

## Management of Cardiovascular Risk Factors in the Postmenopausal Woman

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## Disclosures

### Research support

- Wyeth, Lilly, Organon, Novo Nordisk, Pfizer

### Consultant fees

- Wyeth, Lilly, Merck, Upsher-Smith

### Through marriage...

- Galaxo Smith-Kline, Boston Scientific, Medtronic, CHF Solutions, J&J Scios

## Objective

- Supply techniques for the management of cardiovascular risk factors in postmenopausal women

Misperceptions still exist that cardiovascular disease is not a real problem for women.



## National Study of Women's Awareness, Prevention Action, and Barriers to CV Health

- About 55% of women in America are aware that heart disease and stroke are their greatest threat
  - Whites 62 %
  - Blacks 38 %
  - Hispanics 34 %

Mosca L, et al. *Circulation* 2006;113:525-534.

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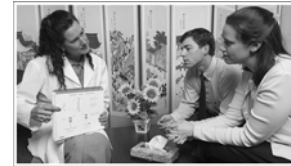
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- When they became aware that personal level was not healthy, women took action to improve risk

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## Educate



Did you know that CHD kills more women than men?



### Health Care Providers Lack Understanding of Women's Risk

Fewer than 1/5 physicians recognize that more women than men die of CHD each year:

- Primary care physicians 8 %
- OBGYN's 13 %
- Cardiologists 17 %


Mosca L, *Circulation*, 2005;111:499

### National Study of Physician Awareness and Adherence to CVD Prevention Guidelines

- Perception of risk was the primary factor associated with CVD preventive recommendations.

Mosca L, et al. *Circulation*, 2005;111:499

**American Heart Association  
Evidence-Based Guidelines for  
Cardiovascular Disease Prevention in  
Women: 2007 Update**



Mosca L, et al. *Circulation* 2007

**Lifestyle  
Interventions**




**Implement Class I Lifestyle  
Recommendations in All Women**

- Smoking cessation
- Heart healthy eating pattern
- Regular physical activity
- Weight management

Mosca L, et al. *Circulation* 2007

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**Soy Protein, Isoflavones, and Cardiovascular  
Health: AHA Science Advisory**

- Earlier research indicating that soy protein has clinically important favorable effects on LDL-C and other CVD risk factors has not been confirmed.
- Because of lack of safety and efficacy data, use of isoflavone supplements in food or pills is not recommended.
- Soy products such as tofu, soy butter, soy nuts, or some soy burgers should be beneficial to cardiovascular health because of their high content of polyunsaturated fats, fiber, vitamins, and minerals and low content of saturated fat.

Sacks FM, et al. *Circulation* 2006;113:1034.

### Low-Carbohydrate-Diet Score and the Risk of Coronary Heart Disease in Women

- 20 year follow up of 82,802 women in Nurse's Health Study who completed food-frequency questionnaires
- Diets lower in CHO and higher in protein and fat were not associated with increased CHD RR 0.94 (.76-1.18)
- Lower risk of CHD if vegetable sources of fat and protein were chosen in low-CHO-diet RR 0.70; p=.002
- Higher glycemic load was strongly associated with increased risk of CHD RR 1.90; p=.003

Halton TL, et al. *N Engl J Med* 2006;355:1991

### Implement Class I Lifestyle Recommendations in All Women

- Smoking cessation
- Heart healthy eating pattern
- **Regular physical activity**
- Weight management



Mosca L, et al. *Circulation* 2007

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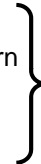
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Mosca L, et al. *Circulation* 2007

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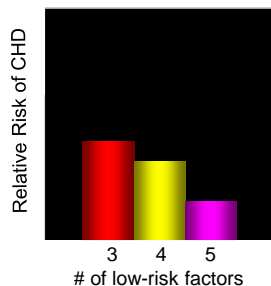
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Mosca L, et al. *Circulation* 2007

### Primary Prevention of CHD through Diet and Lifestyle: Nurses' Health Study

84,129 women with 14 year follow-up



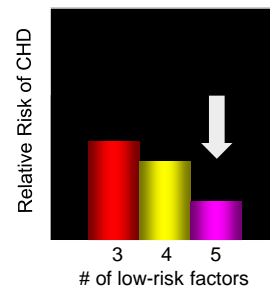
#### Low-risk Factors

- Healthy diet
- Nonsmoking
- Exercise  $\geq$  30 min/d
- BMI < 25 kg/m<sup>2</sup>
- Etoh  $\geq$  5 g/d

Stampfer MJ, et al. *N Engl J Med* 2000;343:16-22.

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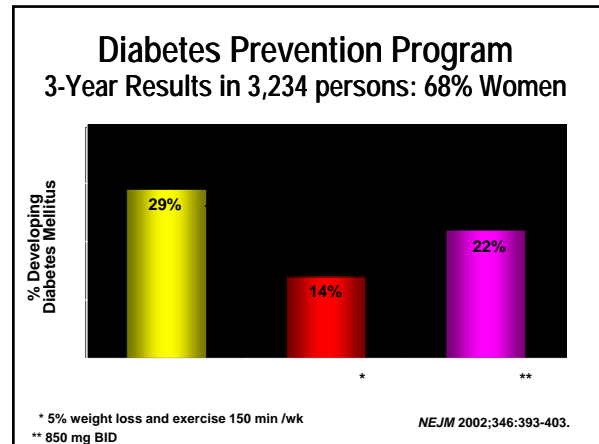
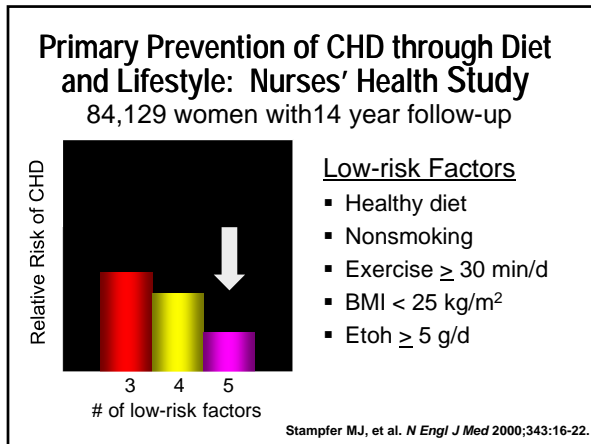
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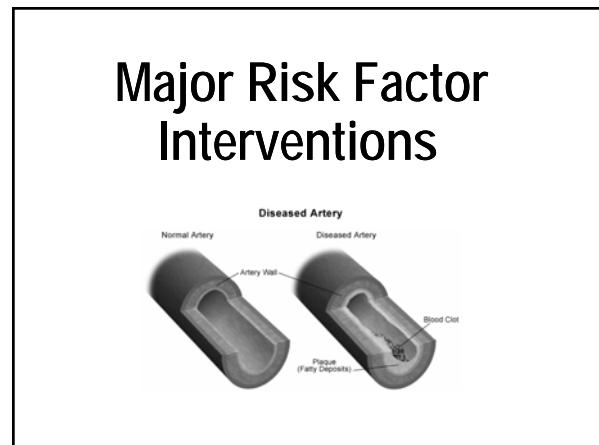


### Lifestyle Interventions

#### Role of Depression?

- Consider screening women with CHD for depression
- Refer and treat when indicated

Mosca L, et al. *Circulation* 2007



### For Women At-Risk

#### Implement Class I Recommendations

- Blood pressure control
- LDL therapy in select women

Mosca L, et al. *Circulation* 2007

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Cardiovascular Disease Prevention in Women  
AHA 2007 Evidence-Based Guidelines

**Blood Pressure Control**

- Through lifestyle approaches, BP goal
  - $\leq 120/80$  mm Hg
- Pharmacotherapy is indicated for BP
  - $\geq 140/90$  mm Hg
  - $\geq 130/80$  if chronic kidney disease or diabetes
  - Start with *B*-blockers, ACE inhibitors/ ARBs
  - Add thiazides as needed

Mosca L, et al. *Circulation* 2007

**For Women At-Risk  
Implement Class I Recommendations**

- Blood pressure control
- **LDL therapy\* in select women**

\*Statins, bile acid sequestrants, niacin, fibrates, and ezetimibe  
Mosca L, et al. *Circulation* 2007

**Optimal Levels of Lipids and  
Lipoproteins in Women**

<u>Lipoprotein</u>	<u>Optimal Level</u>
LDL-C	< 100 mg/dL
HDL-C	> 50 mg/dL
Triglycerides*	< 150 mg/dL
Non-HDL-C	< 130 mg/dL

\*Nonfasting (2-4 hr PP) might be better predictor of CVD risk in women.  
Bansal S, et al. *JAMA* 2007; 298:309; Mosca L, et al. *Circulation* 2007;  
(Non-HDL-C is total minus HDL).

**Lipids—Pharmacotherapy for LDL  
Lowering— At-Risk Women**

- Utilize LDL-C lowering therapy if:  
LDL-C  $\geq 130$  mg/dL on lifestyle therapy
- With multiple risk factors
  - 10-year absolute risk 10-20%

Mosca L, et al. *Circulation* 2007

**Lipids—Pharmacotherapy for LDL  
Lowering— At-Risk Women**

- Utilize LDL-C lowering therapy if:  
LDL-C  $\geq 160$  mg/dL on lifestyle therapy
- With multiple risk factors
  - Even if 10-year absolute risk is < 10%

Mosca L, et al. *Circulation* 2007

**Lipids—Pharmacotherapy for LDL  
Lowering— At-Risk Women**

- Utilize LDL-C lowering therapy if:  
LDL-C  $\geq 190$  mg/dL on lifestyle therapy
- Regardless of presence or absence of other risk factors

Mosca L, et al. *Circulation* 2007

## What about aspirin?



### Randomized Trial of Low Dose Aspirin Primary Prevention of CHD in Women

- 39,876 healthy women  $\geq 45$  yrs followed 10 yrs
- 100 mg of aspirin on alternate days vs placebo
- Cardiovascular events RR 0.91 (.80-1.03)  $p=.13$ 
  - Stroke **RR 0.83** (.69-.99)  $p=.04$
  - Ischemic stroke **RR 0.76** (.63-.93)  $p=.009$
  - Hemorrhagic stroke RR 1.24 (.82-1.87)  $p=.31$
  - No significant effect on fatal/nonfatal MI or death from cardiovascular causes
- GI bleeding/transfusion **RR 1.40** (1.07-1.83)  $p=.02$

Ridker PM, et al. *N Engl J Med* 2005;352:1293

### Randomized Trial of Low Dose Aspirin Primary Prevention of CHD in Women

In subgroup analysis, aspirin significantly reduced the risk of major CVD events among women  $\geq 65$  years of age

- Major CVD events RR 0.74  $p=.008$
- Ischemic stroke RR 0.70  $p=.05$
- Myocardial infarction RR 0.66  $p=.04$

Ridker PM, et al. *N Engl J Med* 2005;352:1293

### Aspirin—At Risk or Healthy Women

- If  $\geq 65$  years, consider aspirin therapy (81 mg daily or 100 mg qod) if
  - BP controlled and
  - Benefit for ischemic stroke and MI prevention is likely to outweigh risk of GI bleeding and hemorrhagic stroke
- If  $< 65$  years, use aspirin when benefit for ischemic stroke prevention is likely to outweigh adverse effects of therapy
- Routine use of aspirin in healthy women  $<65$  years is not recommended to prevent MI

Mosca L, et al. *Circulation* 2007

### Class I Recommendations for Women at High Risk of CVD

- Blood pressure control
- LDL therapy (goal  $< 100$  mg/dL)
- Aspirin/antiplatelet agents
- Beta blocker
- ACE inhibitor/ ARB
- Glycemic control in diabetics
- Aldosterone blocker in select women

Mosca L, et al. *Circulation* 2007

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Mosca L, et al. *Circulation* 2007; \*reasonable goal  $< 70$  mg/dL

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- Blood pressure control
- LDL therapy (goal < 100 mg/dL)
- Aspirin/antiplatelet agents
- Beta blocker
- ACE inhibitor/ ARB
- **Glycemic control in diabetics (A1C<7%)**
- Aldosterone blocker in select women

Mosca L, et al. *Circulation* 2007

### Class III Interventions (Not useful / effective and may be harmful)

- Menopausal therapy (HT and SERMs)
- Antioxidant Supplements
- Folic acid
- Aspirin for MI prevention in women < 65yr

Mosca L, et al. *Circulation* 2007

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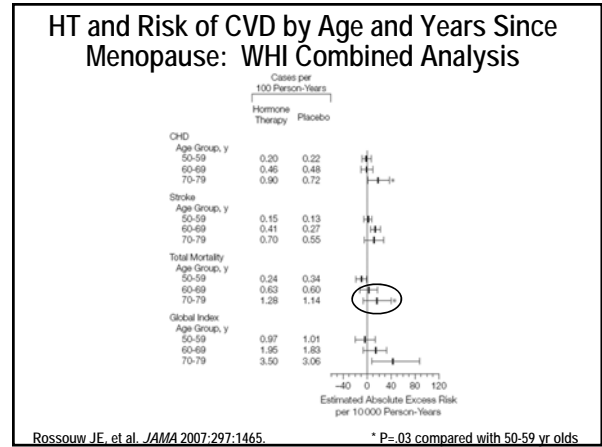
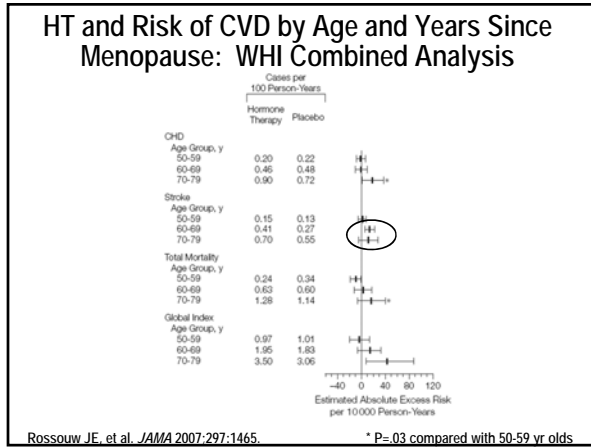
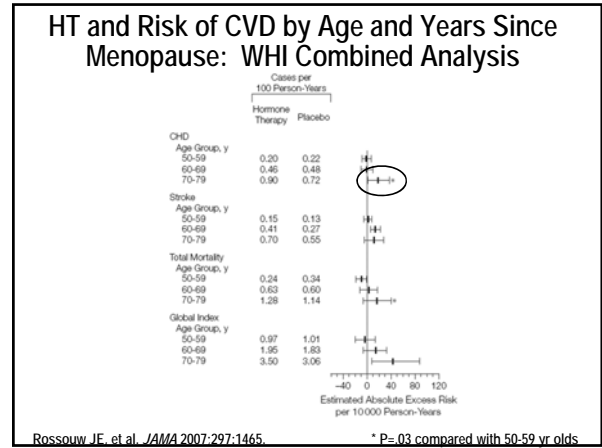
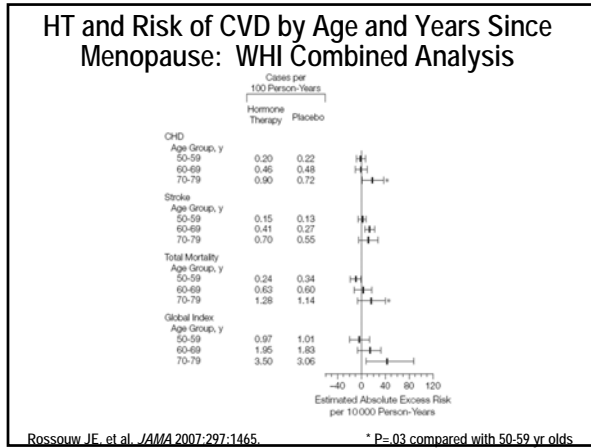
Mosca L, et al. *Circulation* 2007



### Risk of CVD by Age and Years Since Menopause: WHI Combined Analysis

- Included both E+P and E-alone arms of WHI (n=27,347)
- No significant increases in risk due to hormone therapy for any CVD outcome in women ages 50-59 yrs
- The low or absent excess risks of CHD in women with less than 10 years since menopause may be somewhat reassuring to women considering the use of hormones in the first few years after menopause.

Roussouw J, et al. *JAMA* 2007; 297: 1465-1477.



### Clinical Take-Home Message

- The WHI findings in younger women... combined with the low absolute rates of vascular events in this age group, provide some reassurance to recently menopausal women who are considering hormone therapy for the short-term treatment of menopausal symptoms.

Manson JE, et al. Author's reply *N Engl J Med*, September 20, 2007

# Summary and Conclusions

### Prevention of Heart Disease in Women

- Risks for CHD should be identified and aggressively treated in all women, especially those with diabetes or metabolic syndrome
- Modifiable risks (HTN, DM, lipids, smoking) should be treated, and proven therapies for secondary prevention instituted in all women
- Lifestyle may be the most important modifiable risk factor: prudent diet, exercise, stress reduction, and treatment of depression should be encouraged in all women
- Hormone therapy should not be used for primary or secondary prevention of CHD



[www.americanheart.org](http://www.americanheart.org)