

New tools needed to identify men and women at risk for the most aggressive cancers

Twenty years of screening for breast and prostate cancer - the most diagnosed cancer for women and men - have not brought the anticipated decline in deaths from these diseases, argue experts from the University of California, San Francisco and the University of Texas Health Science Centre at San Antonio in an opinion piece published in the *Journal of the American Medical Association*.

Instead, overall cancer rates are higher, many more patients are being treated, and the incidence of aggressive or later-stage disease has not been significantly decreased, the authors conclude. Current screening programs are leading to "potential tumour over-detection and over-treatment," they write in the Oct. 21, 2009 issue of *JAMA*.

"Screening does provide some benefit, but the problem is that the benefit is not nearly as much as we hoped and comes at the cost of over-diagnosis and over-treatment," said Laura Esserman, MD, MBA, professor of surgery and radiology, director of the UCSF Carol Franc Buck Breast Care Centre, and co-leader of the breast oncology program at the UCSF Helen Diller Family Comprehensive Cancer Centre.

Screening is not perfect

"We need to focus on developing new tools to identify men and women at risk for the most aggressive cancers, to identify at the time of diagnosis those who have indolent or 'idle' tumours that are not life-threatening," she added. "If we can identify groups of patients that don't need much treatment, or don't need to be screened, wouldn't that be great? Screening is by no means perfect. We should want to make it better. For both breast and prostate cancer we need to invest in changing our focus from the cancers that won't kill people to the ones that do."

Breast cancer, the most common cancer in women, is a devastating and costly disease, striking more than 200,000 women annually and killing more than 40,000 women each year, reports the American Cancer Society. Prostate cancer is the most common form of cancer in men and the second most common cause of cancer death after lung cancer. This year, an estimated 192,280 men will be diagnosed with the disease and 27,360 men will die from it, according to estimates from the American Cancer Society.

The two diseases account for 26% of all cancers in the U.S., with an estimated 386,560 patients diagnosed annually.

Significant increase in detection

Because of remarkable survival rates when the diseases are treated before they spread, screening for both cancers has been promoted on the assumption that early detection and treatment is the best way to reduce deaths. In turn, much of the U.S. population undergoes routine screening for the cancers: About half of at-risk men have a routine prostate-specific antigen test and 75% have previously had a PSA test, and about 70% of women older than 40 report having had a recent mammogram. More than \$20 billion is spent annually screening for the two diseases in the U.S.

The screenings have resulted in a "significant increase" in early cancers being detected, according to the article authors. Because of PSA testing, the chances of a man being diagnosed with prostate cancer have nearly doubled: In 1980, a white man's lifetime risk of the cancer was 1 in 11; today it is 1 in 6. Similarly, a woman's lifetime risk of breast cancer was 1 in 12 in 1980; today it is 1 in 8. And, if ductal carcinoma in situ is included, the risk of being diagnosed with breast cancer, like prostate cancer, has nearly doubled as well.

But the authors found that while deaths have dropped for both cancers over the last 20 years, "the contribution from screening is uncertain." They also found that many patients are undergoing treatment for cancers that actually pose minimal risk.

Screening increases detection of slow-growing and indolent cancers

A comparison of prostate cancer incidence rates in the U.S. to the United Kingdom, where PSA screening has not been widely adopted, "did not result in significant differences in mortality," the authors write. For breast cancer the relative reduction in deaths from screening has also been limited.

The authors said that breast cancer and prostate cancer screening has not led to a more significant drop in deaths in the U.S. for two primary reasons: Screening increases the detection of slow growing and indolent tumours, and it often misses the most aggressive cancers because many may not be detected early enough for cure.

"In other words, tumour biology dictates and trumps stage, so the basic assumption of these screening programs that finding and treating early stage disease will prevent late stage or metastatic disease may not always be correct," they state.

Periodic screening may find some tumours early, but patients may not be screened often enough for lethal tumours to be detected in time to prevent death, the authors conclude: "Without the ability to distinguish cancers that pose minimal risk from those posing substantial risk and with highly sensitive screening tests, there is an increased risk that the population will be over-treated."

Screening is not the b-all and end-all

"People will think that we're saying screening is bad, and nothing could be further from the truth," said Ian Thompson, MD, who has authored about 400 scientific articles addressing prevention, early detection, and treatment for prostate, kidney, and bladder cancers. "What we are saying is that if you want to stop suffering and death from these diseases, you can't rely on screening alone."

"The basic assumption that screening programs that find and treat early stage disease will then prevent late stage disease, or prevent cancer from spreading, may not always be correct," added Thompson. "If a tumour is aggressive, finding it early may not prevent death."

Thompson is professor and chairman of the Department of Urology and holds the Glenda and Gary Wood Distinguished Chair in Genitourinary Oncology at the Cancer Therapy & Research Centre at the UT Health Science Centre at San Antonio and the Henry B. and the Edna Smith Dielmann Memorial Chair in Urologic Science at the UT Health Science Centre. He led the Prostate Cancer Prevention Trial, a study of 18,882 men from around the U.S. that demonstrated that the drug finasteride reduces a man's risk of prostate cancer by 24.8%.

In contrast to breast and prostate cancer, screening for cervical and colon cancer -- and the removal of

abnormal tissue - has led to a significant drop in invasive cancer. Screening is "most successful when pre-malignant lesions can be detected and eliminated" such as during colonoscopies, said the authors.

The authors suggest that to improve screening, "a new focus is recommended for research and care to identify markers that discriminate minimal-risk from high-risk disease (and) identify less aggressive interventions for minimal-risk disease to reduce treatment burden for patients and society."

Four recommendations

The authors list four recommendations in their call to action for early detection and prevention:

1. Develop tests to distinguish between cancers that are lethal and those that are low-risk.
2. Reduce treatment for low-risk disease. Diagnosing cancers that don't kill the patient has led to treatments that may do more harm than good.
3. Develop tools for physicians and patients to help them make informed decisions about prevention, screening, biopsy and treatment. Offer treatments individually tailored to a patient's tumour.
4. Work to identify the people at highest risk for cancer and use proven preventive interventions.

"Over the years we have worked hard to find new treatments and new ways of finding disease and many of these interventions when appropriately assessed have saved lives," said Otis W. Brawley, MD, chief medical officer of the American Cancer Society, and professor of hematology, oncology and epidemiology at Emory University.

"It is very appropriate that we occasionally step back, assess and reflect on what we in medicine are doing he added. "In the case of some screening for some cancers, modern medicine has overpromised. Some of our successes are not as significant as first thought. Cancer is a complicated disease and too often we have tried to simplify it and simplify messages about it, to the point that we do harm to those we want to help."

Yiwey Shieh, a medical student at the UCSF Medical School and former research assistant with Esserman is also a co-author of the article.

Source: University of California - San Francisco

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