care providers.*
- *Second, disaggregate by sex all performance related data related to the care and treatment of women's heart disease.*
- *Third, institute requirements for all federally funded health research be analysed for sex and gender.*
- *Fourth, develop a comprehensive public policy agenda for prevention of heart disease in women, including research, prevention and interventions [237].*

In a 2006 European policy conference on cardiovascular disease in women several priorities were identified:

- *First, gender specific research in both basic and clinical areas, including subgroup analysis by sex is strongly needed, and should be encouraged by funding agencies.*
- *Second, women specific education on mortality and morbidity should be created for professionals, scientific societies, health authorities, patients associations and general public.*
- *Third, develop a women specific risk assessment data base and process for diagnostics, gendered clinical guidelines for preventive and optimal therapy, extend risk assessment to older age groups, and develop ongoing survey data and registries [202].*

In addition, a comprehensive Canadian review of research literature on sex specific issues related to CVD [107] concludes that clinical trial literature is sparse on sex specific outcomes and has led to inadequate diagnosis and treatment. These authors suggest that gaps in knowledge about sex and gender specific issues may be contributing to the lack of progress in responding to women's heart disease, compared to men's.

The contributions of the social determinants of health can also be quantified. In analyzing the specific effects of poverty and low income on CVD, Raphael (2003) reports that income differentials account for an excess of premature death for lowest income Canadians of 23.7%. Incidence of CVD is also affected by poverty. The overwhelming majority of Ontario hospital admissions for acute MI are from low income neighbourhoods [240]. Raphael estimates that approximately \$4 billion per year (or 20% of total annual cost) is attributable to income differences. The key aspects of poverty that affect CVD are a) material deprivation during early life carried into adulthood, b) psychosocial stress associated with poverty compromising immune systems, and c) the acquisition of health threatening behaviours. All of these factors have sex and gender specific profiles, and Canadian women are more likely to be living on low incomes and experience caregiving stress than men.

In summary, there are multiple levels and opportunities for intervening regarding women and heart health. A key message, however, is that the multiplicity of causal factors of heart disease, or of the preservation and promotion of heart health, requires a multi-level and multi-layered response. The past emphasis on individual "lifestyle" factors as risks, for example, has precluded a clear view of the constellation of social, economic, psychological and biological factors that work together to create and maintain an individual's behaviour. Instead, the language of "lifestyle" factors has led to a limited focus on attempting to change individual level behaviour without parallel efforts to change social and economic conditions. Indeed, this approach is seen as victim blaming, by placing responsibility for all change on the individual. This critique has been made by numerous researchers such as Norma Daykin (1999) who referred to the wider array of factors as creating "landscapes of risk." Referring to the UK strategy, the Health of the Nation, she writes,

"It is often assumed that these improvements can be achieved solely through individual changes in lifestyle, including reducing smoking, improvements in diet and increased physical exercise. However, the strategy has been criticized for overlooking the 'landscapes of risk' faced by disadvantaged groups (particularly women) in their attempts to secure health and well-being....The health priorities of these groups may reflect day-to-day preoccupations and the need for survival in often difficult environments rather than more abstract and distant risks"[241].

From a different vantage point, Lesley Doyal [241] has referred to "opportunities for health" to reflect similar sentiments, and Hilary Graham [242] has referred to "trajectories of disadvantage" to refer to the progress of particular individuals and groups through a variety of experiences and social locations that result in poor health. As Fleury et al. (2000) point out, the "fundamental causes" of CHD in women have not been fully explored" [214p. 968] and they call for a different approach to managing heart disease in women, that moves beyond procedures and pharmacology to examining the social and contextual factors that may also be modified to decrease the burden of CHD.

At the same time, there is room for improvement in various community and institutional arrangements and practices. These include more attention to clinical practices that are directly aimed at reducing gender inequities in diagnosis, treatment and rehabilitation practices [1]. In a growing chorus of researchers and

policy makers who are concerned with understanding the interactive and multiple causes of women's heart disease, there is emphasis on moving to a larger context to develop more effective and relevant interventions [214].

Among the various causes and manifestations of heart health inequity, these critiques challenge both the policy and clinical communities to conceptualize and address the causes of women's heart disease and the preservation of women's heart health using a wider lens and broader perspective. For clinicians in particular, the call is for addressing a range of wider factors and social determinants in their practice, and understanding sex and gender linked issues. For researchers, the challenges are conceptual and methodological, focused on measuring more fully the various interacting contributions of individual characteristics, sex, gender, group and community processes and broad social and environmental factors that converge to affect women's health and women's heart health in particular. For policy makers, the challenge is to address the broader policies that affect women's heart health, and to tailor existing policies in a range of areas specifically to women, while incorporating accurate economic analyses.

4) The Canadian and BC Contexts

Cardiovascular disease is a leading cause of death in Canadian women [219]. Approximately 40% of all deaths in Canada are currently related to cardiovascular disease [1]. Compared to men, the onset of CVD in women is somewhat later (approximately 10 years), and women are less likely to seek care, be investigated and treated with as wide a range of interventions as are men. The range of risk factors that affects the development of CVD in women is, as we have seen, affected by both sex and gender related factors, and has different impacts on various sub-populations of women.

In Canada, Grace et al. (2004) note that first generation immigrants often have a constellation of specific risk factors for cardiovascular disease that reflect culturally specific dietary and smoking patterns [219]. Hence, regional analyses of immigrant groups are important in determining the BC specific high risk groups, either by province or health authority. In addition, two specific sub-populations of concern across Canada are women who are of South Asian ancestry and women who are Aboriginal [12, 115], both important groups for BC based action and study.

In addition, women who have pre-existing diabetes are also at higher risk for CVD [219]. Cross cutting risk factors for women include smoking, depression, low income, elevated lipids, hypertension, obesity and inactivity. As Grace et al. (2004) point out, while low income usually implies a higher prevalence of risk factors, it also appears to have an independent effect that they suggest may manifest as job strain, anger or social isolation among other factors [219]. All of these factors are again affected by sex, gender and diversity.

Risk Factors:

- **Smoking.** In British Columbia, broad population statistics reflect the lowest rate of smoking in Canada [243, 244], but specific sub-populations are at higher risk for smoking, such as Aboriginal people, and girls in particular [245]. Data from 2003 indicates that 16.1% of women 12 years and older in BC were current daily or occasional smoker [245]. Yet, 40% of Aboriginal women in BC were current daily or occasional smokers.
- **Physical activity.** Similarly, broad population based data reflects the highest rate of activity among all provinces, but, again, women experience lower rates of activity than men, and certain sub-populations are most likely to be inactive. Data from 2003 shows that 55.6% of women engage in moderately active leisure time physical activities [245]. Yet, this rate is lower for immigrant women (50.5%) and Aboriginal women (39.5%) in BC.
- **Diet.** According to data from 2003, less than half (45.8%) of BC women regularly consume fruits and vegetables (5 or more times per day) [245].
- **Weight management.** In 2003, 23% of BC women 18 years and older were classified as overweight (BMI of 25- 29.9) [245], and 10.2% were obese (BMI of 30 or higher). For Aboriginal women in BC, these rates are substantially greater, with 32.7% of women classified as overweight and 21% classified as obese.
- **Depression.** Depression is also affected by sex, gender and diversity issues such as poverty and low socioeconomic status [20]. In BC, 22.4% of women reported “a lot” of life stress. As well, the percentage of women in BC who cited a possible or probable risk of depression was 1.7 % and 6.5% respectively [246].

- **Low socioeconomic status.** In BC, women are more likely than men to have incomes under the poverty line. The average income of women in BC was \$23, 500 in 2005, which is lower than the Canadian average of \$26, 800 and only 64% of men's earnings in BC (\$41, 900) [247]. Women also have a slightly higher chance of being exposed to low income for at least one year (19%) compared to men (17%) [247]. It is estimated that ¼ of all BC women and almost ½ of BC's single mothers earn less than the low income cut-off ratio [248].
- **Gendered roles.** In BC there are 21% lone parent families headed by a women [249]. In addition, Canadian women spend an average of 4.4 hours per day on unpaid work [247] compared to 2.7 hours for men. These caregiving and work related burdens fall more heavily on women than men, and in different ways.
- **Social isolation.** In 2006, 250,860 (out of 2,066,720) women in BC lived alone [250].

Sub-populations at Risk:

Clearly, the interactions between these risk factors, both biological and social, along with genetic predispositions, will culminate in creating risks for CVD in particular women or sub-groups of women in BC. Some examples are:

- **Older women.** Azad and Bierman (2007) point out that the onset of coronary heart disease in women in Canada lags behind men by 10 years, but by age 80, prevalence is similar [1]. However, the outcomes in older women with heart disease are often poorer than men due to co morbidities, disability and various psychosocial issues such as lack of social support and poverty.
- **South Asian women.** Anand et al. (2000) report that South Asians in Canada have higher rates of cardiovascular disease, not explainable by smoking, blood pressure, diabetes or high cholesterol [115]. South Asians in Canada, when compared to Canadians of European and Chinese descent experienced higher prevalence of carotid atherosclerosis and glucose intolerance, higher LDL cholesterol, triglycerides and lower HDL cholesterol. They conclude that South Asian ancestry itself is a strong independent risk factor for cardiovascular disease.
- **Aboriginal women.** Anand et al. (2001) report that Aboriginal people in Canada have significantly higher rates of carotid atherosclerosis, smoking glucose intolerance, obesity, abdominal obesity, poverty and unemployment [12]. They suggest that there is an impending epidemic of cardiovascular disease among this group, and that reductions in tobacco use and obesity are the two high priority issues.
- **Women with mental illness and/or addictions.** A literature review by Johnson et al (2006) reveals that smoking among people with mental illness is double that of the general population, and even greater for persons with alcohol and drug dependencies [95], resulting in higher rates of cardiovascular disease. Therefore, there are specific dependence and cessation issues for women with mental illness and/or addictions which must be considered when tailoring interventions.
- **Women with low socioeconomic status.** Anand et al. (2006) used a social disadvantage index to measure employment status, income, and marital status of a diverse group of Canadians [11]. The relationship between social disadvantage and risk factors for CVD was examined. They report that social disadvantage was higher among: older people, women, and non-white ethnic groups. Further, cigarette smoking, glucose, obesity, abdominal obesity, and CRP were higher among individuals with higher social disadvantage, whereas systolic blood pressure, lipids, norepinephrine, and atherosclerosis were not.

According to their results, social disadvantage is an independent predictor of CVD after adjustment for conventional and novel risk markers for CVD (OR for 1 point increase 5 1.25; 95% CI 1.06–1.47).

Considerations for Action:

This synthesis reveals that women's heart disease is a multi factorial problem and heart health promotion for women is a challenge on individual, clinical and policy levels. Evidence in all aspects of sex, gender and women's heart health is still emergent, but continuously evolving. Actions at the policy and program levels can be taken, however, such as initiatives in heart health promotion and prevention of disease. Specific attention can be paid to improvement in outcomes for sub-populations at risk, and, in some cases, attention can be paid tailoring programs and practices to the needs of particular groups of women. Overall, it is important to pursue multifactoral programs and policies, reflecting the multifactoral nature of women's heart health and disease. In all cases, it is critical to evaluate the effectiveness of all such activities in order to contribute to the emergent knowledge about how best to address women's heart health.

Based on this review, there are a number of key messages and areas where action should be considered. They are as follows:

Heart health promotion and prevention of disease

The greatest health benefits and most cost effective solutions come from changes at the prevention level. In particular, the most important risk factors to be addressed include: smoking, physical activity, healthy diet and weight management. Yet, because of the complex nature of women's health, change at the individual level requires change at the policy level to address gender and diversity based differences in risk, and access to health and health care.

Sub-populations at risk

The review reveals that there are identifiable sub populations of Canadian and BC women who face increased risk for heart disease, such as older women, low income women, Aboriginal women, South Asian women, and women with a mental illness and/or addiction. For example, the inverse gradient of CVD and socioeconomic status (SES) is particularly pertinent for women, and particular groups of women who are more likely to live in poverty. These sub-populations of women, therefore, stand the most to benefit from research, programs and policies which address barriers and seek to improve their heart health.

Tailoring of programs and practices

Evidence from this review reveals that there is not a proven universal intervention which can be applied to all women. Instead, programs need to be tailored to women and sub-populations of women. Evidence from this review suggests a number of factors which are important to consider when tailoring, including: changes in women's health through the life-course, addressing health literacy, improving social support and addressing psychosocial factors, and developing women-centred approaches to diet, physical activity and smoking interventions.

For secondary prevention, the greatest strides for improving women's heart health can be made in the form of eliminating gender biases in diagnosis, testing and care. Improved clinical practices that reflect the integration of sex, gender and a range of diversity issues and social determinants into diagnosis and

treatment are key to improving women's treatment and care. Research, policy and program development of cardiovascular screening, diagnostic and treatment for women, needs to account for these factors in order to provide effective secondary prevention and treatment options for women.

Comprehensive programs

More comprehensive and multi-component research studies, policies and programs are required in order to adequately address the complex nature of women's heart health. As shown by the evidence reviewed, the prevention/promotion literature has focused largely on individual change while the treatment literature has focused on intervention effectiveness. Multi-factorial programs and policies are needed which address the broad social, economic and environmental barriers, research policies and practices, health care systems and organizations, as well as the individual level health behaviours.

Conclusion:

In conclusion, the prevention, diagnosis and treatment of heart disease are health priorities for all women in British Columbia. Effectively addressing this will involve comprehensive and multi-factorial research, programs and policies which consider and measure the sex, gender and diversity issues that structure women's health. In particular, women in BC who stand to benefit the most from these potential initiatives include women who are older, Aboriginal, South Asian and living on a low income.

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