CARDIOVASCULAR DISEASE IN WOMEN

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%.

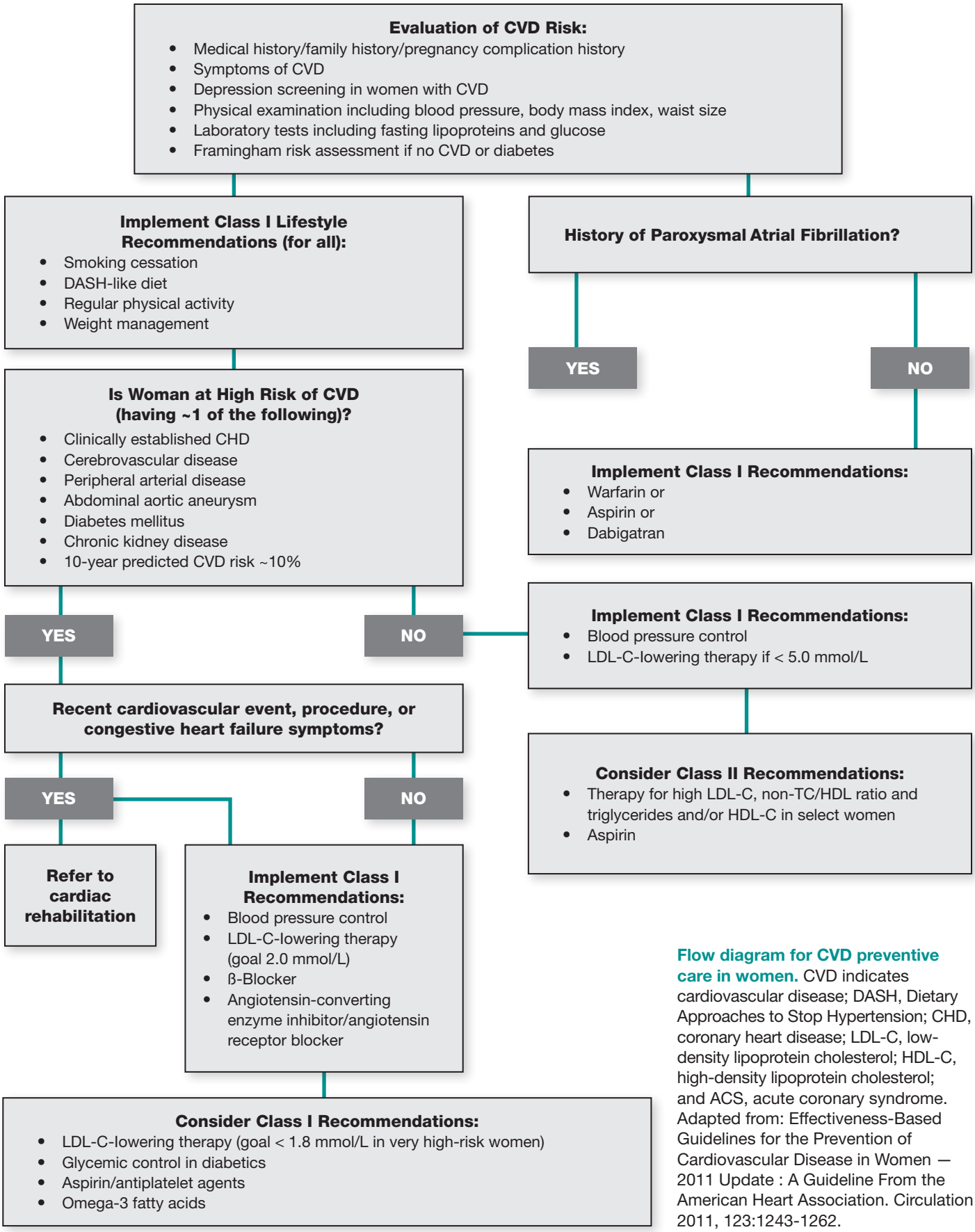
Using common tests to diagnose heart disease in women pose further challenges. Treadmill stress testing, the usual test to diagnose coronary artery disease, can often be falsely abnormal in women. More accurate tests such as stress nuclear heart scanning or stress echocardiograms are necessary to exclude 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.

CV RISK FLOWSHEET

Rx (✓)	Risk Intervention	Date ✓ Achieved	Date ✓ Achieved	Date ✓ Achieved	Date ✓ Achieved	Date ✓ Achieved	Date ✓ Achieved
	Ideal body weight: BMI < 27 kg/m^2 (ideally< 25 kg/ m^2)						
	Girth: *Targets* M < 94 cm (37 inches); F<88cm (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						
	Antiplatelet 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						

PREVENTION OF CVD IN WOMEN



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

UNSTABLE SYMPTOMS
- New onset angina
- Accelerating angina
- Prolonged resting angina

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

	Typical angina		Atypical angina		Non anginal chest pain	
AGE	Men	Women	Men	Women	Men	Women
30-39	69.7	25.8	21.8	4.2	5.2	0.8
40-49	87.3	55.2	46.1	13.3	14.1	2.8
50-59	92.0	79.4	58.9	32.4	21.5	8.4
60-69	94.3	90.6	90.6	54.6	28.1	18.6
	3 of 3 criteria		2 of 3 criteria		1 of 3 criteria	

1)Retrosternal discomfort.2)Provoked by exercise or stress.3)Relieved by rest or NTG

 .....bridging the care gap

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

Patient **unable** to exercise

ECG Normal

ECG Abnormal

Exercise Stress Test

Exercise Myocardial Perfusion Scan*

Exercise Stress Echo

Persantine** Myocardial Perfusion Scan*

Dobutamine Stress Echo

*Avoid in women of child-bearing years **Persantine may be contra-indicated in asthma

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

High Risk

Indeterminate Risk

Optimal Medical Therapy

CT Angiogram

Cardiac Catheterization

Non-Invasive Risk Stratification

CV RISK REDUCTION CHECKLIST

<table>
<tr><th>Rx ✓</th><th>Intervention</th><th>Recommendations</th></tr>
<tr><td></td><td>Smoking: Goal
-Complete cessation</td><td>Strongly encourage patient and family to stop smoking. Provide counselling, nicotine replacement, and formal cessation programs as appropriate.</td></tr>
<tr><td></td><td>Lipid Management:
Primary goal *
LDL < 2.0 (1.8) mmol/L</td><td>Start hypolipidemic diet in all patients: ≤ 30% fat,< 7% saturated fat,< 200mg/day cholesterol. 10% LDL↓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:</td></tr>
<tr><td></td><td>Secondary goal *
Non-HDL Chol
≤ 2.6 mmol/L;
Apo-B<0.8 g/L

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</td><td>
<table>
<tr><th>Lipid Profile</th><th>1st Line Therapy</th><th>2nd Line Therapy</th></tr>
<tr><td>LDL ↑</td><td>Statin</td><td>Ezetimibe</td></tr>
<tr><td>LDL ↑↑ & TG</td><td>Statin</td><td>Comb. Therapy Ezetimibe, Niaspan or Fibrate</td></tr>
<tr><td>LDL ↑& TG ↑↑</td><td>Fibrate or Niacin/Niaspan®</td><td>Combination Therapy</td></tr>
<tr><td>TG ↑& HDL ↓</td><td>Fibrate or Niacin/Niaspan®</td><td>Combination Therapy</td></tr>
</table>
* Primary goal: For patients CHD Risk equivalent: any of CAD, TIA, CVA, AAA, PVD/bruits, DM with one additional categorical risk factor or for patients with very high 10-year risk for total CV events (20%).
• Target initial Rx medication dose required to achieve target LDL <2.0 (1.8) mmol/L or ≥ 50% LDL↓
• For 10 yr CV risk for hard endpoints 10-20%, LDL Rx threshold is 3.5 mmol/L target ≥ 50% LDL↓
• For 10 yr CV risk for hard endpoints < 10%, LDL Rx threshold is 5.0 mmol/L target ≥ 50% LDL↓
• Consider CRP measurement for males >50 & females >60. Initiate lipid lowering if CRP >2.0 mg/L
For specific medications and dosing strategy see Lipid Optimization Tool
</td></tr>
<tr><td></td><td>Hypertension Goal
< 150 systolic(Age ≥ 80)
< 140/90 (non-diabetic CKD)
< 135/85 (Home BP)
< 130/80 (DM+/-CKD)
< 120/80 (LVD) AHA 2007

2013 CHS CHEP
www.hypertension.ca
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.</td><td>• Assess BP at all visits. Assess global CV risk. Lifestyle modifications are cornerstone of anti-hypertensive and anti-atherosclerotic therapy.
• 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
• 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 CK.), < 120/80 LVD. AHA.
• Initial Rx for systolic/diastolic HTN in absence of compelling indication: Low dose thiazide; ß-blocker if age < 60 yr; ACE-I in non-black pts; long-acting CCB and ARB. ISH: LDD/ DHP-CCB/ARB. Combination therapies generally necessary to achieve target BP.
• Consider Rx ASA (once BP controlled) and statin in HTN patients if ≥ 3 CV risks.
• CHF&HTN-Rx ß-blocker; ACE-I (ARB if ACE-I intolerant) & aldosterone antagonist (Class III/IV HF or post MI). Thiazide or loop diuretics, DHP-CCB.
• CKD or Type 2 DM with micro-albuminuria, proteinuria or nephropathy ACE-I/ARB are 1st line Rx. Combination of ACE-I and ARB not recommended in non-proteinuric CKD.
• In DM if ACE combination therapy required: ACE-DHP CCB preferable to ACE-thiazide combinations (ACCOMPLISH)</td></tr>
<tr><td></td><td>Diabetes
CDA 2013
guidelines.diabetes.ca

Guidelines Released April 2013</td><td>• 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: AIC ≤ 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). Rx: ACE-i, ARB, DHP-CCB, thiazide diuretic, then cardio-selective ß blocker or non-DHP-CCB. Alpha blockers not recommended as first line agent.
• Vascular Protection: Macro/microvascular disease: Statin + ACEi or ARB + Antiplatelet (ASA or clopidogrel). DM > 15 years and age > 30 years: statin.</td></tr>
</table>

Rx ✓	Intervention	Recommendations
	Physical activity: Minumum goal 30 mins of moderate activity 5 times a week. Cumulative 150 mins/ week. See website exerciseismedicine.ca	• Assess risk, preferably with exercise test, to guide prescription. • 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) • 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.
	Obesity/weight management:	Start intensive diet and appropriate physical activity intervention, as outlined above, in patients >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 < 25
	Antiplatelet agents/ anticoagulants:	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 antiplatelet therapy for post MI patients unable to to take ASA or dual antiplatelet therapy for up to a year post ACS/PCI (Clopidogrel, Ticagrelor or Prasugrel post ACS with PCI).
	ACE inhibitors/ARBs **Post MI/LV Dysfunction:**	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<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*.
	ACE inhibitors/ARBs **Vascular Disease/ Diabetes**	Rx ACE inhibitors in **all patients** >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** >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*.
	Beta-blockers: **Post-MI**	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 < 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.
	Beta-blockers: **CHF**	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 > 85 kg) or nebivolol 1.25 -> 10 mg daily (Titrate q 2 weeks. Avoid mod-high dose in the elderly).
	Omega-3 fatty acids **HOMOCYST(E)INE**	**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*.
	Estrogens	HRT not recommended for 1° or 2° prevention. Stop HRT in ACS, MI, PTCA, CABG, CHF, other surgery.