Cardiovascular disease (CVD) is the #1 killer of women both in Canada and the US. Average lifetime risk of cardiovascular disease in women is approximately 40%, and increases as the number of risk factors increases. Coronary artery disease is the main form of heart disease that affects both women and men. One in 5 women has been told by their physician that they have heart problems. More women than men die from heart failure and stroke.

The risk factors that lead to the development of heart disease are increasing and we can expect to see more heart disease develop in women over time. Most of these risk factors are the same as for the general population and include obesity, inactivity, poor dietary habits, metabolic syndrome and elevated cholesterol, diabetes, hypertension and smoking. However, additional factors are more prevalent among women than men, are often unrecognized, and have been associated with significantly increased risk of subsequent CVD. These include hypertension in pregnancy, gestational diabetes, preeclampsia and autoimmune diseases. Aggressive management of risk factors can delay the development of heart disease, stroke and congestive heart failure.

Prior to menopause women are relatively protected from the development of heart disease. Hormonal protection delays heart disease by about ten years on average, although the presence of diabetes overrides this protection. Thus, women tend to be older and have more comorbidities than men when they develop heart disease. When women do develop heart disease, particularly at a young age, it tends to be more severe and have a worse prognosis. Women often have delays in diagnosis of heart disease and tend to have more diffuse or widespread disease. Their coronary arteries are smaller and women tend to do poorer with procedures such as angioplasty or bypass surgery.

Heart disease in women can be difficult to diagnose because the usual presenting symptoms are less often present or symptoms are atypical. A recent study of women presenting with heart attack showed that the most frequent preceding symptoms were unusual fatigue (70.7%), sleep disturbance (47.8%), and shortness of breath (42.1%). Only 29.7% reported chest discomfort, a hallmark symptom in men. The most frequent acute symptoms were shortness of breath (57.9%), weakness (54.8%), and fatigue (42.9%). Acute chest pain was absent in 43%.

Using common tests to diagnose heart disease in women pose further challenges. Treadmill stress testing, the usual test to diagnose coronary artery disease, can often be falsely abnormal in women. More accurate tests such as stress nuclear heart scanning or stress echocardiograms are necessary to exclude or diagnose heart disease in women. These tests tend to be less readily available and more costly and sometimes are inappropriately avoided, thus delaying the diagnosis of what are often atypical or unusual presentations of coronary artery disease.

Once coronary artery disease is diagnosed there continue to be problems with inadequate therapy to control symptoms as well as risk. These problems apply to all patients with heart disease and cardiac risk factors.
### Vascular Protection/CAD

**Girth:**
- Targets: M < 94 cm (37 inches); F < 88 cm (34.6 inches). Lower in South Asians M < 90 cm and F < 80 cm. W/H M < 0.95; F < 0.9.

**Physical activity:** Minimum goal > 150 min/week

**Smoking Goal:** Complete cessation

**Lipid Management:**
- **Primary goal:** LDL < 2.0 (1.8) mmol/L or ≥ 50% LDL ↓
- **Secondary goal:** non-HDL chol ≤ 2.6 mmol/L;
  - Apo-B < 0.8 g/L

**Metabolic Syndrome**
- HDL ≥ 1.0 mmol/L M
- HDL ≥ 1.3 mmol/L F
- TG < 1.7 mmol/L

**Apo B:**
- **Hi risk** < 0.8 g/L;
- **Mod risk** < 1.05 g/L;
- **Low risk** < 1.2 g/L

**Blood pressure:**
- Targets:
  - <135/85 mm Hg for HBPM/ABPM
  - <130/80 mm Hg for DM/CAD/CKD
  - <120/80 mm Hg for LVD

**Diabetes:**
- **Targets**
  - FBS 4.7 mmol/L
  - 2hr PC Glucose 5-10 mmol/L
  - HbA1C ≤ 7%
- Consider ≤ 6.5% in selected patients or 7.1 - 8.5% if high risk of hypoglycemia, frail, elderly, multiple co-morbidities.

**MAU:**
- **Targets**
  - Spot urine < 20/mg/L
  - ACR < 2.0 Men
  - ACR < 2.8 Women

**Antiplalet agents:** ASA, Clopidogrel, Ticagrelor or Prasugrel

**Anticoagulants:** Target INR _______ or NOAC

**ACE inhibitor/ARBs:** Post-MI

**ACE inhibitor/ARBs:** Vascular protection/CAD

**Beta-blockers:** Post-MI

**Beta-blockers CHF/LV**
- Dysfunction: LVEF < 40%

**Rx: Omega-3 fatty acids**
- (salmon oil or flax) 1-3 gm/day

**hs-CRP**
- High risk > 3.0 mg/L;
  - Mod risk 1.0-3.0 mg/L;
  - Low risk < 1.0 mg/L

**HRT:** Off

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<table>
<thead>
<tr>
<th>Rx (√)</th>
<th>Risk Intervention</th>
<th>Date √ Achieved</th>
<th>Date √ Achieved</th>
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<td>Ideal body weight:</td>
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<td>BMI &lt; 27 kg/m² (ideally&lt; 25 kg/m²)</td>
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<td><strong>Girth:</strong> Targets: M &lt; 94 cm (37 inches); F &lt; 88 cm (34.6 inches). Lower in South Asians M &lt; 90 cm and F &lt; 80 cm. W/H M &lt; 0.95; F &lt; 0.9.</td>
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<td><strong>Physical activity:</strong> Minimum goal &gt; 150 min/week</td>
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<td><strong>Smoking Goal:</strong> Complete cessation</td>
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<td><strong>Lipid Management:</strong></td>
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<td><strong>Primary goal:</strong> LDL &lt; 2.0 (1.8) mmol/L or ≥ 50% LDL ↓</td>
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<td><strong>Secondary goal:</strong> non-HDL chol ≤ 2.6 mmol/L;</td>
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<td>Apo-B &lt; 0.8 g/L</td>
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<td><strong>Metabolic Syndrome</strong></td>
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<td>HDL ≥ 1.0 mmol/L M</td>
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<td>HDL ≥ 1.3 mmol/L F</td>
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<td>TG &lt; 1.7 mmol/L</td>
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<td><strong>Apo B:</strong></td>
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<td><strong>Hi risk</strong> &lt; 0.8 g/L;</td>
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<td><strong>Mod risk</strong> &lt; 1.05 g/L;</td>
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<td><strong>Low risk</strong> &lt; 1.2 g/L</td>
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<td><strong>Blood pressure:</strong> Targets</td>
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<td>&lt;135/85 mm Hg for HBPM/ABPM</td>
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<td>&lt;130/80 mm Hg for DM/CAD/CKD</td>
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<td></td>
<td>&lt;120/80 mm Hg for LVD</td>
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<td></td>
<td><strong>Diabetes:</strong></td>
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<td><strong>Targets</strong></td>
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<td></td>
<td>FBS 4.7 mmol/L</td>
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<td>2hr PC Glucose 5-10 mmol/L</td>
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<td>HbA1C ≤ 7%</td>
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<td>Consider ≤ 6.5% in selected patients or 7.1 - 8.5% if high risk of hypoglycemia, frail, elderly, multiple co-morbidities.</td>
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<td><strong>MAU:</strong></td>
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<td></td>
<td><strong>Targets</strong></td>
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<td>Spot urine &lt; 20/mg/L</td>
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<td>ACR &lt; 2.0 Men</td>
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<td>ACR &lt; 2.8 Women</td>
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<td><strong>Antiplalet agents:</strong> ASA, Clopidogrel, Ticagrelor or Prasugrel</td>
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<td><strong>Anticoagulants:</strong> Target INR _______ or NOAC</td>
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<td><strong>ACE inhibitor/ARBs:</strong> Post-MI</td>
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<td><strong>ACE inhibitor/ARBs:</strong> Vascular protection/CAD</td>
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<td><strong>Beta-blockers:</strong> Post-MI</td>
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<td><strong>Beta-blockers CHF/LV</strong></td>
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<td>Dysfunction: LVEF &lt; 40%</td>
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<td><strong>Rx: Omega-3 fatty acids</strong></td>
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<td>(salmon oil or flax) 1-3 gm/day</td>
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<td><strong>hs-CRP</strong></td>
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<td>High risk &gt; 3.0 mg/L;</td>
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<td>Mod risk 1.0-3.0 mg/L;</td>
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<td>Low risk &lt; 1.0 mg/L</td>
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<td><strong>HRT:</strong> Off</td>
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</table>
Evaluation of CVD Risk:
• Medical history/family history/pregnancy complication history
• Symptoms of CVD
• Depression screening in women with CVD
• Physical examination including blood pressure, body mass index, waist size
• Laboratory tests including fasting lipoproteins and glucose
• Framingham risk assessment if no CVD or diabetes

Implements Class I Lifestyle Recommendations (for all):
• Smoking cessation
• DASH-like diet
• Regular physical activity
• Weight management

Is Woman at High Risk of CVD (having ~1 of the following)?
• Clinically established CHD
• Cerebrovascular disease
• Peripheral arterial disease
• Abdominal aortic aneurysm
• Diabetes mellitus
• Chronic kidney disease
• 10-year predicted CVD risk ~10%

Recent cardiovascular event, procedure, or congestive heart failure symptoms?

YES

Refer to cardiac rehabilitation

NO

Implement Class I Recommendations:
• Blood pressure control
• LDL-C-lowering therapy (goal 2.0 mmol/L)
• β-Blocker
• Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker

Is Woman at High Risk of CVD (having ~1 of the following)?

YES

Implement Class I Recommendations:
• Warfarin or
• Aspirin or
• Dabigatran

NO

History of Paroxysmal Atrial Fibrillation?

YES

Implement Class I Recommendations:
• Blood pressure control
• LDL-C-lowering therapy if < 5.0 mmol/L

NO

Consider Class II Recommendations:
• Therapy for high LDL-C, non-TC/HDL ratio and triglycerides and/or HDL-C in select women
• Aspirin

Flow diagram for CVD preventive care in women. CVD indicates cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; CHD, coronary heart disease; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; and ACS, acute coronary syndrome. Adapted from: Effectiveness-Based Guidelines for the Prevention of Cardiovascular Disease in Women — 2011 Update : A Guideline From the American Heart Association. Circulation 2011, 123:1243-1262.
CHEST PAIN ASSESSMENT ALGORITHM

STABLE SYMPTOMS – ASSESS PRE-TEST LIKELIHOOD CAD

Prevalence of CAD (%) in Symptomatic Patients According to Age and Sex

<table>
<thead>
<tr>
<th>AGE</th>
<th>Men</th>
<th>Women</th>
<th>Men</th>
<th>Women</th>
<th>Men</th>
<th>Women</th>
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<tbody>
<tr>
<td>30-39</td>
<td>69.7</td>
<td>25.8</td>
<td>21.8</td>
<td>4.2</td>
<td>5.2</td>
<td>0.8</td>
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<td>40-49</td>
<td>87.3</td>
<td>55.2</td>
<td>46.1</td>
<td>13.3</td>
<td>14.1</td>
<td>2.8</td>
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<tr>
<td>50-59</td>
<td>92.0</td>
<td>79.4</td>
<td>58.9</td>
<td>32.4</td>
<td>21.5</td>
<td>8.4</td>
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<tr>
<td>60-69</td>
<td>94.3</td>
<td>90.6</td>
<td>90.6</td>
<td>54.6</td>
<td>28.1</td>
<td>18.6</td>
</tr>
</tbody>
</table>

3 of 3 criteria 2 of 3 criteria 1 of 3 criteria

Low Likelihood
CAD < 10% risk
Consider no test

Intermediate Likelihood
CAD 10-90% risk

High Risk
CAD >90% risk
Consider non-invasive assessment to determine severity and extent of CAD or cardiac catheterization based on severity of symptoms.

Patient able to exercise

ECG Normal
Exercise Stress Test
Exercise Myocardial Perfusion Scan*
Exercise Stress Echo

Patient unable to exercise

ECG Abnormal
Persantine** Myocardial Perfusion Scan*
Dobutamine Stress Echo

Test Results: If suspected false + Exercise Stress Test (EST) — consider Stress Echo or Stress Nuclear study. If inconclusive EST — consider Persantine Nuclear study.

Normal
Equivocal or Mild Symptoms
Abnormal Low/Moderate Risk
Abnormal High Risk
ACS Protocol

Optimal Medical Therapy
CT Angiogram
Cardiac Catheterization
Non-Invasive Risk Stratification
CV RISK REDUCTION CHECKLIST

**Rx** | **Intervention** | **Recommendations**
--- | --- | ---
Smoking: Goal | - Complete cessation | Strongly encourage patient and family to stop smoking. Provide counselling, nicotine replacement, and formal cessation programs as appropriate.

Lipid Management: Primary goal | LDL < 2.0 (1.8) mmol/L | Start hypolipidemic diet in all patients: ≤ 30% fat, < 7% saturated fat, < 200mg/day cholesterol. 10% LDLL achievable with diet. Assess fasting lipid profile. Baseline lipid profile < 24 hrs. after acute event. In post-MI patients, lipid profile may take 4 to 6 weeks to stabilize. Add drug therapy according to the following guide:

**Lipid Profile** | **1st Line Therapy** | **2nd Line Therapy**
--- | --- | ---
LDL ↑ | Statin | Ezetimibe
LDL ↑ & TG | Statin | Comb. Therapy Ezetimibe, Niaspan or Fibrate
LDL ↑ & HDL ↓ | Fibrate or Niacin/Niaspan® | Combination Therapy
TG ↑ | Fibrate or Niacin/Niaspan® | Combination Therapy

**Secondary goal** | Non-HDL Chol ≤ 2.6 mmol/L; Apo-B<0.8 g/L | 2012 Update–CCS GUIDELINES for the Dx and Tx of Dyslipidemia for the Prevention of CVD

**Tertiary goal** | Metabolic Syndrome TC/HDL < 4.0mmol/L HDL > 1.0mmol/L (men)/ > 1.3mmol/L (women) | 2012 Update–CCS GUIDELINES for the Dx and Tx of Dyslipidemia for the Prevention of CVD

**Hypertension Goal** | < 150 systolic (Age ≥ 80) | 2013 CHS CHEP www.hypertension.ca
| < 140/90 (non-diabetic CKD) | Measure BP at all appropriate visits. Assess overall cardiac risk. Home BPM an important monitoring tools. Treat to target. Lifestyle modifications to reduce BP and CV risk. Lifestyle and Rx to achieve BP targets. Combination Rx. Focus on adherence.
| < 135/65 (Home BP) | • Assess BP at all visits. Assess global CV risk. Lifestyle modifications are cornerstones of anti-hypertensive and anti-atherosclerotic therapy.
| < 130/60 (DM/-CKD) | • Initiate Rx immediately if hypertensive urgency. Dx HTN on second visit if: target organ damage, DM, chronic kidney disease (CKD) or BP > 180/110. Dx HTN on 3rd visit if BP ≥140-179 or ≥90-109
| < 120/80 (LVD) AHA 2007 | • Validate hypertension with: 1) Office BP(<140/90), ambulatory BP(<135/85 daytime average/ or 130/80-24 hr average) or Awake ABPM ≥ 135 or 85. 24-hour ≥ 130 or 80 DM, or 130/<80 DM, and/or DM nephropathy. Target <140/90 (non diabetic CKD), <120/80 LVD. AHA.

**Diabetes** | CDA 2013 guidelines.diabetes.ca
| Guidelines Released April 2013 | • Dx DM: FPG ≥ 7.0 mmol/L or 2 hr PC Glucose ≥ 11.1 mmol/L (Normal A1C < 5.5; FPG < 5.6 mmol/L; 2 hr PC FPG < 7.8 mmol/L). Dx Impaired Glucose Tolerance: FPG < 6.1 mmol/L and 2 hr PC PG 7.8-11.0 mmol/L.
| At diagnosis target euglycemia ASAP: A1C ≤ 8.5 | • At diagnosis target euglycemia ASAP: A1C ≤ 8.5 - Initiate diabetes education, diet to achieve weight loss (5-10%), exercise and lifestyle (+/- metformin). If not at target 2-3 mo - Start/Increase metformin. If A1C > 8.5 start metformin immediately. Consider initial combination therapy. If symptomatic hyperglycemia with metabolic decompensation, initiate insulin immediately.
| Aggressive BP Control (Target<130/80) | • Aggressive BP Control (Target<130/80). Rx: ACE-I, ARB, DHP-CCB, thiazide diuretic, then cardio-selective β blocker or non-DHP-CCB. Alpha blockers not recommended as first line agent.
| Vascular Protection | • Vascular Protection: Macro/microvascular disease: Statin + ACEi or ARB + Antiplatelet (ASA or clopidogrel). DM > 15 years and age > 30 years: statin.
<table>
<thead>
<tr>
<th>Rx</th>
<th>Intervention</th>
<th>Recommendations</th>
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<tr>
<td></td>
<td><strong>Physical activity:</strong>&lt;br&gt;Minimum goal 30 mins of moderate activity 5 times a week. Cumulative 150 mins/week. See website exerciseismedicine.ca</td>
<td>- Assess risk, preferably with exercise test, to guide prescription.&lt;br&gt;- Encourage minimum of 30 minutes of moderate intensity activity 5-7 times weekly (walking, jogging, cycling or other aerobic activity) supplemented by an increase in daily lifestyle activities (e.g., walking breaks at work, using stairs, gardening, household work)&lt;br&gt;- Max benefits 5 to 6 hours per week. Medically supervised programs for moderate to high-risk patients. Resistance exercise 3 times/week does not adversely influence BP.</td>
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<td><strong>Obesity/weight management:</strong></td>
<td>Start intensive diet and appropriate physical activity intervention, as outlined above, in patients &gt;120% of ideal weight for height. Particularly emphasise need for weight loss in patients with hypertension, elevated triglycerides or elevated glucose levels. Ideal body weight BMI &lt; 25</td>
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<td><strong>Antiplatlet agents/anticoagulants:</strong></td>
<td>Start aspirin 81-325 mg per day if not contraindicated. Consider clopidogrel 75mg OD post MI, post CABG, CVA, PVD in ASA intolerant or allergic patients CAPRIE Trial. Consider clopidogrel 75mg OD + ASA for ACS: unstable angina/non-ST elevation MI CURE Trial: duration of therapy 9-12 months. No chronic benefit of ASA+ clopidogrel CHARISMA. Consider alternate antplatelet therapy for post MI patients unable to to take ASA or dual antplatelet therapy for up to a year post ACS/PCI (Clopidogrel, Ticagrelor or Prasugrel post ACS with PCI).</td>
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<td><strong>ACE inhibitors/ARBs</strong>&lt;br&gt;Post MI/LV Dysfunction:</td>
<td>Start early post-MI in stable high risk patients (anterior MI, previous MI, Killip class II (S3 gallop, rales, radiographic CHF). Continue indefinitely for all with LV dysfunction (EF&lt;40%) or symptoms of CHF. Use as needed to manage HPT or symptoms in all other patients. In ACEi intolerant patients consider Valsartan VALIANT or Candesartan CHARM.</td>
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<td><strong>ACE inhibitors/ARBs</strong>&lt;br&gt;Vascular Disease/ Diabetes</td>
<td>Rx ACE inhibitors in all patients &gt;55 yrs with evidence of vascular disease or DM and one other risk factor: HOPE Trial - Ramipril 2.5 – 10 mg OD or all CAD patients &gt;18 yrs EUROPA Trial -Perindopril 4 – 8 mg OD. If LVF preserved, patient non diabetic and other risk factors optimized may not need ACE inhibitor PEACE.</td>
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<td><strong>Beta-blockers:</strong>&lt;br&gt;Post-MI</td>
<td>Start acutely or within a few days of event in all post-MI patients (unless contra-indication). Continue indefinitely if residual ischemia, heart failure LV dysfunction, heart failure, severe LV dysfunction with EF &lt; 40% or symptomatic arrhythmias. No mortality benefit of Beta blockers beyond 1 year post MI, in chronic CAD without MI or in patients with CAD risk factors. (JAMA , Vol 308, No. 13, pp. 1340-1349). Rx as needed to manage angina or HTN.</td>
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<td></td>
<td><strong>Beta-blockers:</strong>&lt;br&gt;CHF</td>
<td>Rx Add Beta-blocker to ACE-inhibitor/diuretic/-/ digoxin in stable Class II-IV CHF/LVEF ≤ 40% Bisoprolol 1.25 – 10 mg OD, carvedilol 3.125 mg BID – 25 mg BID (50 mg BID if weight &gt; 85 kg) or nebivolol 1.25 - 10 mg daily (Titrare q 2 weeks. Avoid mod-high dose in the elderly).</td>
</tr>
<tr>
<td></td>
<td><strong>Omega-3 fatty acids</strong>&lt;br&gt;HOMOCYST(E)INE</td>
<td>Rx: Omega-3 fatty acids 1-3 gm/day. No identifiable benefit in lowering elevated homocysteine with vitamin supplements combining folic acid, B6 and B12 in patients with CVD, DM or post MI. HOPE 2/NORVIT.</td>
</tr>
<tr>
<td></td>
<td><strong>Estrogens</strong></td>
<td>HRT not recommended for 1* or 2* prevention. Stop HRT in ACS, MI, PTCA, CABG, CHF; other surgery.</td>
</tr>
</tbody>
</table>

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Heart Disease in Women – April 2014
Prepared by Dr. J. Niznick/Dr. J. Heshka
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