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## Prostate Cancer Incidence and Screening

Cancer of the prostate is the most common cancer among American men and the second leading cause of cancer deaths in men, according to the American Cancer Society. While PSA screening is widely used for the early detection of prostate cancer, it is also associated with a high rate of overdiagnosis, which can lead to unnecessary treatment and anxiety.



Andrew Vickers, Research methodologist and study author

(Overdiagnosis is commonly characterized as the diagnosis of a disease or condition that will never cause symptoms or death during a person's lifetime.)

Compared to other common cancers, tumors in the prostate typically grow very slowly and, in most cases, do not lead to death. In general, a man's lifetime risk of death from prostate cancer is approximately 3 percent. However, for men with an aggressive form of the disease, early diagnosis and treatment is essential and physicians do not yet have a way to accurately distinguish between early-stage prostate tumors that will become aggressive — and potentially deadly — and those that will cause no harm.

Despite recommendations that men between ages 50 and 70 get an annual PSA tests, only about half of US men do so.

"We felt that if we were able to predict which men were at higher risk of getting an aggressive prostate cancer and then focused screening on those men, we could shift the balance of harms and benefits associated with screening," says lead author and Memorial Sloan Kettering research methodologist <a href="Andrew Vickers">Andrew Vickers</a>, <a href="PhD">PhD</a>. "We also thought that men who were told that they were at high risk would be much more likely to return for screening."

Back to top ^

## A 'Natural Experiment'

The study, also led by Memorial Sloan Kettering clinical chemist Hans Lilja, MD, PhD, was conducted in collaboration with investigators from Lund University, in Sweden, and was published in the September 14 online issue of the *British Medical Journal* [PubMed Abstract]. It analyzed the PSA levels in blood samples from nearly 1,200 Swedish men who had given blood as part of a 1981-82 cardiovascular study. The men were all 60 years old at the time of testing and were followed until either the age of 85 or their death.

"Our study is a sort of 'natural experiment' for establishing links between PSA and long-term risk of prostate cancer," notes Dr. Vickers.

During the 25 years of follow-up, a total of 126 men received a diagnosis of prostate cancer. Of these, 35 died of the disease. Researchers wondered if

these outcomes could have been predicted by prior PSA concentrations.

As it turned out, PSA levels were a highly accurate predictor of long-term risk. For example, investigators found that men with a PSA of 2 nanograms per milliliter (ng/ml) or higher were on average 27 times more likely to die from prostate cancer than those with concentrations below 2 ng/ml.

However, says Dr. Vickers, "if a man is close to 60 years of age and has a PSA level of 1 nanogram per milliliter or less, he can be reassured that he is at very low risk of getting an aggressive prostate cancer and, consequently, does not need to continue with screening."

The study found that some men in this low-risk category may in fact have prostate cancer, although it would be a non-aggressive form of the disease that is not likely to produce symptoms or shorten their lives by the age of 85.

Conversely, Drs. Vickers and Lilja found that those in the top quarter of PSA values — the equivalent of a PSA of 2 ng/ml or greater — represented 90 percent of the prostate cancer deaths that occurred over the next 25 years.

"These men need to be told that they are at high risk of getting a prostate cancer that could kill them and really do need to come back for regular screening," adds Dr. Vickers.

Back to top ^

## The Future of Predicting Prostate Cancer

According to the researchers, the study's results could have important clinical implications, helping to determine which men should be screened after the age of 60 and which men may not benefit substantially from continued prostate cancer screening. "It is our ability to determine the risk of the really aggressive cancers that makes this approach of such great potential value," Dr. Vickers explains.

But Dr. Vickers and his colleagues note that more research is needed to confirm and refine the findings. Questions remain, including what to do before men reach the age of 60. Could an earlier baseline PSA screening value determine who should and should not continue to be screened?

"We are conducting a similar analysis on men at age 50," Dr. Vickers reports, "to see whether an even earlier PSA test can predict the risk of prostate cancer death."

Back to top ^



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