Analysis: Major Prostate Cancer Screening Trials Agree on Mortality Reduction

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Thursday, September 7, 2017

Prostate Cancer (/prostate-cancer)

Genitourinary Cancers (/genitourinary-cancers) Screening (/screening)

An analysis that corrected for differences in implementation found that the two main trials of prostate cancer screening in Europe and the United States both show a reduction in prostate cancer mortality with screening. In the study's primary analysis, the European trial found a reduction, while the US trial did not.

The US.Preventive Services Task Force (USPSTF) determined in 2012 that there is "very low probability of preventing a death from prostate cancer in the long term" using PSA screening. "Since then, rates of PSA screening and prostate cancer incidence have decreased significantly in the United States," wrote study authors led by Alex Tsodikov, PhD, of the University of Michigan in Ann Arbor.

That recommendation relied on results of the European Randomized Study of Screening for Prostate Cancer (ERSPC) and of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO). The former found a reduction in prostate cancer mortality, while the latter did not. However, they used slightly different screening programs, including a shorter screening interval in the PLCO (1 year vs every 2 to 4 years) and a higher PSA threshold for biopsy referral.

To reconcile those differences, investigators conducted an analysis of the trials using a method known as mean lead times (MLTs). This is generally defined as the average time by which a diagnosis is advanced with screening, relative to the date of diagnosis without any screening. For this study, they restricted that analysis to a certain follow-up period (11 years). The results were published (http://annals.org/aim/article/doi/10.7326/M16-2586) online ahead of print in *Annals of Internal Medicine.*

The analysis included 72,473 screening patients in the ERSPC, and 88,921 control patients; and 38,340 screening patients in the PLCO, and 38,343 control patients. The intervention groups in the two trials had similar MLTs, but the PLCO control patients had longer MLTs, reflecting "contamination" due to a more intensive screening setting.

An extended analysis that accounted for MLTs found no evidence for different effects of screening on mortality between the trials (*P* for interaction = .37 to .47 [range across estimation approaches]). A longer MLT was significantly associated with a lower risk for prostate cancer death.

Each year of MLT was associated with a 7% to 9% reduction in the risk of prostate cancer death. Over the full 11 years of follow-up, this would translate to a reduction in the expected risk for prostate cancer death of 25% to 31% in the ERSPC setting, and 27% to 32% in the PLCO setting.

In an accompanying editorial (http://annals.org/aim/article/doi/10.7326/M17-2012), Andrew J. Vickers, PhD, of Memorial Sloan Kettering Cancer Center in New York, wrote that this study should "finally put to rest" the question of whether screening with PSA testing actually reduces prostate cancer mortality. This does not, however, suggest that debate over best screening practices is over.

"PSA-based screening does reduce prostate cancer mortality, but whether this benefit outweighs the harms of overdiagnosis and overtreatment depends on how screening is implemented," he wrote. "Unfortunately, the way screening has been implemented in the United States leaves much to be desired." He suggested several changes to screening practices, including avoiding screening in older men who are unlikely to derive benefit from it, restricting biopsy to those who screen positive and are at high risk for aggressive disease, among other ideas.

"The controversy about PSA-based screening should no longer be whether it can do good but whether we can change our behavior so that it does more good than harm," he wrote.