

Hormone-Replacement Therapy: Could Estrogen Have Saved 50,000 Lives?

By [Alexandra Sifferlin @acsifferlin](#) July 20, 2013 16 Comments

For more than a decade, doctors have cautioned women about the risks associated with hormone-replacement therapy. But those warnings may have put one group of women at increased risk of dying early, according to the latest study.

Researchers at Yale University say nearly 50,000 women may have died prematurely after they stopped taking hormone-replacement therapy (HRT) to treat menopause symptoms, following a much publicized 2002 study that revealed the treatment increased risk of [heart disease](#) and [breast cancer](#).

The 2002 [Women's Health Initiative](#) (WHI) study, a 15-year investigation into the factors that contribute to the health of postmenopausal women, was [stopped](#) three years early when a preliminary review of the data showed that women taking the combination of [estrogen](#) and progestin had a higher rate of [breast cancer](#), [heart disease](#) and stroke than women taking a placebo. The results stunned both the public and the medical community, since doctors had been prescribing the hormones not just to treat menopausal symptoms like hot flashes, but for extended periods of time to protect women against heart disease.

Almost immediately, doctors and public-health officials began shifting women away from such long-term use of hormones, recommending that postmenopausal women restrict hormone use to the few months surrounding menopause to address the most intense symptoms. In 2012, the U.S. Preventive Services Task Force [confirmed](#) the WHI trial's findings, concluding after a review of 51 studies published since 2002 that the risks of HRT outweighed the benefits, which were limited to a reduced risk of fractures.

But the WHI scientists had always cautioned that their findings might not be broadly applicable to all women past menopause. They noted that the trial included women who were at least a decade beyond menopause, and that the participants used one specific formulation of HRT called Prempro, which is a combination of conjugated estrogens and a synthetic form of progesterone known as medroxyprogesterone acetate.

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The WHI also continued to evaluate women who had had a hysterectomy, and therefore could take estrogen alone; women with an intact uterus are not advised to take estrogen without the

protective effect of progesterone since estrogen is linked to a higher risk of uterine cancer. In 2007, the WHI reported that women with a hysterectomy who took estrogen alone had fewer calcium-based plaques in their arteries, and therefore may have enjoyed some protection against heart disease. This finding was supported by a 2011 [study](#) published in the *Journal of the American Medical Association (JAMA)* that found a slightly lower risk of breast cancer and no significantly increased risk of heart disease, blood clots, stroke or early death among women taking estrogen only compared with women with hysterectomies who took a placebo.

Based on those results, the Yale scientists decided to study this group of women further, to determine whether widespread coverage about the risks of HRT — the combination of estrogen and progestin — had persuaded these women to stop taking their estrogen-only therapy, and whether that decision impacted their mortality. Could women without a uterus benefit in some way from estrogen-only therapy, and were they putting their health at risk if they avoided the hormone therapy?

Their analysis, [published](#) in the *American Journal of Public Health*, confirmed their suspicions. Before the WHI study, about 90% of women who had a hysterectomy would have relied on estrogen therapy to replace what their reproductive system no longer produced. Following WHI, however, 10% of these women used the hormone, and based on a formula the researchers created to estimate their survival rates, they determined that 50,000 women died during the study period, between 2002 and 2011, prematurely. Dr. Philip Sarrel, professor emeritus of obstetrics, gynecology and reproductive sciences at Yale University School of Medicine and lead author of the study, said in a [video](#) discussing the study that none of these women, who were aged 50 to 59 at the start of the study, lived to reach their 70s. Most died of heart disease, bolstering the connection that earlier studies had found between estrogen-only therapy and a lower risk of heart problems among women who had a hysterectomy.

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The analysis highlights the challenges in crafting and distributing public-health messages so that they are interpreted correctly and applied to the right people. Following the surprisingly negative effects of HRT that WHI revealed, most in the medical community focused on warning women away from hormone therapy en masse, and the more nuanced message that some women might be able to continue taking estrogen alone became lost in that effort. “All we really knew [in 2002] was that this one kind of HRT used late in menopause resulted in a modest degree of harm,” says Dr. David Katz, the director of the Yale University Prevention Research Center and one of the authors of the new paper. “We developed a cultural aversion to HRT and unfortunately it was

shared by doctors and patients alike, and it extended to all women and all forms [of the hormones].”

Katz says it’s not just the media that is responsible for such overgeneralizing — research journals do it too. And he suspects that many patients probably never discussed the results of the 2002 study in depth with their doctors, to determine if the findings applied to them, heightening the perception that hormone therapy of any kind was not a good idea for any postmenopausal woman.

“We would like to think that physicians are a case apart, that we are always guided by high professional standards and meticulously reading the literature,” says Katz. “If that were the case, every doctor would’ve read the WHI study, every doctor would’ve read the 2011 study and we wouldn’t have this problem. But actually the practice of medicine is consumed in the prevailing current in our culture.”

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And as is the case with any scientific finding, not everyone in the medical community is convinced that the 50,000 women would have lived had they taken estrogen therapy. But most experts agree that the results should start a serious discussion about how to communicate public-health messages so they are applied to the right populations in the correct way.

“What makes it a challenge is that there is not a simple set of evidence. There is not one truth about estrogen,” says Andrea LaCroix, the co-project director of the Clinical Coordinating Center for the Women’s Health Initiative and author of the 2011 study. “Anytime something is less straightforward and more complicated, it’s difficult in a quick media sound bite to get the message across. We tried very hard when we published that data to show that the findings were different for different age groups of women. In terms of the challenge, I actually agree with these authors that there was a lot of media attention when the 2011 paper came out, but there was not a lot of discussion about translation for women afterwards.”

In that spirit, LaCroix says the Yale results should not necessarily drive all women who have had a hysterectomy to take estrogen pills. More research will need to tease apart how estrogen may or may not be contributing to premature death in these women. “I find it incredibly brash in a way and almost arrogant to recommend the use of a pill to prevent death in women when it is totally unproven to do that in women of any age group. If the results of this paper were true and has public-health significance, we would’ve seen deaths in U.S. women age 50 to 59 increase concomitant with the decline in estrogen use,” she says. “The death data exists, and it would be

important to do a study relating the decline in estrogen use to changes in mortality directly in our country.”

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In the meantime, women should be asking their doctors about hormone therapy, and whether any version of the treatment is right for them. These discussions that could clear up confusion over what the latest data shows about the risks and benefits of hormones. “The primary messenger for all messages ought to be the doctors to the patients,” says Dr. Georges Benjamin, executive director of the American Public Health Association. “The public hears a lot from trusted messengers that may not be knowledgeable.”

Read more: <http://healthland.time.com/2013/07/20/hormone-replacement-therapy-could-estrogen-have-saved-50000-lives/#ixzz2ahkeydDt>