You may have thought that the controversy over prescribing hormone therapy for cardiovascular protection was resolved in 2002 when the Women’s Health Initiative was abruptly halted due to the finding that study participants who took hormone therapy had increased risk of negative health events. Recently, however, some scientists have begun to speculate that initiating hormone therapy early in menopause is the key to cardiovascular protection. Although there is insufficient scientific evidence to support these claims, many have insisted on promoting these guesses in the popular media, misleading women once again about benefits and risks of hormone therapy. Earlier this year, a series of journal articles went as far as to speculate that HT can actually be cardio protective if taken during early menopause! This fact sheet will help you distinguish between proven scientific facts and conjectured hypotheses regarding hormone therapy and cardiovascular disease. In women who are at least 10 years beyond the menopausal transition, scientists agree that hormone therapy increases the risk of heart disease; if women in this stage of life choose to take hormones for menopausal symptoms, it should be for the shortest period of time at the lowest possible dose. However, some scientists have recently speculated that starting prescription hormones during the menopausal transition (either before, or within a year or two after the last menstrual period) could prevent the development of heart disease, and subsequently cardiac events such as heart attacks. This theory has been called the “Unified Hypothesis” or the “Window of Opportunity Theory” of hormone therapy. “Window of Opportunity” theorists propose that the ability of estrogen to lower coronary atherosclerosis means that it can be prescribed to prevent heart disease. They suggest that hormone therapy may have a beneficial effect on heart health if it is initiated early in menopause when a woman’s arteries are still likely to be relatively healthy. They concede that HT may have a harmful effect if started in late menopause when advanced atherosclerosis may be present. However, it is essential that patients and physicians understand that this opinion is only a hypothesis and has not been supported by any randomized controlled clinical trials. The WHI Investigators who formalized this hypothesis actually state in a medical journal article that this theory has not been tested: “as yet there has been no clinical trial that has tested the unified hypothesis directly.” Moreover, the rationale behind this idea has fundamental flaws. According to the “Window of Opportunity” line of reasoning, we should be questioning not the age at
which HT is initiated, but rather the arterial health of the woman because this is what, so these theorists say, decides the effect of HT on a woman’s cardiovascular system. Due to the ongoing global obesity epidemic, atherosclerosis is occurring at younger ages. A younger woman early in menopause who is overweight is likely have advanced atherosclerosis, in which case - according to the rationale behind the “Window of Opportunity” hypothesis - HT cannot be deemed beneficial. Thus, the idea that a certain age, a numeric figure, can be the deciding factor as to whether HT will have beneficial or adverse effects for all women is imprecise. A more sensible implication of this hypothesis is that clinicians can be reassured about cardiac risks when considering short term use of HT for menopausal symptom relief in such women. Women have a right to know this critical point - that currently there is no scientific evidence to support the “Window of Opportunity” theory as a clinical recommendation for women’s heart health.

To date, the most reliable evidence on hormone therapy use by women in the early stages of menopause is from the Women’s Health Initiative. Although critics often state that the WHI was a clinical trial of “older” women in their 60’s & 70’s, over 12 percent of WHI participants were aged 50 to 54 at baseline (n = 2,029), making it the largest randomized clinical trial of hormone therapy ever conducted in this age group. Statistical analyses of the WHI data did not indicate significant differences by age in the effect of estrogen and progesterone (E+P) on the risk of heart disease; in other words, younger WHI participants who took E+P were at no less risk nor were they more protected from heart disease compared to older participants. Another recent analysis of the WHI data on women who had undergone hysterectomy also found that estrogen alone did not provide significant cardiovascular protection in women aged 50-59.7 The American Heart Association and a National Institutes of Health Consensus Panel have both clearly stated that hormone therapy should NOT be used as a protective agent against cardiovascular disease. A health care practitioner who prescribes hormones as a protective measure against heart disease for younger women in their forties or fifties is making an irresponsible clinical decision without sufficient scientific evidence, and may actually be endangering the health of the patient. Clinical studies that are cited to support the “Window of Opportunity” theory are fairly short-term. Longer term follow up studies are necessary if studies are to have predictive value as to the relationship between HT and cardiac events to have more predictive value. The Women’s Health Initiative, the largest long term RCT to look into the effects of HT, did not find any statistically significant reduction in CHD risk among women who initiated HT earlier in their menopausal transition. Moreover, the risk of stroke was elevated among all women, regardless of at what point in their transition they initiated HT.8 In an attempt to separate fact from fiction, the “Window of Opportunity” hypothesis is now being tested in two ongoing clinical trials of hormone therapy in younger menopausal women: the KEEPS trial at the Kronos Longevity Institute and the ELITE trial at the University of Southern California. Both of these studies began enrolling participants in 2005; study results were expected in 2008 at the earliest, but there have been no reports of results so far.

Contact Us
The National Women’s Health Network is committed to ensuring that women have access to accurate, balanced information. For more information, email us at healthquestions@nwhn.org or call the Women’s Health Voice at (202) 682-2646. Stay informed, connect with us on Facebook and Twitter.

References
4. Manson, J, “Invited Commentary: Hormone Therapy and Risk of Coronary Heart Disease — Why renew the


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