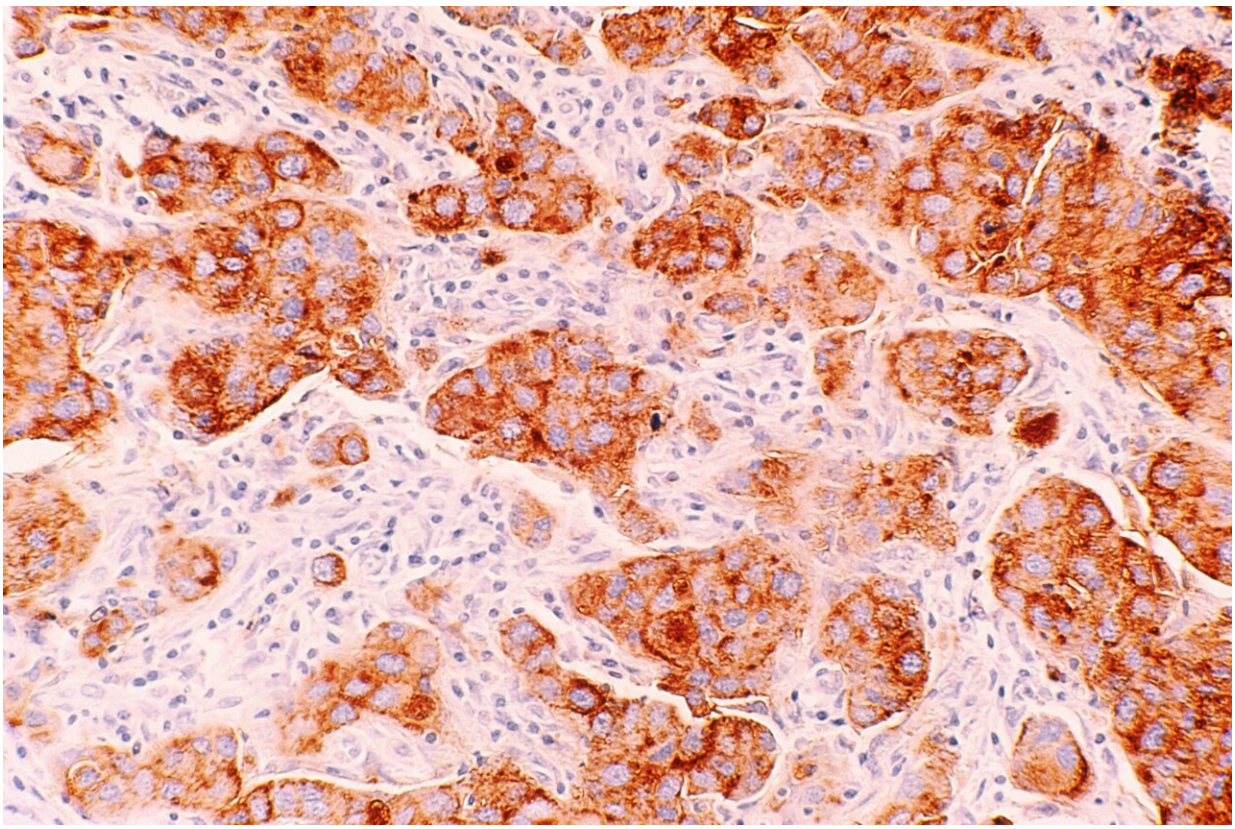
Women with elevated breast cancer risk could see mortality benefit from estrogen-blocking drugs

December 1 2022



Credit: Unsplash/CC0 Public Domain

While it has long been recognized that drugs that block the cancer-promoting activity of estrogen reduce risk of developing new breast

cancers, a new computer modeling study led by researchers at Georgetown Lombardi Comprehensive Cancer Center and colleagues shows that these treatments could also reduce the risk of dying from the disease in women who are at high risk.

The finding appeared December 1, 2022, in the *Journal of Clinical Oncology.*

"Recent studies have shown that women diagnosed with estrogen receptor (ER) positive tumors continue to experience breast cancer recurrence and death for as long as 30 years after their primary diagnosis," says Claudine Issacs, M.D., Leader of the Breast Cancer Program, medical director of the Fisher Center for Hereditary Cancer and Clinical Genomics Research at Georgetown Lombardi and one of the study's two senior authors.

She says this new evidence prompted researchers to reexamine the lifetime benefits and harms of risk-reducing medications developed for the primary prevention of breast cancer to see if the drugs could, over the long run, reduce the rate of death from the disease.

"Based on the available data, recommendations for preventing ER-positive breast cancer with tamoxifen or aromatase inhibitors presumed that women at elevated risk who took the drugs simply reduced their chances of developing the disease, but our modeling study found that over the long run, there could also be a significant impact on mortality," Isaacs says. "Giving an estrogen blocker to a woman in her 30s who is at high risk could potentially forestall death due to breast cancer for 20 years or more, which would be significant."

Over the past several decades, a number of large, federally-funded randomized clinical trials have shown that risk-reducing antiestrogen medications such as tamoxifen and aromatase inhibitors could decrease

the incidence of ER-positive breast cancer by 30 to 50 percent in women who are at high-risk of developing the disease. Despite evidence from these trials, the drugs have remained underutilized, perhaps due to the risk, albeit low, of endometrial cancer conferred by the drugs as well as other factors.

"What has been missing from our conversation until now is our ability to say to women that these drugs can not only prevent them from getting breast cancer but they can ultimately prevent them from dying of the disease," Isaacs says.

Studies have shown that chemoprevention drugs are most effective if taken for five years and not longer. This latest study shows that the impact on mortality could confer a long term and persistent benefit for a decade or more.

The study used computer models developed by the Cancer Intervention and Surveillance Modeling Network (CISNET), a National Cancer Institute sponsored consortium, to determine the lifetime benefits and harms of estrogen blockers for women with a five-year risk of developing breast cancer equal to or greater than three percent. The researchers evaluated the effects of estrogen blockers along with annual screening mammograms (and magnetic resonance imaging, or MRI, if necessary) to calculate the risk of invasive breast cancer, breast cancer death, side-effects, false positives and chances of overdiagnosis.

Tamoxifen, and the use of annual mammography (and MRIs, if necessary), reduced the risk of developing new invasive breast cancers by 40% and reduced the risk of breast cancer deaths by 57%. This translates to 95 fewer invasive breast cancers and 42 fewer breast cancer deaths per 1,000 women compared to women who didn't get a mammogram, an MRI, or risk-reducing drugs. The scientists noted that the drugs were not without downsides, as tamoxifen could increase the

number of new endometrial cancers by up to 11 per 1,000 women.

"The Institute of Medicine [now the National Academy of Medicine] suggests that modeling approaches such as ours are going to provide the most definitive answers about the value of these drugs because, given size and cost considerations, a clinical trial would be impractical, even putting aside the fact that evidence of benefit from a clinical trial would take close to 20 years to accrue," says Isaacs.

More information: Reassessing the Benefits and Harms of Risk-Reducing Medication Considering the Persistent Risk of Breast Cancer Mortality in Estrogen Receptor Positive Breast Cancer: A Simulation Modeling Study, *Journal of Clinical Oncology* (2022). DOI: 10.1200/JCO.22.01342

Provided by Georgetown University Medical Center