

Center News

The value of WHI's combined hormone therapy trial, weighed in lives and dollars saved

The landmark study that prompted millions of women to stop taking combined hormone therapy resulted in \$37.1 billion net economic return, thousands of lives saved, a new study finds

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By Diane Mapes

In 2002, the Women's Health Initiative came out with a stunning – and decidedly unpopular – finding: combined hormone therapy (CHT) was not the fountain of youth it was touted to be. Yes, the daily hormone pills helped women combat hot flashes, bone loss and other symptoms of menopause, but at a cost. CHT significantly raised a woman's chances of [developing cardiovascular disease, stroke and breast cancer](#).

The landmark WHI estrogen + progestin study – led by National Heart, Lung and Blood Institute researcher Dr. Jacques Rossouw and Fred Hutch's [Dr. Garnet Anderson](#) and [Dr. Ross L. Prentice](#) -- made huge headlines, triggering a rapid decline in the use of the pill, protests from flummoxed doctors and frustrated patients and an ongoing debate regarding risk vs. benefits.

But what if there had been no WHI study? What kind of outcomes and costs would patients – and health insurers – have faced then?

Investigators at the Hutchinson Institute for Cancer Outcomes Research (HICOR) answered that question today with the release of a new study in the *Annals of Internal Medicine* on the economic impact of the WHI's combined hormone therapy trial.

"The economic return from the trial is substantial," lead author [Dr. Joshua Roth](#) announced Friday during a presentation at the annual WHI investigator conference. "The original NIH trial cost was \$260 million (in 2012 dollars) and the net economic return was \$37.1 billion. That's a return of approximately \$140 on every dollar invested in the trial."

And even more critically, the 2002 WHI study sparked a sea change with regard to women's health. The analysis projected that approximately 4.3 million fewer women used CHT which resulted in 126,000 fewer breast cancer cases, 76,000 fewer cases of cardiovascular disease (including coronary heart disease and stroke) and 80,000 fewer cases of venous thromboembolism (deep vein thrombosis or pulmonary embolism) in the decade following the trial.

But there were down sides to the drop in CHT use, too: the authors projected 263,000 more women suffered osteoporotic fractures and 15,000 more were diagnosed with colorectal cancer. However, the quality of life, mortality and cost impacts of these increases were more than offset by decreases in breast cancer, cardiovascular disease and VTE, Roth said.

All in all, these clinical effects translated into 145,000 additional "quality-adjusted life years" or QALYs, which Roth said is a health economic evaluation that measures "how long you live and how well you live."

A post-doctoral fellow at both Fred Hutch and Group Health Research Institute, Roth said he was surprised by just how many women were impacted by the landmark WHI trial.

"It really brings the point home when you crunch the numbers," he said. "You see that millions of U.S. women likely stopped or never used CHT and that this change resulted in important reductions in disease incidence and associated medical spending."

Anderson, co-author of the study, director of the Hutch's Public Health Sciences division and the current principal investigator of the WHI national coordinating center based at the Fred Hutch, called the new results "astonishing," adding that at the time of the WHI's E+P study more than 5 million women were on combined hormone therapy.

"Doctors were increasingly putting women on hormones from the time they became menopausal for the rest of their lives," she said. "That's what was happening before we started our study. They were trying to get women on hormones to prevent osteoporosis and heart disease."

From push to pushback

While pharmaceuticals weren't advertised on television during the 1980s and '90s when CHT was regularly prescribed, Anderson said hormones were pushed on menopausal women in countless other ways.

"There used to be full page ads in Parade magazine. There were celebrities pushing hormone therapy," she said. "There was a lot of direct-to-consumer marketing for hormones. The message was very clear that this was the way to go."

After the 2002 WHI study came out, that push turned into pushback -- both from menopausal women who were left in the lurch with no way to control their symptoms and from OB/GYNs, many of whom strongly believed women should be on hormones for the rest of their lives.



"There's been a lot of discussion about the cost of the trial which was one of the most expensive studies ever funded by the National Institutes of Health," said Roth of the economic pushback surrounding the study. "So we asked, given the large investment of the trial, what was the return?"

Envisioning a 'no WHI world'

To find out, Roth and his team used WHI findings, scientific literature and other data to determine disease incidence, survival, health-related quality of life and direct medical expenditures in the years following the WHI finding.

They then extrapolated a parallel universe where no WHI study was ever conducted and women continued to blithely use combined hormone therapy, not knowing they were upping their odds for cancer, stroke and heart disease.

Using a simulation model, they estimated the clinical and economic influence of the "no WHI world" with its thousands of additional cases of heart disease, breast cancer, stroke and related medical expenditures. Then they added up the costs and compared the two scenarios.

Of the \$37.1 billion in net economic return attributable to the WHI E+P trial, \$26.4 billion was attributable to medical expenditure savings, specifically the cost of CHT prescriptions and the cost of treating disease. The remaining \$10.7 billion represents the value of additional quality-adjusted life years resulting from lower incidence of breast cancer, cardiovascular disease, and venous thromboembolism (study authors applied the standard cost of a QALY -- \$100,000 -- to arrive at this amount).

"The major driver of value was reduced spending on combined hormone therapy prescriptions," said Roth.

The value of WHI

Fred Hutch's Dr. Scott Ramsey, coauthor of the study and director of HICOR, said the findings point to the value of large initiatives like WHI.

"It's important to consider the potential value of studies when making decisions about how to invest limited public research dollars," he said. "Many stakeholders have talked about the high cost of the WHI estrogen plus progestin trial, but few have considered the potential value of the trial. These findings show that the trial was a high-value use of public funds that provided a substantial return on investment."

Anderson, who worked on the original study, agreed.

"The motivation for the first WHI trial was to see if we could prevent heart disease, the No. 1 killer of women," she said. "That's why we did it. The economics never occurred to us. But these findings underscore the significant role clinical trials play in science and the importance of continuing to find ways to strategically invest public research funds to maximize value to society."

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Solid tumors, such as those of the breast, are the focus of Solid Tumor Translational Research, a network comprised of Fred Hutchinson Cancer Research Center, UW Medicine and Seattle Cancer Care Alliance. STTR is bridging laboratory sciences and patient care to provide the most precise treatment options for patients with solid tumor cancers.

Diane Mapes is a staff writer at Fred Hutchinson Cancer Research Center. She has also written extensively about health issues for nbcnews.com, TODAY.com, CNN.com, MSN.com, Columns and several other publications. She also writes the breast cancer blog, doublewhammied.com. Reach her at dmapes@fredhutch.org.



Fred Hutchinson Cancer Research Center
1100 Fairview Ave. N., PO Box 19024, Seattle, WA 98109
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