

# PSA Tests Cut Metastatic Prostate Cancer Rate by 50%

Alexander M. Castellino, PhD | October 28, 2015

Screening for early cancer detection may reduce the rate of related metastatic disease, but not always. In a perspective published today in the *New England Journal of Medicine*, the authors describe trends in metastatic breast cancer and prostate cancer prior to and more than a decade after the widespread use of mammography — a radiographic test — and prostate-specific antigen (PSA) testing — a blood test.

The trends are startlingly different. The incidence of metastatic prostate cancer fell by approximately 50% within 7 years of the start of widespread PSA use in 1990; however, rates of metastatic breast cancer remained remarkably stable following the initiation of widespread mammography screening in women from 1985 to the current day.

Median age at diagnosis reflects the differences in the observed trends, say the authors, led by H. Gilbert Welch, MD, of the Dartmouth Institute for Health Policy and Clinical Practice, in Lebanon, New Hampshire.

For individuals aged 40 years and older, the median age at diagnosis has fallen from 71.8 years to 69.8 years for advanced prostate cancer — a difference of 2 years. But for patients with metastatic breast cancer, the median age at diagnosis, 63.7 years, has not changed.

Dr Welch and colleagues looked at the incidence of metastatic disease for breast and prostate cancer using the Surveillance, Epidemiology, and End Results (SEER) Program database for incidence of initial diagnoses of metastatic disease, not early-stage disease that progressed to metastasis.

They say that their findings are instructive about how variability in cancer dynamics — in this case, the difference between prostate cancer and breast cancer — may influence the impact of screening and how different screening strategies — in this case, a test that searches for an anatomic abnormality and one that seeks a systemic tumor marker — may also influence screening outcomes.

## How PSA Testing Reduces Incidence of Metastatic Prostate Cancer

Dr Welch and colleagues indicate that "the rapid uptake of PSA screening led to a dramatic spike in overall prostate cancer diagnoses during the early 1990s — one that's unrivaled in US cancer data."

Although the authors speculate that interventions to reduce prostate cancer risk or reductions in environmental carcinogens might contribute to a reduction in the incidence of prostate cancer, they believe that "it's hard to imagine another factor [other than PSA screening] changing and exerting an effect so quickly."

Prostate cancer expert Anthony V. D'Amico, MD, PhD, of the Brigham and Women's Hospital and Dana Farber Cancer Institute, Boston, who was not involved with the new essay, agreed.

"The initial spike in all prostate cancer incidence following PSA screening was due to the test identifying all the undiagnosed clinically occult disease missed on digital rectal examination," he told *Medscape Medical News*.

"Earlier detection of prostate cancer means that diagnosis of metastatic disease at presentation is less likely to occur," Dr D'Amico said.

This is a result of the dynamics of most prostate cancer, he suggested.

"Because prostate cancer is generally a slow-growing disease, picking it up early through annual PSA screening

would be expected to reduce the occurrence of late-stage [ie, metastatic] disease," he said.

Thus, much of prostate cancer appears to fit the "Halsteadian paradigm" of cancer development — a dynamic in which a "cancer arises at a single location, grows there, and eventually migrates to local lymph nodes and then to more distant organs," write Dr Welch and colleagues.

However, the authors also believe that in some men, microscopic metastasis may develop early in the disease course, making it a systemic disease — known as the Fisher paradigm.

In any case, Dr D'Amico said that the latest recommendation against PSA screening by the United States Preventive Services Task Force is likely to reverse this trend in the incidence of metastatic disease.

"With the current recommendation by the Task Force against PSA screening, we are likely to see a rebound to more high-risk nonmetastatic and metastatic disease at presentation," he predicted.

"We will not see this for another 7 years, but expect death rates to incline in 7 years, given that the survival curves from the European Randomized Study of Screening for Prostate Cancer and Göteborg PSA-based screening studies started to separate in favor of PSA screening approximately 7 years following randomization to PSA screening vs usual care," Dr D'Amico continued.

Nancy Lynn Keating, MD, MPH, professor of healthcare policy and medicine at Harvard University and physician at the Brigham and Women's Hospital, Boston, who also was not involved with the new essay, provided a different view.

"Even though PSA is associated with decreases in the incidence of metastatic prostate cancer, studies of PSA screening have been disappointing, suggesting a very modest improvement in prostate cancer mortality with substantial overdiagnosis and overtreatment," she told *Medscape Medical News*.

Dr D'Amico responded: "Fortunately, with the increase in the use of active surveillance in appropriate men with low-risk prostate cancer, overtreatment is being reduced. Moreover, with the advent of multiparametric magnetic resonance imaging, the opportunity to diagnose and target high-grade prostate cancer is expected to reduce the feared risk of underdiagnosing or surveying occult high-grade and potentially lethal prostate cancer."

Dr D'Amico also indicated that in 1997, following the publication of a practice-changing study, the adoption of the earlier use of hormonal therapy for nonmetastatic but high-risk prostate cancer also likely contributed to the decline in mortality and occurrence of distant metastatic disease following treatment.

"The importance of earlier detection and earlier hormonal therapy use is responsible not only for the decline in developing metastatic disease but also in mortality," he said.

Although screening is expected to reduce prostate cancer mortality, it does not decline proportionately, according to Dr Welch and colleagues. In one study, the decline in mortality was 20%, whereas the decline in the incidence of metastatic disease was almost 50%.

### **Why Metastatic Breast Cancer Rates Are Still the Same Despite Mammography**

The authors explain why the metastatic disease trend seen with prostate cancer did not occur with breast cancer. Breast cancer is a systemic disease — conforming to the Fisher paradigm — and screening mammography is unable to detect disease at an earlier stage for cancers destined to become metastatic, they say.

"Breast cancer has shown no clear declines in the incidence of metastatic breast cancer in the mammography era

and is consistent with the Fisher paradigm of advanced disease," Dr Keating concurred.

Dr Keating agreed with Dr Welch and colleagues that the inherent differences in screening tests for breast and prostate cancer may likely explain the discordance between the paradigms they have chosen to highlight.

Mammography looks for structural abnormalities, whereas PSA is a biochemical assay that detects a tumor marker, Dr Welch and colleagues indicate.

"Were a similar breast-cancer assay discovered — and a similar organ-wide sampling strategy used (the typical prostate biopsy now involves at least 12 needle cores throughout the organ) — then perhaps fewer women would present with metastatic breast cancer," Dr Welch and colleagues write.

When asked whether the new guidelines for screening mammography will have an impact on the future incidence of metastatic breast cancer, Dr Keating said: "I don't expect the new recommendations to change the incidence of metastatic breast cancer; the incidence has remained steady despite no mammography, increasing use of mammography (including periods where mammography was recommended yearly starting at age 40), and in recent years."

*Dr Welch has financial ties with Beacon Press, which publishes his books, including one on overdiagnosis of disease. Dr D'Amico and Dr Keating report no relevant financial relationships.*

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