Rates of Advanced Prostate Cancer Continue to Increase

The US Preventive Services Task Force (USPSTF) has recommended against prostate-specific antigen–based (PSA) screening studies, first in 2008 for men aged 75 years and older and then in 2012 for all men. Recent studies have reported a shift in US prostate cancer incidence rates when stratified by stage of disease beginning in 2008, with rates increasing for regional-stage and distant-stage disease and declining for local-stage disease.

A new study by American Cancer Society (ACS) researchers led by Ahmedin Jemal, DVM, PhD, scientific vice president of surveillance and health services research, has examined whether those trends continued through 2016, which could suggest a longer-lasting impact. “We wanted to know if this previous observation was a short-term bump or if it persisted over the longer term,” says study-co-author, Stacey Fedewa, PhD, an epidemiologist and senior principal scientist in the ACS’s surveillance and health services research program.

Their article in the *Journal of the National Cancer Institute* (published online May 20, 2020. doi:10.1093/jnci/djaa068) confirmed increased rates of regional-stage and distant-stage prostate cancer in men aged 50 years and older residing in the United States, along with fewer cases of early-stage disease, during the 5 years after the USPSTF’s 2012 decision.

**Study Details**

Dr. Jemal and his colleagues, including Dr. Fedewa, used data from the US Cancer Statistics Public Use Research Database to study prostate cancer incidence from 2005 to 2016 in men aged 50 years and older. The men were examined with regard to cancer stage (local, regional, and distant) and stratified by age (age 50-74 years and age 75 years and older) as well as race and ethnicity to determine the annual percentage change in rates of invasive prostate cancer.

The researchers could not study incidence rates after 2018, when the USPSTF again revised its guidelines to include screening as an option for men aged 55 to 69 years and recommended against screening for men aged 70 years and older, because registry data for that time frame were not yet available.

**Study Results**

Of all US prostate cancer cases diagnosed among men aged 50 years and older during the study period, approximately 86.8% were of local stage, 1.5% were of regional stage, and 5.1% were of distant stage. The incidence rates for local-stage prostate cancer decreased by an average of 6.4% for men aged 50 to 74 years each year from 2007 to 2016. For men aged 75 years and older, the incidence declined by an average of 10.7% per year from 2007 to 2013. In addition, the investigators reported that regional-stage and distant-stage cancers increased by 6%. Although the increase was steepest among non-Hispanic White men, it remains twice as high among Black men aged 50 to 74 years as in White men in that age group.
distant-stage disease increased in both age groups during the study period.

Dr. Jemal, Dr. Fedewa, and their colleagues also reported that:

- The incidence of distant-stage disease increased by an average of 2.4% per year from 2008 to 2012.
- From 2012 to 2016, the incidence of distant-stage disease increased by an average of 5.6% per year in men aged 50 to 74 years and by 5.2% per year from 2010 through 2016 in men aged 75 years and older.

There was a significant decrease noted between the 2 periods investigated (2005-2006 and 2015-2016) with regard to the incidence disparity for distant disease between non-Hispanic Black and non-Hispanic White men aged 50 to 74 years. Researchers say that this coincides with a steeper increase in the incidence of distant-stage disease among non-Hispanic White men. They also note that the incidence of distant-stage disease in non-Hispanic Black men remains much higher than that in non-Hispanic White men among those aged 50 to 74 years and those aged 75 years and older. The factors contributing to these racial disparities were not clear but could be related to lifestyle, biological susceptibility, and a lack of the availability of medical care. Dr. Fedewa says there is a focus on non-Hispanic Black men because of their greater burden of disease, and estimates for some racial/ethnic groups were unstable due to sparse data.

According to Dr. Fedewa, it is important to note that the previously reported increases in distant-stage prostate cancer continued through 2016. “Specifically, distant-staged disease increased by 5% per year between 2010 and 2015 and regional-stage disease increased by 11% per year between the years 2012 to 2016,” she says. “We also found that localized prostate cancer incidence has declined by about 7% per year between 2007 and 2016.” Despite these patterns, Dr. Fedewa says most men still are diagnosed at an early stage.

The ACS investigators computed absolute numbers because they can be helpful for cancer control efforts, Dr. Fedewa says. She notes that in 2016, a total of 3590 more men were diagnosed with distant-stage disease than would have been observed had the incidence rates for distant stage remained at the lower 2008 level. There were 115,438 fewer men diagnosed with localized prostate cancer in 2016 than would have been observed had the incidence rate for local-stage disease remained at its peak.

Dr. Fedewa says the takeaway message from the study should be that increases in the incidence of regional-stage and distant-stage prostate cancer have endured over the past 5 years, whereas those for localized disease have declined. Moreover, she believes the results of the study could help to inform clinical approaches and attitudes. “Our research, along with other studies on what occurs after prostate cancer patients are diagnosed—specifically how they are treated, their outcomes, and side effects—can inform guidelines and the balance of benefits versus risks of routine PSA screening across the population,” she says.

Andrew Julian Vickers, PhD, a biostatistician and attending research methodologist at Memorial Sloan Kettering Cancer Center in New York City, says that in terms of breaking new ground, this study is not unique. “Others have also reported increased incidence of metastasis for late-stage prostate disease,” he says. “However, Dr. Jemal’s group at ACS is the gold standard, so you can rest assured that what they have reported is what is actually happening in the US.”

Dr. Vickers notes that the ACS researchers do not attribute the incidence trends to the changes in guidelines. “They don’t come out and say that the recommendations from USPSTF have caused these results,” he says. “Of course it’s very difficult to disentangle whether it was the USPSTF or was it just people generally being more skeptical about PSA screening or the results of the PLCO trial (the Prostate, Lung, Colorectal and Ovarian [PLCO] Cancer Screening Trial), which was a very flawed trial. So there are probably a number of contributing factors. Nonetheless, people seemed to take the [USPSTF] recommendations at face value and said ‘screening doesn’t work, so let’s not do it.’”

Based on his perspective as a statistician, Dr. Vickers emphasizes that clinicians should not think of PSA testing as “...a single intervention...that can only be given in one way, and so the harms and benefits are a sort of take-it-or-leave-it.”

“We can screen in a variety of different ways, and how we screen affects the ratio of harms to benefits,” he says. “We can dramatically reduce the harms of PSA screening—overdiagnosis and overtreatment—by drastically limiting screening in men over 70, avoiding routine biopsy in men with elevated PSA but restricting biopsy to those men shown to be at high risk of aggressive disease by a secondary test such as a blood or urine marker (there are several now available) or MRI [magnetic resonance imaging], and putting almost all men with low-risk disease on active surveillance rather than subjecting them to treatment. Indeed, it is straightforward to show that overdiagnosis and overtreatment could be
reduced by 70% or more by putting in place well-established knowledge.”

Furthermore, Dr. Fedewa says that although the USPSTF modified its recommendation in 2018 toward individual decision making for men aged 55 to 69 years and said men aged 70 years and older should not be screened, continued research regarding how this decision impacted PSA testing, shared decision making, and prostate cancer incidence and outcomes is needed. “The American Cancer Society guidelines have also recommended shared or individual decision making for PSA testing since 1997, though other studies we’ve conducted suggest most men have not had this discussion with their physician.”

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