Newsletter

Prostate Cancer 101, Inc.

http://prostatecancer101.org

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The Prostate Cancer Information and Support Group of the Mid-Hudson

All you need to know about the PCA3 test

Prostate cancer is a common cancer among males. There are often no symptoms in the early stages, but screening can help people detect prostate cancer while it is still treatable.

Screening tests look for markers. These are unusual levels of proteins and other substances that can indicate that cancer is present.
Current tests include the prostate-specific antigen (PSA) blood test, which tests for high levels of the PSA protein. However, this can sometimes produce a false-positive result, suggesting that prostate cancer is present when it is not. This may lead to anxiety and unnecessary further testing.

Prostate cancer is the second most common cancer among males in the United States, after skin cancer. In fact, according to the American Cancer Society (ACS), 1 in 9 men will receive a diagnosis of prostate cancer during their lifetime.

Effective treatment is available in most cases. Those who receive a diagnosis in the early stages are almost certain to survive for at least another 5 years.

For this reason, scientists have been looking for other reliable markers to screen for. Testing for a substance called prostate cancer antigen 3 (PCA3) may be one solution.

Trade names for this test include Progensa and GenProbe.

Problems with current screening methods

A PSA blood test looks for high levels of the PSA protein.
The ACS advise that males with an average risk of prostate cancer should start screening from the age of 50. Those with a higher risk should start earlier.

Currently, the standard way of screening for prostate cancer is with the PSA blood test. Experts do not recommend the digital rectal exam (DRE).

High PSA levels can indicate prostate cancer, but they can also indicate other conditions. This is because both cancerous and noncancerous cells in the prostate gland can produce PSA.
Other factors that can affect PSA levels include:

- age, as higher levels are more common among older adults
- having a large prostate gland
- having an enlarged prostate, or benign prostatic hyperplasia
- inflammation or infection, such as prostatitis or a urinary tract infection
- stimulation of the prostate, which can happen during a DRE
- medications, some of which increase PSA levels and some of which reduce them

If a test shows that PSA levels are high, the doctor will likely recommend a biopsy to test for cancer. This is an

invasive procedure, and it can lead to anxiety, discomfort, and possibly complications.

In a 2018 statement of recommendations, the U.S. Preventive Services Task Force (USPSTF) noted that routine PSA testing may over diagnose prostate cancer by 20–50%. They expressed concerns about the physical and emotional risks of receiving a false-positive result, which can lead to unnecessary biopsies and even treatment.

The statement concluded that although PSA testing may save lives, the choice to attend screening should be a personal one. The authors urge males ages 55–69 years to make the decision after talking to their doctor.

The USPSTF do not recommend PSA screening for men aged 70 or above.

Also, experts disagree on what "normal" PSA levels should be. One 2004 study, for example, found that doctors had diagnosed some high grade prostate cancers in males with normal PSA levels.

Finally, the studies that researchers used to work out the typical PSA range mostly involved white males.

According to the National Cancer Institute (NCI), "There is no clear consensus regarding the optimal PSA threshold for recommending a prostate biopsy for men of any racial or ethnic group."

A PCA3 test may help a doctor decide whether or not to perform a biopsy on a person with high PSA levels.

What happens during a prostate biopsy? Find out here.

What is a PCA3 test?

The PCA3 test may provide more accurate results than other screening methods.
The PCA3 test may be one way to obtain more accurate results when screening for prostate cancer.
PCA3 is a gene that exists in all prostate gland cells. It causes these cells to make small amounts of certain proteins. It is also present in urine.

Prostate cells that are cancerous can make 60–100 times more of this protein than noncancerous cells. When this happens, the extra proteins will eventually leak into the urine.

If tests detect this protein in the urine, it can signal that prostate cancer is present.
Initial studies showed that these proteins were present in around 95% of prostate cancer samples. They were also more likely to be present in high levels in cancerous tissue, compared with benign tissue. In other words, a person who does not have cancer is unlikely to have significant amounts of this protein.

The PCA3 test may therefore be helpful when PSA test results are abnormal.
Examples of such results include:

- having a high PSA level but a negative biopsy
- having cancer despite also having low PSA levels

having a high PSA level as well as prostatitis

The advantage of the PCA3 test is that noncancerous conditions do not affect PCA3 levels. High levels of PSA may indicate cancer, but they can also result from other factors — ranging from older age to an infection.
The authors of a 2015 study involving 407 men concluded that the PCA3 test could be useful as both a diagnostic tool and in working out the prognosis for prostate cancer. They found that it was more likely to indicate prostate cancer than two types of PSA test.

In addition, people with more aggressive tumors tended to have a higher PCA3 score.
The Gleason score is one way of describing the grade of cancer cells. Learn more here.

What to expect during a PCA3 test

No special preparations are necessary before undergoing a PCA3 test, but knowing what to expect can help put a person at ease.
If a doctor offers a PCA3 test, people should check whether their insurance covers it before going ahead.

The procedure

A urine test is one part of the PCA3 test.
A PCA3 test has two parts:

Rectal examination: First, a health professional will carry out a rectal examination. As well as feeling for lumps or other changes, they may also massage the prostate. This will encourage more PCA3 proteins to enter the urine before the next part of the test.

Urine test: Immediately after this, the person will provide a urine sample that the doctor will send to a laboratory for analysis.
The results should be available within a few days.

After the test

After receiving the results of a PCA3 test, a discussion about the next steps will take place.
Depending on the results, the doctor may recommend:

- continuing with routine screening, if the result is negative
- taking a "watch and wait" approach, with testing at intervals, to see if the results change further testing, to confirm if cancer cells are present

Additional testing may include:

- a biopsy, which means removing a few cells for testing in a laboratory
- a transrectal ultrasound of the prostate cell

an MRI scan of the prostate gland, to look for growths

Outlook

The PCA3 test is not currently a standard test for prostate cancer. Instead, a urologist might order it when an initial PSA test result is abnormal.

Not everyone will have a PCA3 test, but the Food and Drug Administration (FDA) have approved its use in certain cases.

For example, a doctor may use it to help decide whether or not to recommend repeat biopsies for males aged over 50 or who have had a previous negative biopsy.

They may also use it to help confirm whether or not prostate cancer is present in males who have a negative biopsy but who continue to have high PSA levels.

The PCA3 test remains a relatively new way of screening for prostate cancer, and its use is not yet widespread. However, it may hold promise for the future.

The NCI note that researchers are looking into ways of combining the PCA3 test with other tests for a more accurate result during screening.

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Presentation by Dr. Jaspreet Singh, D.O. from Premier Medical Group on February 28 ,2020

By Diane Sutkowski

For those of you who missed the sterling presentation by Dr. Jaspreet Singh, D.O. from Premier Medical Group on February 28 – it was a winner. We were all impressed by his knowledge, willingness to answer any and all questions and his friendly demeanor, all of which showed how much he truly cares about his profession and his patients.

We can't thank Boston Scientific and Michael Perkins, their wonderful representative for sponsoring this lecture. They paid for the postage, post card printing and the nominal fee for the use of the main hall at the Hurley Church.

Michael brought snacks and water and even helped set up and take down the chairs, as did his boss who came to see what we were all about. Our sincere and heartfelt thanks to both of you and Boston Scientific.

Dr. Singh's talk was on "Life (or Sex) after Prostate Cancer" and covered the serious topics of the after effects that many men suffer – bladder leakage and erectile disfunction after surgery involving prostate cancer. His primary message is -there is hope if you suffer with any of these issues.

Dr. Singh performs surgery in prostate and kidney cancer. Prior to that surgery he does all he can to prepare his patients to try to prevent any of the long term after effects and to educate them on the procedures available to mitigate those effects should they encounter them. Being prepared gives you a much better chance of conquering problems both emotional and physical with after effects. He is data driven in all aspects of his treatment – checking continually to see what is most effective in each case. That is the sign of a true physician and healer.

Dr. Singh is a board-certified urologist with degrees from NY College of Osteopathic Medicine; internship at Brookdale University Hospital; surgical residencies at Albert Einstein Medical Center and Hahnemann University Hospital. Externships at Memorial Sloan Kettering and Children's Hospital of Philadelphia. He keeps up with the latest trends and procedures and is always broadening his horizons in his chosen field.

One of his patients, Howard Montanya, was comfortable enough to tell of his difficulty with ED prior to consulting with and then having an implant done by Dr. Singh and his satisfaction afterward. Howard was amazingly forthright in telling us of his journey. He gave me his card and permission to give his email to any man who would like to speak with him. It is paulahow52@yahoo.com.

You can also visit www.edcure.org for further information regarding ED.

And I have Howard's phone number too.

You can find more on Dr. Singh on the Premier Medical Site or call for a consultation at 845 437-5031 to speak with Christina Langston, LPN or for Patient Service Coordinator, Mari Martinez at 845 437-5024.

Diane Sutkowski

Goodbye Poke and Hope!

by Bernadette M. Greenwood, BSc., PG Cert., RT (R) (MR)(ARRT), PhD Candidate -Radboudumc, Dept. of Radiology and Nuclear Medicine; Clinical Instructor -UC Riverside School of Medicine, Department of Internal Medicine; Chief Research Officer -HALODx

The days of poke and hope are over! For decades prostate biopsies have been performed in a random, systematic fashion. An ultrasound probe is inserted into the patient's rectum and an image of the shape of the prostate gland is obtained. Random, systematic cores are taken out at the apex level (bottom), the mid-gland level and the base (top). This is conventionally known as transrectal ultra-sound guided biopsy or TRUS biopsy, and has been the standard for decades. This procedure is usually performed in an outpatient setting.

With the advent of multiparametric MRI, we are now able to look at detailed images of the prostate gland and aim the biopsy needle toward a specific target rather than systematically sampling 10, 12 or 18 cores or more. MRI allows us to see anatomic and morpho-logic features as well as functional information like perfusion, or blood flow and diffusion, movement of water molecules between cells. These functional sequences add great value and improve diagnostic performance. A special attribute of diffusion-weighted imaging (DWI) is that we can mathematically calculate some-thing called apparent diffusion coefficient value or ADC. This number is derived from the diffusion sequence and reflects the amount of restriction of water movement. This is referred to as "restricted diffusion." The lower the ADC value, the more likely malignancy is present –there is an inverse, linear relationship between ADC value and tumor aggressiveness. This relationship has been well-published in the radiology and urology literature.

It is important to note that there are other things besides cancer that can cause a low ADC, for example infection or inflammation. The best part about MRI is that we are able to aim at a target within a target; in other words, if a lesion has one particular area that looks most suspicious, we can take aim at that part of the tumor with pinpoint precision. The benefit is more accurate Gleason scoring and better tissue-based genomics. If a random biopsy is performed, there can be misclassification of dis-ease, especially if the tumor is far toward the front of the prostate gland, which can be missed with TRUS biopsy.

For the patient, the procedure is very straightforward. He lies on the MRI scan table on his stomach. A needle guide smaller than an adult's index finger is inserted into the rectum. The needle guide functions two ways: it is both a receptacle for instruments to be insert-ed and it functions as a fiducial marker. Our specialized computer software allows us to see the needle guide and its relationship to the target area. The software gives us coordinates that allow us to aim at the area of interest with a high degree of accuracy. We can angle left, right, front, back and insert or retract the device to aim squarely at the target. Once the needle has been deployed, the technologist takes an image of it in the fixed position. We have our pathologist include this image in our report so that it is indisputable where the tissue came from. The procedure takes only about a half an hour and does not require anesthesia. Numbing gel is used to ease any possible discomfort and patients tolerate the procedure extremely well. There is also an extremely low risk of infection on the order of 0.6%, which we presented at the annual American Urological Association meeting in San Francisco. Once the biopsy specimens are collected, they are sent to a specialized laboratory for the pathologist to evaluate them and generate a report of findings. Our pathologist is specifically trained in prostate cancer evaluation. In many cases we send the specimens to another laboratory for genomic testing. This test looks at 22 genes known to be associated with prostate cancer. The report will designate the patient as low-, intermediate-or high-risk as it relates to potential for metastasis, or spread of cancer outside the prostate gland to lymph nodes or skeletal structures. This in-formation can be a very helpful piece of a complicated jigsaw puzzle.

Another important piece of the puzzle is PSA density. This is the patient's PSA divided by their prostate gland volume. This helpful prognostic indicator combined with imaging findings and genomics can be very helpful. To use an example: if one man has a prostate the size of an apricot and an-

other man has a prostate the size of a grapefruit and they both possess a PSA level of 4 ng/mL, the one with the smaller gland will have a higher PSA density then the man with the larger gland.

MRI allows us to measure the prostate gland in order to accurately calculate PSA density. The functional MRI sequences also allow us to monitor response to treatment over time so we could tell if a patient is responding well to whichever therapy they choose. Even if they are on active surveillance or watchful waiting, the MRI allows us to monitor the patient and keep him safe. In the United Kingdom and the European Union guidelines have been published mandating MRI prior to biopsy and recently the American Urological Association published their policy statement agreeing with those guidelines and implementing it in the United States. We tell our patients to never allow anyone to put a finger, a needle or a scalpel any-where near your prostate gland unless they have done an MRI first. If you want more information about MRI targeted biopsy you can visit our website at www.halodx.com.

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Testing with combined biopsy method improves prostate cancer diagnosis in NCI study

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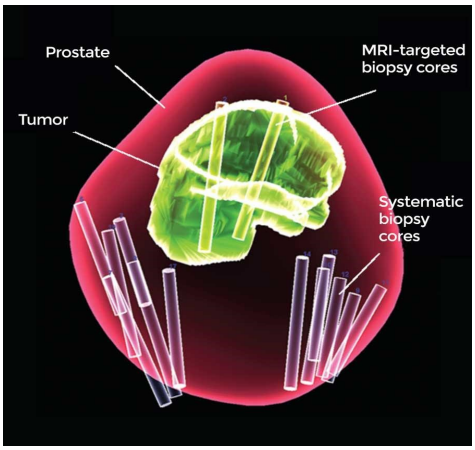

A 3-dimensional map of the prostate using combined MRI -targeted and systematic biopsies.

Using both types of biopsy greatly improved prostate cancer diagnosis in a new study.

Credit: National Cancer Institute

A method of testing for prostate cancer developed at the National Cancer Institute (NCI) leads to more accurate diagnosis and prediction of the course of the disease, according to a large study. This method, which combines systematic biopsy, the current primary diagnostic approach, with MRI-targeted biopsy, is poised to greatly improve prostate cancer diagnosis, thereby reducing the risk of both overtreatment and undertreatment of the disease. NCI is part of the National Institutes of Health.

The findings were published March 5, 2020, in the *New England Journal of Medicine*. The study was conducted at the NIH Clinical Center in Bethesda, Maryland.

"Prostate cancer has been one of the only solid tumors diagnosed by performing systematic biopsies 'blind' to the cancer's location. For decades this has led to the overdiagnosis and subsequent unnecessary treatment of non-lethal cancers, as well as to missing aggressive high-grade cancers and their opportunity for cure," said Peter Pinto, M.D., of the Urologic Oncology Branch in NCI's Center for Cancer Research and senior author of the study. "With the addition of MRI-targeted biopsy to systematic biopsy, we can now identify the most lethal cancers within the prostate earlier, providing patients the potential for better treatment before the cancers spread."

Prostate cancer can vary widely in severity and its potential to spread. Low-grade prostate cancer is associated with a very low risk of cancer-specific death and often doesn't require treatment, whereas high-grade cancers are much more likely to spread and are responsible for most prostate cancer deaths. This makes the correct assessment of the cancer grade very important for treatment decisions.

Unlike biopsies for most other

types of cancer, which target abnormalities found by imaging, systematic biopsy uses a non-targeted method of taking systematically spaced samples across the prostate gland to find a cancer. Because this method can potentially miss areas of cancer, doctors may then overtreat a patient with low-grade disease, fearing there is high-grade disease they missed. Or, if an aggressive cancer is missed, a patient may be undertreated.

MRI-targeted biopsies, which merge previously taken MRI images of suspected cancer with real-time ultrasound technology, are better able to detect more high-grade cancers than systematic biopsies. The goal of this study was to determine whether it would be better to replace systematic biopsy with MRI-targeted biopsies or use both tests together.

In the study, 2,103 men who had MRI-visible lesions underwent both MRI-targeted and systematic biopsies. Of these men, 1,312 were diagnosed with cancer and 404 underwent prostatectomy, a full removal of the prostate. By comparing diagnoses from systematic biopsy alone to systematic biopsy plus MRI-targeted biopsy, the researchers found that adding MRI-targeted biopsy to systematic biopsy led to 208 more cancer diagnoses than systematic biopsy alone. The addition of MRI-targeted biopsy also led to 458 upgrades, or changes in diagnosis to a more aggressive cancer, based on analysis of the biopsy tissue by histopathology.

The researchers also determined that combined biopsy provided more accurate diagnosis than MRI-targeted biopsies alone. Among the men who underwent prostatectomy, the researchers found that systematic biopsy alone underdiagnosed about 40% and MRI-targeted biopsy alone underdiagnosed about 30% of the cancers, while combined biopsy underdiagnosed 14.4% of the cancers. In addition, while systematic biopsy underdiagnosed 16.8% and MRI-targeted biopsy underdiagnosed 8.7% of the most aggressive cancers, combined biopsy missed only 3.5% of the most aggressive cancers.

MRI-targeted biopsies were first developed more than 10 years ago by a team of NCI researchers led by Dr. Pinto; Bradford Wood, M.D.; Baris Turkbey, M.D.; and Peter Choyke, M.D., all co-authors of the new study. The team, which included other researchers from NCI and other organizations, worked with Philips Healthcare to develop software that could overlay MRI images onto ultrasound images in real time, providing a view of lesions to be sampled that's not possible with systematic biopsy.

"Seeing this technology really make a difference in how we diagnose and treat prostate cancer is validation of the work we have done and continue to do at NIH," said Dr. Pinto. "But the change that matters most to us is how this impacts the patients we see every day, for whom we can now make more informed treatment decisions."

Reference

Ahdoot M, Wilbur AR, Reese SE, et al. MRI-Targeted, Systematic, or Combined Biopsy for Prostate Cancer Diagnosis. *N Engl J Med*. March 5, 2020. DOI: 10.1056/NEJMoa1910038 Source URL: Testing with combined biopsy method improves prostate cancer diagnosis in NCI study

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Cleveland Clinic Researchers Validate Link Between Genetic Variant and Poor Outcomes in Men with Advanced Prostate Cancer
Findings lay the foundation for more personalized treatments

Nima Sharifi, M.D.

In a new Cleveland Clinic-led study published in *JAMA Oncology*, researchers show that a testosterone-related genetic variant – *HSD3B1* (1245C) – is associated with more aggressive disease and shorter survival in men with metastatic prostate cancer.
This study – the first clinical trial validation of the relationship between *HSD3B1* status and clinical outcomes – suggests that genetic testing for *HSD3B1*(1245C) may help physicians identify patients most likely to benefit from additional and more aggressive treatment.

Nima Sharifi, M.D., of Cleveland Clinic's Lerner Research Institute, and colleagues retrospectively analyzed data from 475 participants enrolled in a large, multi-center national clinical trial testing the efficacy of androgen deprivation therapy (ADT) alone or in combination with docetaxel in prostate cancer. They compared clinical outcomes between men who carried the variant versus those who did not.

The researchers found that *HSD3B1*(1245C) inheritance is associated with faster progression to treatment resistance and shorter overall survival in men with low-volume metastatic prostate cancer regardless of the use of docetaxel. Interestingly, the genetic variant led to shortened survival despite the administration of any other therapies following the development of treatment resistance.

"These findings lay the groundwork for more personalized and effective treatments for prostate cancer," said Dr. Sharifi, senior author of the study. "If men carry this specific testosterone-related genetic abnormality we may be able to individualize their therapy."

In addition, *HSD3B1* (1245C) was not found to influence clinical outcomes in men with high-volume prostate cancer. Dr. Sharifi notes this is not surprising as previous studies have shown that disease progression and burden is vastly different between high- and low-volume prostate cancer.

Taken together, these findings suggest that the presence or absence of this genetic variant can be used to help identify men with low-volume metastatic prostate cancer most at risk for quick progression to treatment resistance and earlier death – a discovery with significant implications for clinical care and genetic counseling.

A limitation of the study was a lack of diversity due to the patient population enrolled in the original clinical trial and genetic variant frequencies. Validating this association with a more diverse population will be an important next line of investigation.
In 2013, Dr. Sharifi made the discovery that the *HSD3B1*(1245C) variant helps prostate cancer cells evade ADT, the first line of defense against the disease. ADT works by cutting off cells' supply of testicular androgens, hormones that fuel cancer cells to grow and spread.

He showed that in men with the genetic change, cancer cells adapt to produce their own androgens, which leads to treatment-resistant prostate cancer. In 2017, he received the national Top Ten Clinical Achievement Award from the Clinical Research Forum for his discoveries linking *HSD3B1*(1245C) with poor prostate cancer outcomes.

"These findings represent a seven-year research story that started at the lab bench and has now reached the patient bedside," said Dr. Sharifi. "As the team has shown here, incorporating genetic testing in prostate cancer as part of routine care has significant potential to improve treatment success and quality and length of life for men with prostate cancer who carry the *HSD3B1*(1245C) variant. This work is another step in that direction."

Dr. Sharifi holds the Kendrick Family Chair for Prostate Cancer Research at Cleveland Clinic and directs the Cleveland Clinic Genitourinary Malignancies Research Center. He has joint appointments in the Glickman Urological & Kidney Institute and Taussig Cancer Institute.

Jason Hearn, M.D., Department of Radiation Oncology, University of Michigan, is first author on the study, which was supported in part by the National Cancer Institute, part of the National Institutes of Health, the U.S. Department of Defense and the Prostate Cancer Foundation.

About Cleveland Clinic
Cleveland Clinic is a non-profit multispecialty academic medical center that integrates clinical and hospital care with research and education. Located in Cleveland, Ohio, it was founded in 1921 by four renowned physicians with a vision of providing outstanding patient care based upon the principles of cooperation, compassion and innovation. Cleveland Clinic has pioneered many medical breakthroughs, including coronary artery bypass surgery and the first face transplant in the United States. *U.S. News & World Report* consistently names Cleveland Clinic as one of the nation's best hospitals in its annual "America's Best Hospitals" survey. Among Cleveland Clinic's 67,554 employees worldwide are more than 4,520 salaried physicians and researchers, and 17,000 registered nurses and advanced practice providers, representing 140 medical specialties and subspecialties. Cleveland Clinic is a 6,026-bed health system that includes a 165-acre main campus near downtown Cleveland, 18 hospitals, more than 220 outpatient facilities, and locations in southeast Florida; Las Vegas, Nevada; Toronto, Canada; Abu Dhabi, UAE; and London, England. In 2019, there were 9.8 million total outpatient visits, 309,000 hospital admissions and observations, and 255,000 surgical cases throughout Cleveland Clinic's health system. Patients came for treatment from every state and 185 countries.

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Less Frequent Prostate Cancer Screening a Good Idea PSA Testing Pioneer Warns About Overdiagnosis-Mortality Trade-Off

Lengthening the interval between prostate cancer (PCa) screenings for men with low PSA levels was, unsurprisingly, predicted to modestly reduce the risk of overdiagnosis, according to a modeling study by Dutch and American investigators. But the results also showed that a longer screening interval would eventually lead to higher mortality rates from the disease compared with screening every two years, reported Eveline A.M. Heijnsdijk, PhD, of Erasmus MC University Medical Center in Rotterdam, The Netherlands, and colleagues online in the Journal of the National Cancer Institute.

Compared with biennial PSA testing from ages 45-69, the group calculated that if men with PSA levels <1.0 ng/mL at age 45 were screened every eight years instead of every two years, there would be approximately 47% fewer tests done and approximately 1-2% fewer overdiagnoses.

However, approximately 3-4% fewer lives would be saved using PSA-stratified screening approach. Another model where, instead, screening was stopped altogether at age 60 if levels were below 1.0 ng/mL was estimated to result in approximately 5.5-24.0% fewer overdiagnoses but 5.0-13.1% more deaths compared with continued biennial PSA screening until age 69.

"Less intensive PSA screening in men with low PSA levels can substantially reduce the testing burden. Both models project that stratifying screening by PSA level is expected to reduce overdiagnosis by a modest amount while preserving the majority of the benefit of screening," the team wrote.

Asked for his opinion of the results, William Catalona, MD, of Northwestern University Feinberg School of Medi-cine in Chicago said he disagreed with lengthening PSA screening intervals.

"In my practice, I now see daily the sad effects of men who have had a hiatus in their PSA testing or have not been tested because their doctors have told them that PSA testing caused more harm than good," he stated.

"I believe that suggesting less PSA testing is desirable could compromise many men. "For the study, Heijnsdijk and co-investigators used different predictive models – the Erasmus University Medical Center-Microsimulation Screening Analysis (E-MISCAN) and the Fred Hutchinson Cancer Research Center (FHCRC) model –to arrive at their calculations. "Using the calibrated models, we simulated cohorts of men in the U.S., age 45 or 50 in 2017 and followed until age 85," the team explained. The calculations were based on these screening strategies:

▪Screening from ages 45 to 69 at two-year intervals

▪Lengthening screening to eight years for men with a PSA level <1.0 ng/mL at age 45, but decreasing it again to two years if the levels rose to >1.0 ng/mL on a later screening

▪Stopping screening completely if the PSA level remained at less than 1.0 ng/mL at age 60 and older

▪Using a combination of

the last two strategies Using the combination strategy, the E-MISCAN model projected a 52.2% reduction in the number of screening tests carried out, a 24.4% reduction in overdiagnosis, and a 14.8% reduction in the number of lives saved.

The FHCRC model projected a 51.1% reduction in the number of screening tests done, a 5.7% reduction in overdiagnosis, and a 7.5% reduction in lives saved. Compared with no PSA screening, the two models "projected that screening 10,000 men ages 45-69 biennially would require more than 110,000 screenings, yield 277 (E-MISCAN) to 348 (FHCRC) overdiagnoses, save 110 (E-MISCAN) to 160 (FHCRC) lives and gain 921 (E-MISCAN) to 1,312 (FHCRC) life-years," the authors say.

The predicted reduction in PCa-specific-mortality was 38.6% for the E-MISCAN vs. 53.3% for the FHCRC model, compared to a no-screening model. Both models predict-ed that discontinuing screening at age 60 would reduce overdiagnoses by approximately 80%, but about 50% more lives would be lost vs. a policy where men are screened until age 69.

"The models agree qualitatively across all settings that PSA-stratified strategies will lead to modest reductions in both overdiagnoses and lives saved," Heijnsdijk and co-authors stated. "Depending on how these harms and benefits are valued, our results confirm that PSA-based stratification could lead to more efficient use of the PSA test in early detection of PCa," the team concluded.

Catalona agreed that results support a risk-stratified approach to PCa screening. "However, statistical modeling studies have limitations in accurately reflecting real-world scenarios, and statistical modeling are usually not considered sufficiently rigorous to support hard recommendations for clinical adoption," he said.

Catalona also noted that the current benefit-harm analysis does not include the frequency of metastases at diagnosis, which is determined only by early detection and, said the authors "fail to con-sider preventing suffering and treatment of metastatic disease, which is a burden to patients and their families.

"In addition, Catalona said prolonging screening intervals >two years delays the diagnosis of the most aggressive cancers. "This makes a recommendation of lengthening screening intervals to four or eight years or completely discontinuing screening when PSA is below 1.0 ng/mL at the age of 60 particularly concerning," he said. MedPage Today21 February 2020

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COVID 19

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Be Safe!

Be Well!

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