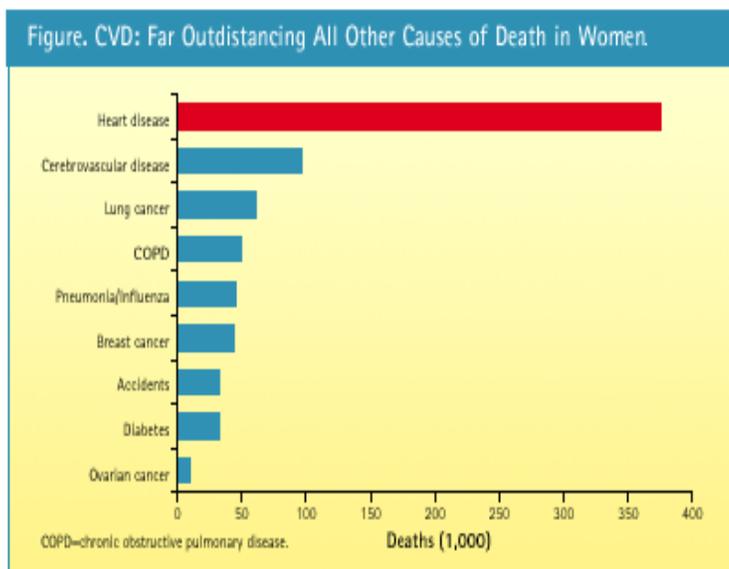


# CVD in Women: Controlling Risk Is Doable

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Cardiovascular disease (CVD), which includes coronary heart disease (CHD) and strokes, is the leading killer of women in America, far outdistancing all other causes of death (Figure below). In 1997, CVD accounted for 43% of all deaths in women in the U.S.<sup>i</sup> In each year since 1984, CVD has killed more women than men, and the gap continues to widen. Even more alarming, 63% of those deaths occur in women with no evidence of prior disease. For the nearly 50 million American women who will be more than 50 years of age this year, there is no greater health-related issue than preventing CVD and controlling this risk.



Adapted from Anderson RN et al. *Monthly Vital Statistics Report*. 1997;45(suppl 2).

As recommended in last year's revised AHA/ACC *Guidelines for Women*<sup>ii</sup>, women should be carefully evaluated for CHD risk factors and managed aggressively to prevent heart disease. Epidemiological studies and

randomized clinical trials provide compelling evidence that CHD is quite preventable.

## CVD Risk in Women: Current Thinking

- CHD risk increases with age, and this increase is more dramatic in women.
- The favorable gender effect on risk factors in women diminishes with age.
- Women generally develop CHD later than men: 10 years later for onset of angina and 20 years for the onset of first MI.
- Overall CHD rates are higher in men, but more women die of CVD. [There is no gender difference in mortality after CHD is manifest.]
- Compared to men, women have much greater risk if they have diabetes and are at slightly increased risk if they have high cholesterol, high triglycerides, high blood pressure or are obese, inactive, or smoke.
- Estrogen has long been thought to confer decreased risk in women because of its beneficial effects on the arterial wall, promoting vasodilation by stimulating the release of nitric oxide, inhibiting proliferation of vascular smooth muscle cells, and its beneficial impact on serum lipids. While its effects on inflammation are inconclusive, it is believed to decrease platelet aggregation and increase fibrinolysis.

## Clinical Trials

The degree to which changes in lifestyle reduce the incidence of CHD and its complications in women have not been well documented.

Furthermore, the role of hormone-replacement therapy (HRT) in the primary and secondary prevention of CHD in women has not been firmly established. Two new studies appearing in the August 24, 2000 issue of the *New England Journal of Medicine* and an accompanying editorial shed valuable light on a plan for promoting coronary health in postmenopausal women. As yet, they still do not clarify the role of HRT in primary and secondary prevention.

Results of the Estrogen Replacement and Atherosclerosis (ERA) study<sup>iii</sup> show that HRT with or without progestin did not affect progression of atherosclerotic disease in postmenopausal women with previously diagnosed disease when compared to placebo (secondary prevention).

ERA principal investigator Herrington said, “For secondary prevention, I believe that the ERA trial, in combination with the HERS (Heart and Estrogen/Progestin Replacement Study)<sup>iv</sup>, provide pretty compelling evidence to suggest that in women with established disease, there may be little or no benefit of HRT for the heart. That’s not to say there may not be other good reasons to use estrogen, but (for now)...it does not appear that women should take estrogen with the expectation of CV benefit.”

The ERA and HERS trials, one looking at clinical events, and the other looking at progression of disease that causes these events, failed to show any benefit of HRT for secondary prevention. In addition the HERS trial suggested that there was an early increase in risk. The re-analyses in the Nurses Health Study and a press release in April from the Womens Health Initiative corroborate this suggestion. **Evidence from these studies should prompt physicians to concentrate on the use of therapies proven to reduce clinical events in postmenopausal women with known disease, i.e. aspirin, statins, beta-blockers and ACE-inhibitors.**

In the same issue, the Nurses Health Study (NHS)<sup>v</sup>, a primary prevention study, looks at the incidence of CHD as it evolved over the last two decades and relates those changes to dietary and lifestyle patterns over time. It attributes at least some of the decline in CHD among women seen in the last decade to the increasing use of postmenopausal HRT among women who were free of CHD at baseline.

During the 14 years of follow-up of 85,941 nurses in an observational study, the incidence of CHD declined by 31%, after adjustment for the effects of age. Smoking declined by 41%, the rate of use of HRT by postmenopausal women increased by 175%, and diet improved considerably. Taken together, the changes in these variables explained two-thirds of the 31% overall decline (21%) in the incidence of CHD.

The Nurses Health Study’s lead investigator Hu says, “**Cardiovascular disease in women is really an important issue that hasn’t been paid enough attention in the past in terms of prevention and treatment.** I think our paper and another paper also published by our group a couple of months ago<sup>vi</sup>, suggests that heart disease is basically a preventable disease through diet and lifestyle modification. The factors we’re talking about, like diet, obesity, physical activity and smoking, they’re all modifiable risk factors. Hormone use is just an option, but these other options are more viable and safer, and can have multiple benefits beyond heart disease.” The large sample, the high rate of follow-up and detailed information make the results of this study quite powerful.

Although his study was primary prevention, Hu agrees with Herrington, concurring that HERS and ERA show that hormone therapy, “is not likely to be beneficial,” in the secondary prevention group. However, Elizabeth Nabel in an accompanying editorial<sup>vii</sup> feels that trials now ongoing using the selective estrogen-receptor

modulators (SERMS), a new type of non-hormonal therapy that may overcome some of the problems seen with hormonal preparations, and the WHI (Women’s Health Initiative) will provide better information than the ERA.

Nabel concludes, ”The message from the two studies described in this issue of the *Journal* is clear. Adherence to a healthful lifestyle and use of HRT, when prescribed for current indications, reduce the risk of primary CHD in women. The role of postmenopausal hormone therapy, including SERMs, in secondary prevention awaits a definitive answer in ongoing clinical trials.”

### Key Messages

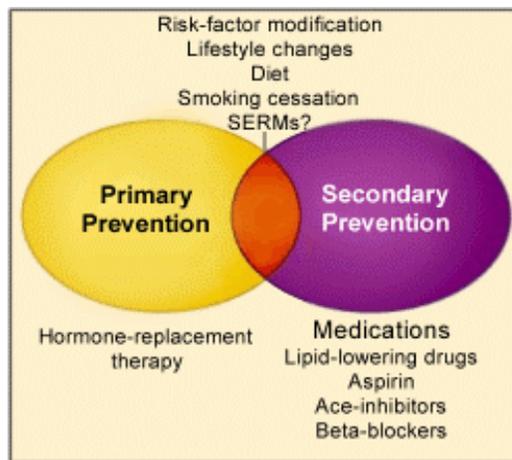
Clinicians evaluating postmenopausal women for CVD risk must:

- assess both key and lesser risk factors
- consider all evidence on the preventive role of dietary / lifestyle modification and pharmacologic treatment
- evaluate the total patient within the context of her overall clinical profile and risk group.

Patients also should be instructed about their part in aggressively reducing their risk factors for primary and secondary CHD. All patients with known CVD should be appropriately treated with medications proven to decrease clinical events [secondary prevention].

The use of HRT for the prevention of CHD should be individualized. Potential beneficial effects of HRT on CHD should be considered, but final treatment decisions should be based on the likely outcome of therapy.

Interventions that may be effective in primary and secondary prevention of CHD are shown below. Controlling risk is do-able!



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*Heartbeat* is available at KHS-WTD library (856-582-2675) or at [www.newsrounds.com/](http://www.newsrounds.com/) under Cardiology. E-mail [maiese@dnmail.com](mailto:maiese@dnmail.com) with questions or comments.

<sup>i</sup> Hoyert DL et al. Deaths: final data for 1997. *Natl Vital Stat Rep.*1997; 47:1-104.  
<sup>ii</sup> Mosca L et al. Cardiovascular disease in Women: a statement for healthcare professionals from the AMA. *Circulation* 1997; 96:2468-82.  
<sup>iii</sup> Herrington DM et al. Effects of estrogen replacement on the progression of coronary atherosclerosis [ERA]. *N Engl J Med* 2000; 342:522-29.  
<sup>iv</sup> Hully S et al. Randomized trial of estrogen plus progesterin for secondary prevention of CHD in postmenopausal women. *JAMA* 1998; 280:605-13.  
<sup>v</sup> Hu FRB et al. Trends in the incidence of CHD and changes in diet and lifestyle in women. *N Engl J Med* 2000; 342:530-37.  
<sup>vi</sup> Stampfer MF et al. Primary prevention of CHD in women through diet and lifestyle. *N Engl J Med* 2000; 343:16-22.  
<sup>vii</sup> Nabel EG. Coronary Heart Disease in Women-an ounce of prevention. *N Engl J Med* 2000; 343:572-74.