Women’s Cardiovascular Health

This issue of the Women’s Health Bureau Information Forum focuses on women’s cardiovascular health. In British Columbia in 1996, heart disease and stroke killed 164 of every 100,000 women, whereas 26 of every 100,000 women died as a result of breast cancer.1 Interestingly, it is breast cancer that has always received more attention. Now, thanks to a slowly increasing body of women-centred and gender-inclusive research and resulting media attention, women are finding out that cardiovascular disease (CVD) is a serious problem that does affect them. Most interesting is that this new awareness is proving to be a double-edged sword. Women are realising that they, too, are affected by CVD and that they can play an important role in its prevention, but women often receive information that is not evidence-based and/or is presented in a misleading way. This issue will serve to outline cardiovascular health issues for women, including: risk factors, symptoms, treatment and prevention of CVD, the importance of gender-inclusive research and barriers to giving women access to accurate information about their health.

Risk Factors

Heart Disease

Women have many of the same risk factors for heart disease that men do. However, the effects of some of the factors differ between the sexes. Cardiac events, when they occur in women, tend to happen an average of 10 years later than for men, and when events occur later (as with women), recovery is less likely. Women need to realise that although it appears they “have more time” to work on lowering the influence of modifiable risk factors, they should adopt a heart-healthy lifestyle as early as possible. Risk factors are listed and briefly explained in Table 1. Note that many of the listed risk factors are preventable and can be improved.

Table 1. Risk factors for heart disease in women.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advancing Age</td>
<td>Affects all women; after menopause, the rate of heart disease in women increases dramatically. It is not necessarily age or menopause themselves, but conditions associated with advanced age that affect risk</td>
</tr>
<tr>
<td>Tobacco Use</td>
<td>A preventable risk factor for heart disease in women. Smoking is increasing more in young women than in young men</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>Increases risk of death from heart disease in women more than men. Often associated with obesity and lack of physical activity in women.</td>
</tr>
<tr>
<td>Lipoprotein Abnormalities:</td>
<td></td>
</tr>
<tr>
<td>Especially low levels of High</td>
<td></td>
</tr>
<tr>
<td>Density Lipoprotein (HDL)</td>
<td>By 55 years, women have higher concentrations of total blood cholesterol than men.</td>
</tr>
</tbody>
</table>
Many of the risk factors for stroke are the same as those for heart disease, and several are preventable or improvable. These include hypertension, smoking, diabetes mellitus, high blood cholesterol, obesity, alcohol use, knowledge of family history and oral contraceptives use. Unique to stroke are transient ischemic attack (TIA – stroke-like features, but temporary duration), migraine headaches and presence of heart disease. \(^1,2\) Another major risk factor is atrial fibrillation (a form of arrhythmia) that affects women more than men and is more common as age increases. \(^3\) Some risk factors, however, are unique to women. These include use of oral contraceptives and pregnancy. \(^1\)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated Triglyceride Levels</td>
<td>After 64 years, women have higher mean triglyceride levels than men.</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Increases with age (especially after menopause) and is more common in women than men over 55 years.</td>
</tr>
<tr>
<td>Physical Inactivity</td>
<td>Can reduce incidence of heart disease especially through its effects on blood pressure, cholesterol and weight. In adulthood, and even in childhood, women get much less exercise than men.</td>
</tr>
<tr>
<td>Obesity</td>
<td>Increases risk of heart disease and stroke; linked with several health problems.</td>
</tr>
<tr>
<td>Psychosocial Factors*</td>
<td>Intake of fats affects both blood pressure and cholesterol. Stress and depression have possible links with increased risk. Continued research is needed on these factors in women.</td>
</tr>
<tr>
<td>Alcohol Use</td>
<td>Low to moderate consumption has possible protective effects in women, however, moderate consumption is also linked to hypertension. Excess drinking increases the risk of heart disease.</td>
</tr>
<tr>
<td>Family History</td>
<td>Increased risk of heart disease if there is a family history of early evidence of heart disease.</td>
</tr>
<tr>
<td>Use of Oral Contraceptives(\dagger)</td>
<td>Age, smoking, and high blood pressure further increase chances of heart attack in women who take oral contraceptives.</td>
</tr>
<tr>
<td>Menopause(\ddagger)</td>
<td>After menopause, the risk of heart disease increases dramatically.</td>
</tr>
</tbody>
</table>

Information for this chart was obtained from the Heart and Stroke Foundation of B.C. and Yukon: http://www.hsf.ca/stats/Womanhrt.pdf


**Stroke**

While men and women share many of the signs and symptoms of heart disease, the manifestation of these can be different. The two major warning signs of heart disease are angina (chest pain) and myocardial infarction (MI – heart attack). Women are more likely to experience angina as a first sign, while men more often suffer a heart attack as the first warning sign. Important to note is that when women experience heart attack as the first signal, they are more likely than men to suffer fatal or severe outcomes. \(^2\)

**Signs and Symptoms of CVD in Women**

**Heart Disease**

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Interpreting symptoms of heart disease can also be different between women and men. When experiencing a heart attack, for example, both men and women can experience crushing chest pain and breathlessness. However, women experience several symptoms they may not interpret as a heart attack. These include discomfort resulting from what seems like indigestion and/or pressure in the chest, as well as nausea and back pain. Further, their response to symptoms can also differ. Even when women recognise that something is wrong, they are more likely than men to ignore the symptoms and not get the help they need as quickly. Although women see physicians more frequently than men, they may reason that nausea is not something needing immediate medical attention. Women need to be aware of symptoms and get help when they are experienced. Table 2 lists different types of heart disease (including MI and angina) and the symptoms that accompany each.

Stroke

The symptoms of stroke are the same for women and men. All symptoms will appear suddenly. These include:

- Weakness, numbness or tingling in face, arm or leg
- Temporary inability to speak or understand speech
- Double vision or loss of vision (particularly in one eye)
- Severe and unusual headache
- Loss of balance that often accompanies another symptom mentioned above

Information Sources: The Importance of Good Research

The key to understanding CVD and making the decision about its treatment/prevention is knowing the source and quality of your information. This section is a discussion of gender-inclusive research, levels of evidence for clinical decisions and how research results get translated into information for public consumption.

The Importance of Gender-Inclusive Research

What constitutes gender-inclusive research? Gender-inclusive research is research that takes gender into account throughout the entire investigative process, that is, from asking the research question (including the concepts used to define the issue), to collecting the information, through to analysing the data. To determine whether research is gender-inclusive (whether you are conducting the study or reading published material), you should consider the following questions:

- In the design of the research, is the group being studied reflective of the people to whom conclusions will be applied (sex, age, race, etc.)?
- Does the design of the study allow for the determination of group differences? For example, should different groups be studied/measured in the same way?
- What kind of statistics should be used to analyse group differences?
- Do the conclusions being drawn help you to understand the implications for different groups?

What are the implications of research that is not gender inclusive?

A great deal of medical research has studied men and then been applied to both men and women. Researchers have typically excluded women as participants because women’s biological cycles create variables that are difficult to control in studies. However, applying the results from “uncomplicated” men to “complicated” women, which has been the standard of practice until recently, does not make sense and can cause serious problems. At best, this creates misunderstandings that can be corrected in the future; at worst, the people being treated are subjected to irreversible damage. What does make sense is increasing the focus on women-centred studies and research that looks at differences, as well as similarities, between women and men. Serious gaps in the literature have also led to a lack of understanding of women’s coping mechanisms. With CVD, for example, little attention is given to the fact that women need a strong social support component for successful rehabilitation. Women are generally older when experiencing a first cardiac event and, as such, are more likely to be living alone without family support. Women also tend to receive less spousal support than men do. Knowledge of women’s unique needs affects all aspects of their well-being.

To Medicate or not to Medicate: The Need for Unbiased, Evidence-Based Information

The media as an information source

Women are just as likely to get information about health from the media as from health professionals, and these sources, especially magazines, are surprisingly influential. According to Statistics Canada, 55.7% of Canadian women report reading magazines at least once a week; 3/4 of women include magazines as reading material at least once a year. In the United States, women are bombarded with drug advertisements and health-focussed magazine articles. In Canada, it is illegal for pharmaceutical companies to place ads in magazines for public consumption although ads still appear despite the law.
And Canadian magazines often carry legal, but misleading articles focussed on health, and American magazines are as common or even more plentiful on the shelves of Canadian book and convenience stores than “drug ad-free” Canadian magazines.

Women who take their health information from the popular media would do well to consider the sources of the information. Health writers, under time constraints, may report on new findings without in-depth understanding of the nature and relevance of research. And a great deal of health information in the media is contained in advertisements and related articles produced by pharmaceutical companies or by people receiving funding from them. Pharmaceutical companies market their products by presenting findings or statistics that emphasize the benefits of these treatments. Health related articles directed at women that downplay the effectiveness of lifestyle changes, and raise fears about gender inequality in medical treatment or risk of death from certain conditions, create a mentality open to the arguments of medication proponents. The B.C. Office of Health Technology Assessment (BCOHTA) reviewed the print material available in seven American and two Canadian women’s magazines related to cholesterol and heart disease. The drug advertisements and magazine articles revolved around the themes above: heart disease kills more women than any other disease, women do not have equal access to treatment and behavioural changes are not enough, especially in post-menopausal women. BCOHTA concluded that these particular messages lead to a very pro-medication standpoint that targets high cholesterol levels as the disease and not heart disease itself. Otherwise healthy or low-risk women become more open to and often ask their physicians for prescriptions for medications with marginal benefits and potential harm.

Levels of evidence
Another roadblock in the pursuit of accurate information involves the level of evidence of that information. There is a great deal of research on CVD. But how valuable is that information as a basis for medical recommendations? Medical advice should be based on levels of evidence where large, double-blind, randomised, controlled trials (RCTs) with clinically relevant outcomes are the gold standard. An RCT is research where the people studied are randomly assigned to a treatment level and where people receiving treatment are compared to people receiving a “placebo” (inactive/fake treatment). A double-blind study is one where neither the participants nor the people giving the treatments are aware of the treatment condition they are receiving/giving. Other forms of research are less conclusive and not, by themselves, adequate to make medical recommendations. These include RCTs that are very small, non-blinded and/or do not have relevant outcome measures, studies where participants are not selected randomly, observational studies, case studies or cross-sectional studies. Expert opinions also do not form an adequate basis for medical recommendations and are the lowest form of evidence. As consumers, when dealing with primary prevention* or secondary prevention, it is important to find out the source of your information. The most reliable information is that are from sources independent of pharmaceutical companies, their surrogates or anyone with a stake in the outcome of the research. Also, if you are interpreting statistics explaining the risk of getting disease when you take a medication, make sure you are being given the “absolute risk” instead of the “relative risk”.

For more information about these terms and how to interpret risk statistics, see sources such as: http://www.cma.ca/cmaj/vol-152/0351.htm

<table>
<thead>
<tr>
<th>Example</th>
<th>Heart Attack</th>
<th>Total Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>14</td>
<td>1000</td>
</tr>
<tr>
<td>Control</td>
<td>20</td>
<td>1000</td>
</tr>
</tbody>
</table>

Relative Risk 0.014/0.020 = 0.7
There is only a 70% risk of heart attack when treatment taken.

Relative Risk Reduction 1 - 0.7 = 0.3
Treatment reduces risk of heart attack by 30%.

Absolute Risk Reduction 0.02 - 0.014 = 0.006
0.6% of the patients are spared from heart attack by taking treatment.

* Note that levels of prevention are medically defined here to remain consistent with research terminology (see Therapeutics Initiative). Primary prevention occurs with persons with no evidence of CVD. Secondary prevention occurs when CVD is present.
Treatment and Prevention

Information on estrogen/hormone therapy, cholesterol-lowering drugs (statins, in particular) and non-medication alternatives will be critically discussed in light of the earlier discussion on levels of evidence.

Estrogen/Hormone Therapy

The effects of estrogen on the cardiovascular system are well-known; cholesterol, carbohydrate metabolism and blood vessel tone, for example, are mechanisms that appear to benefit from estrogen. Indeed, after menopause and the accompanying drop in estrogen levels, women show rates of heart disease that are comparable with men in the same age group (up to three times greater than during pre-menopause). The obvious answer might be to put all women on estrogen therapy (ET) or on a combination of estrogen and a progestin (hormone therapy – HT) following the onset of menopause. And, in fact, a large number of women entering post-menopause are prescribed one of these therapies for long-term use. The results of long-term ET/HT use, however, are not fully understood due to a lack of RCTs that follow women taking these therapies over long periods of time. A number of questions then arise. Should ET/HT be given to healthy women, that is, women who show little or no risk of CVD? As the disease thought to be most affected by estrogen occurs much later in life, on average, should hormone therapies be initiated as early as age 50? Do hormone therapies have more impact on this disease than other interventions such as physical activity programs and diet changes? And finally, as a broader question, are we “treating” menopause or preventing CVD?

To date, RCTs examining hormone therapy use and secondary prevention are very few. The key study, the Heart and Estrogen/progestin Replacement Study (HERS), found that while low density lipoprotein (LDL – or “bad cholesterol”; see section on cholesterol below) was significantly reduced by 11% and high density lipoprotein (HDL – or “good cholesterol”) was similarly increased (10% net increase), there did not appear to be any cardiovascular benefit to HT. This was also found when estrogen was taken alone. Further, there appeared to be more adverse effects in the HT group (thromboembolic events; 2.5% vs. .9% and gallbladder disease; 6.1% vs. 4.5%). Other potential harmful effects that have been noted in observational studies and that require further investigation are possible increased risks of endometrial and breast cancers. Interestingly, the National Toxicology Program in the US voted in 2000, almost unanimously, that steroidal estrogen be placed on the federal list of cancer-causing substances. Conjugated estrogens are already on this list.

There is no equally rigorous RCT looking at primary prevention although data are forthcoming. What remains is a large body of observational research that, in contrast, supports the use of ET/HT for primary and secondary prevention. Based on the quality of evidence, it is difficult to recommend hormone therapy for either primary or secondary prevention of CVD. In light of inconclusive research, women and their physicians must use the information available to decide whether ET/HT is the right choice.

Cholesterol

Cholesterol, a naturally occurring steroid, is produced in the human liver and other tissues. About a fifth of the body’s cholesterol comes from one’s diet, while the body itself produces the other 80%. Cholesterol levels are affected by the types of food consumed, weight changes, level of activity and various medications. When determining cholesterol levels, we measure LDL, protein that carries most of the blood cholesterol and deposits it on artery walls, and HDL, protein that carries very little cholesterol, but removes it from artery walls. Reasonably, it is good to have high HDL levels and low LDL levels. The following discussion includes information on statins. Other drug alternatives, such as niacin, fibrates, cholestyramine and colestipol will not be reviewed here due to lack of RCT data and/or data pertaining to women.

Cholesterol screening

Recommendations for who should be tested vary greatly. These recommendations range from testing everyone every five years starting at age 20 to a more restrictive set of age and risk factor conditions. What is common about many of these sets of recommendations is that they are not based on research. BCOHTA notes that, based on evidence, only people displaying actual symptoms should be tested, and of these people, only men over 35 and post-menopausal women should be included. Those without symptoms, regardless of risk factor status, would not be tested based on evidence. Other factors make widespread testing seem unreasonable. Test inaccuracy (measurement error) and natural, within-person fluctuation of cholesterol levels both may contribute to inaccurate readings, misclassification, and unnecessary treatment.
Cholesterol Lowering Drugs - Focus on Statins

The most widely known, effective, safe, and expensive class of cholesterol lowering drugs is statins. Statins act to lower cholesterol by blocking the production of cholesterol in the liver. Several RCTs have been conducted to examine the effects of statins on CVD although none of these studies included information about primary prevention tactics to reduce CVD in women. Currently there is no data available on the effects of long-term usage of statins. Of the research available on secondary prevention, most has used male samples or samples with small representations of women, and the results are conflicting. One trial (18% women) focussing on secondary prevention with simvastatin showed a 25% reduction in total cholesterol, and 8% of patients were spared from mortality due to CVD with treatment. Differences between the two groups prior to treatment made gender analyses difficult to interpret. Another trial (14% women) examined pravastatin treatment in secondary prevention. With treatment, there was a 20% reduction in total cholesterol and a trend toward greater reduction in major coronary events in women. Negative effects of statin use include a potential risk of breast cancer and a link between use of these drugs and muscle disintegration and kidney failure when they are used in combination with other cholesterol-lowering drugs. If comparing the efficacy of hormone therapy and statin treatment in secondary prevention in women, there is more evidence to support the use of statins, but caution should be used when making the decision to use statins in prevention of CVD.

Other Alternatives to Combating CVD

Drug therapy regimes are relatively easy and immediate solutions to dealing with CVD risk; however, the available evidence indicates that there are few guarantees for success. Improving lifestyle by changing personal behaviors, such as those listed in Table 1, is the key to preventing CVD. A healthy lifestyle not only reduces CVD risk, but also involves fewer uncertainties about health status, improves general health and well being, and leads to greater personal satisfaction and empowerment. An RCT meta-analysis examining dietary therapies showed a 12% reduction in cholesterol lower incidence of death due to heart disease (absolute risk reduction of 6.6%). Several observational studies demonstrate the positive effects of lifestyle changes such as smoking cessation and exercise regimens on primary prevention of CVD in women. Further, 10% of post-menopausal women participating in a secondary prevention trial avoided diagnosis of CVD after a 10-year follow-up by using a walking program intervention.

Information Sources

If you are considering taking a medication to deal with primary or secondary prevention of CVD, speaking with a physician and a pharmacist who understand the research behind the drugs is important. There are also web sites and organisations available to provide evidence-based information on pharmaceuticals. The Therapeutics Initiative web site (http://www.ti.ubc.ca) and the Service for Medication Information, Learning and Education in British Columbia (http://www.ubcpharmacy.org/SMILE) are two excellent sources of information. You may also contact SMILE by telephone, only after consulting with your pharmacist, at 604-822-1330 or 1-800-668-6233.

Bibliography:

2. Heart and Stroke Foundation of B.C. and Yukon. Resource Library http://www.bc.heartandstroke.ca/cgi-bin/English/Catalog/Public/bR.cgi


Table 2. Key features of heart disease and heart disease warning signs.

<table>
<thead>
<tr>
<th>Angina (chest pain)</th>
<th>Valvular Disorders</th>
<th>Arrhythmias</th>
<th>Congestive Heart Failure</th>
<th>Heart Attack</th>
<th>Peripheral Vascular Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest/arms; tightness, pressure, squeezing, aching</td>
<td>Chest pain</td>
<td>First degree Heart Block: No symptoms</td>
<td>Shortness of breath</td>
<td>Crushing/ squeezing pain in chest</td>
<td>Pain in limbs that is affected by narrowed arteries</td>
</tr>
<tr>
<td>Persistent feeling of indigestion</td>
<td>Excessive fatigue</td>
<td>Second degree: Heart Block: either no symptoms or minor ones such as lightheadedness</td>
<td>Swollen ankles or legs</td>
<td>Pains in left arm and jaw</td>
<td>Severe blockage can cause extremities (i.e., feet) to appear bluish or pale and feel cold to the touch</td>
</tr>
<tr>
<td>Sharp, burning/ cramping pain</td>
<td>Heart palpitations</td>
<td>Third degree Heart Block: fatigue, lightheadedness or fainting</td>
<td>Sudden weight gain</td>
<td>Breathlessness</td>
<td></td>
</tr>
<tr>
<td>Ache starting in or spreading to neck, jaw, throat, shoulder, back or arms</td>
<td>Thumping sensation in chest</td>
<td>AV Block: No symptoms</td>
<td>Tiredness and/or loss of energy</td>
<td>Nausea</td>
<td></td>
</tr>
<tr>
<td>Discomfort in neck or upper back, particularly between shoulder blades</td>
<td>Shortness of breath</td>
<td></td>
<td>Loss or change in appetite</td>
<td>Sweating</td>
<td></td>
</tr>
<tr>
<td>Swollen ankles, wrists or stomach</td>
<td></td>
<td></td>
<td></td>
<td>Anxiety</td>
<td></td>
</tr>
</tbody>
</table>

Vague chest discomfort/ pressure in chest or severe heart burn

Especially women

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