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# HOTSHEET

APRIL 2011

## STUDY KNOCKS DIAGNOSTIC VALUE OF PSA VELOCITY

If prostate biopsy is based on PSA velocity (PSAV) alone, the number of unnecessary biopsies would be almost 4 times the number of additional cancers diagnosed, data from a large clinical trial showed.

In the absence of other predictive factors, PSAV would have identified 115 prostate cancers at a cost of 433 unnecessary biopsies, according to Andrew Vickers, PhD, of Memorial Sloan-Kettering Cancer Center in New York City and colleagues. If used as sole justification for a biopsy, PSAV would trigger about 1 of every 7 prostate biopsies, they reported online in the *Journal of the National Cancer Institute*.

To examine the predictive value of PSAV, Vickers and colleagues analyzed data from the Prostate Cancer Prevention Trial (PCPT), which included an end-of-trial prostate biopsy for all study participants. The analysis included 5,519 men from the placebo arm of the trial. A linear regression model was constructed incorporating various predictors of prostate cancer on biopsy. They compared results in models with and without PSAV as well as an analysis that limited the definition of prostate cancer to high-grade disease (Gleason score 7 to 10).

(Continued on page 3)

## IMAGING MISSES MARK IN PROSTATE CANCER

A large percentage of low-risk prostate cancer patients are getting expensive imaging studies that are not recommended by treatment guidelines – but, paradoxically, 39% of high-risk patients who should be receiving scans don't get them, researchers reported at the 2011 ASCO Genitourinary Cancers Symposium (GUS).

About 36% of men with low-risk prostate cancer underwent magnetic resonance imaging (MRI), computer-assisted tomography (CT) or positron emission tomography (PET) imaging studies, said Sandip Prasad, MD, a fellow in urologic oncology at the University of Chicago Medical Center. "The chances of finding relevant disease outside the prostate in these patients on one of these scans is less than one percent," Prasad told MedPage Today at his poster presentation. "We think that the percentage of patients getting these exams should be 0%."

Similarly, Prasad said that no men diagnosed with intermediate prostate cancer should be getting these diagnostic scans. Yet in his study based on Surveillance Epidemiology and End Results (SEER-Medicare), governmental databases showed that 49% of men diagnosed with this type of prostate cancer underwent one of the screening tests.

(Continued on page 5)

## LARGEST STUDY TO DATE SHOWS LITTLE NEED FOR PSA BEYOND 10 YEARS POST-SURGERY

Is it reasonable to discontinue PSA testing 10 years after radical prostatectomy (RP) if the patient has remained disease-free to that point? Stacy Loeb, MD, a urology resident at Johns Hopkins University, in Baltimore, MD, presented the findings at the 2011 ASCO Genitourinary Cancers Symposium (GUCCS).

"A lot of issues are addressed by prostate cancer guidelines," Dr. Loeb told *Medscape Medical News* in an interview. "But one issue not addressed is how long patients need to continue PSA testing after RP." Results from the largest study carried out to date – and with the longest follow-up – suggest that the answer is yes.

Previous studies have shown that biochemical recurrence usually occurs within 5 years of surgery; even when cancers return after 5 years, they're usually associated with less risk for morbidity and mortality.

This retrospective study followed 10,609 men from the Hopkins database, some for as long as 25 years after RP. Dr. Loeb reported that 1,684 men in the cohort had BCR, defined as a PSA level above 0.2 ng/mL, without previous hormonal or radiation therapy. Dr. Loeb

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## PSA TESTING DECLINES A BIT

After interim results from 2 landmark prostate cancer screening trials were published, PSA testing declined "slightly" – but statistically significantly – in men 74 years and younger, according to a new study of Veterans Health Administration (VHA) practice groups.

The drop happened from August 2009 to March 2010 – a time that followed long-awaited news from the Prostate, Lung, Colorectal and Ovarian (PLCO) screening trial, and the European Randomized Study of Screening for Prostate Cancer (ERSPC) trial, which were simultaneously published in March 2009.

The fall-off was not dramatic – from 5.5% to 9.1% (or 2.2 to 3.0 absolute percentage points), depending on the age group examined.

The new study provides a "preliminary indication" that patients and physicians "may have interpreted the evidence from the trials negatively" and subsequently reduced their use of PSA testing, write study authors, led by Steven Zeliadt, MD, from the Veterans Administration Puget Sound Health Care System in Seattle, Washington. The study appears online on 24 February 2011 in the *Journal of the National Cancer Institute*.

It's not a surprise that the decline in testing was modest, say the authors of an editorial that accompanies the study. That's because the data from the 2 trials were "neither strongly supportive nor decidedly unfavorable" of PSA testing, write Siu-Long Yao, MD, and Grace L. Lu-Yao, PhD, who are from, respectively, the Merck Research Laboratories in Kenilworth, New Jersey, and the Cancer Institute of New Jersey at the University of Medicine and Dentistry of New Jersey in New Brunswick.

The ERSPC study showed a 20% relative reduction in prostate cancer mortality in the screened group, write the 2 editorialists, but the PLCO study did not show any statistically significant change in prostate cancer mortality. In the eyes of Dr. Yao and Dr. Lu-Yao, the "net results" do not "clearly argue for or against screening," and people are likely to continue in their earlier mindsets.

Both the editorialists and the study authors point out that PSA testing in the VHA might not represent what's hap-

pening in the general community. Interestingly, they disagree about who gets more testing – the study authors say it's veterans and the editorialists say it's the general American population – and both cite studies to back up their positions.

When the 2 screening trials were published, they received "broad media coverage, potentially influencing the way PSA testing is viewed," say the study authors. Last year, after prostate cancer screening was repeatedly in the news, a prominent urologist cited media coverage as an agent of change in PSA testing.

"The controversy over PSA testing is now being played out in many mainstream venues, like the New York Times and the Wall Street Journal, and not necessarily urology publications," Peter Carroll, MD, MPH, from the University of California, San Francisco, told Medscape Medical News. "One of the top 10 news stories of 2009 on CNN is about how men may not need to get a PSA test," he said. "I find that very disturbing."

To examine possible changes in PSA testing patterns, the investigators conducted a cross-sectional study. In it, they assessed the frequency of PSA testing among 8 group practices in the VHA Pacific Northwest Network from August 2004 to March 2010. They broke up the timeline into 6 periods; the final period (August 2009 to March 2010) looked at PSA testing patterns soon after the publication of the screening trials.

During each of the 6 periods, they calculated the proportion of men who had a PSA test from all eligible men with a primary care or urology clinic visit in the 8 group practices. The total number of eligible men ranged from 125,000 to 140,000 in each period, they report.

Throughout the study periods, the investigators observed that about one third of eligible younger men (40 to 54 years) got tested, as did about one half of eligible middle-aged/older men (55 to 74 years), and about one quarter of eligible oldest men (75 years and older). However, they found a downturn in PSA testing among the 3 age groups examined by 3.0 percentage points, 2.7 percentage points, and 2.2 percentage points, respectively, after the publication

(Continued on page 8)

## GENETIC MAP OF PROSTATE CANCER CRACKED

The genetic code of one of the most deadly cancers has been mapped by scientists for the first time in a breakthrough that could “transform” our understanding of the disease. The blueprint uncovers many of the mutations and genetic damage that drives prostate cancer and could lead to better diagnosis and may lead to a patient’s personalized “cancer chart” that could be used to provide “made to measure” personal care.

Dr Mike Berger, lead author at the Broad Institute at MIT and Harvard, said: “This is a transforming moment in understanding the underlying biology of prostate cancer. “It offers the potential of new targets for treatment and earlier diagnosis of the more aggressive strains of the disease.” The latest research is published in the journal *Nature*.

Dr Berger and colleagues sequenced the genomes of 7 different prostate cancer tumors and compared them to healthy tissues to find where they had been damaged or mutated. They found more than 21,000 mutations – like spelling mistakes – in the 7 tumors as well as more than a 100 “rearrangements” where whole sections of DNA have broken free and reattached to other parts of the genome.

By sequencing many more cancer patients over the next few years, the researchers hope to narrow down to a handful of targets to hit with treatments such as chemotherapy and radiotherapy.

“Whole genome sequencing gives us fascinating new insights into a category of alterations that may be especially important in prostate cancer,” said Dr Levi Garraway. “This first whole genome view shows us tantalizing evidence for several new prostate cancer genes that likely would have remained undiscovered had we not been taking a genome-wide approach.”

Dr Kate Holmes, the Prostate Cancer Charity’s Research Manager, said: “This is interesting research that highlights a new approach to understanding the way prostate cancer develops. However, only 14 tissue biopsy samples were analyzed in total. The next stage will be to repeat the study on a much larger scale, which will be an extensive piece of work.”

*The Telegraph UK, 11 February 2011*

## VALUE OF PSAV IN SCREENING QUESTIONED *(Continued from page 1)*

In a univariate analysis, PSAV had a significant association with biopsy outcome ( $P < 0.001$ ). As a component of a multivariable prediction model, however, the association was substantially diminished. Varying the definition of PSAV, the authors found marginally significant odds ratios (OR) with log (PSA) values one year before diagnosis (OR 0.74,  $P = 0.037$ ) and annualized PSAV (OR 0.98,  $P = 0.047$ ).

Receiver operating characteristic analysis showed minimal improvement in the area under the curve (AUC) when PSAV was added to other predictors of prostate cancer risk (AUC 0.702 vs. AUC 0.709). Even less improvement in predictive accuracy was observed for detection of high-grade or clinically significant cancers.

“There was little evidence that PSAV adds an important level of predictive accuracy to either standard predictors or to PSA alone,” the authors wrote.

“Superior risk stratification can be achieved simply by choosing a different PSA cut point, especially for the endpoints of high-grade cancer or clinically significant cancer,” they added.

The findings have implications for clinical guidelines from the American Urological Association (AUA) and the National Comprehensive Cancer Network (NCCN) that include PSAV in criteria for prostate biopsy.

NCCN guidelines, for example, recommend a biopsy in men who have a PSAV greater than 0.35 ng/mL/year. In support of the recommendation, the guideline authors cited a single study showing that PSAV predicted diagnosis of fatal prostate cancer 10 to 15 years later.

“We found no reason to believe that implementation of the guideline would improve patient outcomes; indeed, its use would lead to a large number of unnecessary biopsies,” Vickers and co-authors wrote in conclusion. “We therefore recommend that organizations issuing policy statements related to PSA and prostate cancer detection remove references to PSAV.”

The PCPT used a PSA cutoff of 4.0 ng/mL as a biopsy trigger, resulting in a biopsy rate of approximately one in 20

with no appreciable loss in diagnostic accuracy, Siu-Long Yao, PhD, and Grace L. Lu-Yao, PhD, of the University of Medicine and Dentistry of New Jersey, wrote in an accompanying editorial. The study by Vickers et al. serves as a reminder that “the use of PSA as a screening tool leaves much to be desired,” wrote Yao and Lu-Yao. “Indeed, after more than 20 years of PSA screening, it has been estimated that approximately one million men may have been unnecessarily treated for clinically insignificant prostate cancer.”

The authors did acknowledge that current clinical guidelines for prostate cancer have a strong evidentiary base for many aspects of diagnosis, evaluation, and treatment; in particular, use of PSA and free PSA levels to diagnose cancer.

The analysis was supported by the Prostate Cancer Foundation and the National Institutes of Health.

*MedPage Today, 24 February 2011*

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## PSA TESTING 10 YEARS POST-RP NOT NEEDED

(Continued from page 1)

said that 77% of BCRs occurred within 5 years of RP, 16.6% occurred 5 to 10 years after RP, 4.9% occurred 10 to 15 years after RP, and 1.5% occurred more than 15 years after RP.

“Late recurrences were associated with more favorable pathologic features,” Dr. Loeb said. “Even when cancers did recur, they were unlikely to metastasize or cause the patient to die from prostate cancer.” Having a low initial Gleason score was a favorable factor, she said.

“No patient with a Gleason [score of] 6 or less had metastases or death, even if they had late recurrence. So for those men, and also for men with a limited life expectancy, it’s probably safe to discontinue PSA testing 10 years after surgery.”

Jonathan Tward, MD, a radiation oncologist at the Huntsman Cancer Institute in Salt Lake City, UT, said that he found the study very useful. “It’s not like a lot of studies where it’s unclear how to translate the findings to clinical practice. This directly guides physicians as to what they can tell patients.”

He noted that prostate cancer is associated with a lot of anxiety before treatment, but also after treatment. “Every few months when PSA is drawn, it causes patients a lot of worry; it can be almost like a [posttraumatic stress disorder], quite frankly. So knowing when you can safely stop testing is really important information.”

Both Dr. Tward and Dr. Loeb did stress, however that in very young patients it’s probably a good idea to continue testing beyond 10 years. “Even looking at data going out 20 years, it may only be a few who will develop metastases, but you don’t want them having to live with that risk,” Dr. Tward said.

Both physicians also agreed that rather than stopping PSA testing completely after 10 years, a reasonable option might be to continue to testing, but at much less frequent intervals.

### Reference:

Podium presentation given at the 2011 ASCO GUCCS), Abstract 179

*Medscape Medical News, 21 February 2011*

## DISEASE FREE SURVIVAL FOLLOWING SALVAGE CRYOTHERAPY FOR BIOPSY-PROVEN RADIO-RECURRENT PROSTATE CANCER

Williams AK, Martínez CH, Lu C, Ng CK, Pautler SE, Chin JL

**Eur Urol 22 December 2010**  
Epub ahead of print

*University of Western Ontario, Departments of Urology and Oncology, London, Ontario, Canada*

The optimum treatment of prostate cancer recurrence following radiation therapy (RT) remains controversial due to the lack of long-term data.

Our aim was to review the survival of patients who underwent salvage cryotherapy to the prostate gland for biopsy-proven recurrent prostate cancer and establish prognostic indicators.

A retrospective analysis was performed on all patients undergoing salvage cryotherapy at an academic urology unit for biopsy-proven locally recurrent prostate cancer after RT from 1995 to 2004. Patients' preoperative, perioperative, and postoperative data were reviewed and recorded.

Two freeze-thaw cycles of transperineal cryotherapy were performed under transrectal ultrasound guidance by a single surgeon.

The primary outcome was survival. Secondary outcomes were disease-free survival (DFS), metastasis-free survival, and progression to androgen-deprivation therapy.

Of 187 patients, 176 had records available for follow-up (follow-up rate: 94%). Mean follow-up was 7.46 yr (range: 1-14 yr). Fifty-two patients were followed for >10 yr. DFS at 10 yr was 39%. Risk factors for recurrence were pre-salvage prostate-specific antigen (PSA), pre-radiation, and pre-salvage Gleason score. A PSA nadir >1.0 ng/dl was highly predictive of early recurrence.

Salvage cryotherapy led to an acceptable 10-yr DFS. Pre-salvage PSA and Gleason score were the best predictors of disease recurrence. A PSA nadir >1 ng/dl following cryotherapy indicated a poor prognosis, and recurrence of disease was universal in these patients.

## NEW ON WWW.USTOO.ORG

### Recent additions to the Us TOO website include:

- New report on prostate cancer's impact on bone health: *Bone Health In Focus*
- Financial Assistance Resources - including co-pay relief, travel, how to ask for a reduced medical bill, early access programs for drugs and treatments in clinical trial, legal issues, and more
- Updates to the Treatment Options page for Hormone-Resistant Prostate Cancer, added new info on Autologous Cellular Immunotherapy
- “Ten Things I Learned from Loving in Sickness and in Health” - new article on *My Prostate Cancer Roadmap.com*
- Read the monthly letter from Us TOO President & CEO Tom Kirk
- Latest issues of *HotSheet* & the *Us TOO Chapter NEWS... in color!*
- Added more items to Calendar of Events

## IMAGING MISSES MARK

(Continued from page 1)

While those tests may be wasteful of scarce resources, Prasad said he was more concerned that 39% of men diagnosed with high-risk prostate cancer – and for whom guidelines recommend additional screening tests – did not receive any of these studies. “All of these men should have received the tests,” Prasad said. “Our numbers should have been 0%, 0% and 100% for the high risk patients. Instead we saw 36%, 49% and 61%. These are troubling figures.”

“I’m not surprised to see these figures,” commented Badar Mian, MD, associate professor of urology surgery at Albany Medical College in New York. “I do find these figures concerning.” Mian said that overuse of scans is more likely to occur at large private practices rather than at academic institutions. “At academic institutions, residents such as Dr. Prasad perform critical checks and balances by being encouraged to question various procedures,” he told MedPage Today. “In other situations doctors may just be going by gut feelings on the need for these tests.”

In his study, 9,640 men were diagnosed with low-risk prostate cancer; 12,966 men were diagnosed with intermediate prostate cancer and 7,577 men in the study were diagnosed with high-risk prostate cancer. Prasad said the unnecessary tests among the 30,183 men in the SEER-Medicare database may have cost the American taxpayer \$35 million. “When you consider that private insurers for younger men may reimburse at a higher rate, the unnecessary expense may be far higher,” he explained.

“Despite existing guidelines of the AUA and the NCCN, costly and unnecessary imaging studies continue to be performed in men with low-risk and intermediate-risk prostate cancer, while a significant number of men with high-risk disease do not receive adequate staging prior to treatment,” he said.

### Reference:

Prasad M, et al “Inappropriate utilization of radiographic imaging in men with newly diagnosed prostate cancer.” Poster presented at the 2011 ASCO GUS, Abstract 120

MedPage Today, 19 February 2011

## STUDY SUGGESTS LOWER PSA CUTOFF FOR BIOPSY

An initial PSA <3 ng/mL predicted a low risk of prostate cancer and a remote likelihood that a man would die of the disease, showed the results of a large screening study presented at the 2011 ASCO Genitourinary Cancers Symposium.

The median time to diagnosis of prostate cancer in men with the lowest initial PSA values exceeded 8 years, said Monique Roobol, MD, of Erasmus University Medical Center in Rotterdam, Netherlands. The low cancer risk and prolonged interval to diagnosis have potentially major implications for use of PSA to screen for prostate cancer.

“These results provide justification for a PSA threshold of  $\geq 3$  ng/mL for prostate biopsy,” Roobol said. “The results can also contribute to individual risk stratification and management of men in PSA-based screening programs,” she said. “For example, the favorable outcomes in men with initial PSA values of less than 1 ng/mL – who accounted for 45% of men between the ages of 55 and 74 – supports prolongation of the screening interval up to, for example, 8 years.”

“I believe that this study gives us some confidence that annual PSA screening is going to soon become a thing of the past,” said Nicholas Vogelzang, MD, urologic oncologist from the Comprehensive Cancer Centers of Nevada, who moderated an earlier news briefing.

“A low PSA, particularly men with a PSA less than 1, and probably those with a PSA less than 2, could be considered for substantially longer intervals of PSA screening. We formerly learned that a PSA of 4.0 was the threshold for a prostate biopsy. This study suggests the number should drop to 3.”

Supporters that PSA screening works point to the near-100% five-year survival except for the cancers associated with distant metastasis. detractors of PSA screening argue that the test merely uncovers clinically insignificant cancers that would not have posed a mortality threat if they had never been discovered. Diagnosis of early stage-prostate cancer has led to significant overtreatment, morbidity and cost, they argue.

A key issue in the controversy relates to the most appropriate PSA value for identifying men with an increased risk

of prostate cancer. The European Randomized Study of Screening for Prostate (ERSPC) used a PSA value of 3.0 ng/mL as the cutoff for a prostate biopsy.

Roobol reported findings from an analysis of a Dutch cohort included in ERSPC. The cohort comprised 42,376 men ages 55 to 74 and living in the Rotterdam area. The researchers randomized 19,950 of the participants to serial screening PSA tests, and men who had initial PSA values  $\geq 3$  ng/mL underwent prostate biopsy. Roobol and her co-investigators focused on the 15,758 (79%) men who had PSA values <3.0 ng/mL at their first screening test. Follow-up screening occurred at four-year intervals.

From 1993 through 2008, 915 (5.8%) of the 15,758 men had prostate cancer diagnoses and 23 (0.15%) died during a median follow-up of 11 years. The investigators determined 182 of the cancers were detected between screenings, and 169 (1.1%) had characteristics associated with more aggressive cancer (clinical stage >T2c, Gleason score >8, PSA at diagnosis >20 ng/mL, and spread to lymph nodes or distant sites).

Within the range of PSA values from undetectable to 3 ng/mL, prostate cancer incidence and mortality increased. Of the 7,126 men with PSA values <1 ng/mL, 129 (1.8%) eventually had prostate cancer diagnoses, and three (0.04%) of the men died of prostate cancer. Of the 6,156 men with PSA values of 1.0 to 1.9 ng/mL, 415 developed (6.7%) prostate cancer, and 11 (0.18%) died of the cancer. The remaining 2,476 men had PSA values of 2.0 to 2.9 ng/mL; 371 (15.7%) of them developed prostate cancer and nine (0.36%) died of the disease.

As compared with men with initial PSA <1.0 ng/mL, men with first-time values of 1.0 to 1.9 ng/mL had a significantly higher incidence (hazard ratio, HR 4.0,  $P < 0.001$ ), proportion of aggressive cancers (HR 2.7,  $P < 0.001$ ), and prostate cancer mortality (HR 3.9,  $P = 0.038$ ).

Corresponding hazards for men in the PSA range of 2.0 to 2.9 ng/mL were HR 10.3 for incidence ( $P < 0.001$ ), HR 6.9 for aggressive cancers ( $P < 0.001$ ) and HR 7.5 for prostate cancer mortality ( $P = 0.003$ ).

MedPage Today, 15 February 2011

*Editors' note:* In the spirit of information sharing, we have invited certain physicians and others to provide comments and opinions for Us TOO's *HotSheet*. It is our desire to enrich the content of the *HotSheet* to empower the reader. The columns by Drs. Chodak, Moyad and Myers contain the opinions and thoughts of its author and is not necessarily those of Us TOO International.

## ASK DOCTOR SNUFFY MYERS

Do the common side-effects of hormonal therapy typically increase toward the end of the therapy, and what is the typical time frame for recovery from side-effects after the completion of the hormonal therapy?

The pattern differs from side effect to side effect. Hot flashes commonly reach their peak at 3-4 months and may actually decrease in intensity as time passes. On the other hand, muscle loss, weight gain, and cardiovascular risk all increase steadily until treatment stops. Bone loss also progresses as long as the testosterone and estradiol levels are suppressed. After hormonal therapy is over, the pace of recovery depends on the patient.

The key element of recovery is the return of testosterone. Younger patients recover faster than older patients. The longer you are on hormonal therapy, the slower you will recover. The more weight you have gained during treatment, the slower your recovery will be. This is because fat cells convert testosterone to the female sex hormone estradiol. If you have done aerobic exercise and weight lifting during hormonal therapy and minimized your weight gain, you will recover much more rapidly.

With those variables in mind, some of my younger patients have started to recover serum testosterone within 4 months. However, most patients start to recover serum testosterone between 6-12 months after the end of hormonal therapy. If you have been on treatment for two years or more, are older and/or have gained a lot of weight, your testosterone level may never return to normal.

Most patients do not realize that the recovery of their body--muscle, hair distribution, sex drive, penis size will not be instantaneous with testosterone recovery. The recovery of testosterone just means that the hormones are in place for these other problems to correct themselves. You will not gain muscle and lose fat unless you also exercise and watch your diet. Normal male hair distribution will take at least 6 months additional time.

## DOC MOYAD'S WHAT WORKS & WHAT IS WORTHLESS COLUMN, ALSO KNOWN AS "NO BOGUS SCIENCE" COLUMN

**"Perhaps if we improved our diets and did more resistance exercises many of us would no longer need calcium and vitamin D supplements!? Let the controversy begin!"**

Mark A. Moyad, MD, MPH,  
University of Michigan Medical Center, Department of Urology

**Bottom Line:** Men lifting weights + getting aerobic activity just 3 times per week and already getting adequate dietary calcium and vitamin D had better bone changes compared to the group that received calcium and vitamin D supplements! Where is this commercial?

That wacky Charlie Sheen has been providing me with all sorts of entertainment so I actually almost forgot to write this column! In the meantime, lets talk about less = more.

Last month, we talked about vitamin D supplementation and how it is over hyped! Now comes a new amazing and unique lifestyle study that once again proves that you should be really critical and analytical before taking ANY pill my friends and enemies! An 18-month study of 180 men aged 50-79 years was just completed and men had been placed into one of 4 groups: exercise (3 days a week of combined aerobic and weight lifting exercise); calcium (1000 mg/d) and vitamin D (800 IU/d) supplementation; exercise + these supplements; and control (do nothing) group. However, keep in mind that the average man in this study was already getting 900-1000 mg of calcium in his diet daily and had a vitamin D blood level of 35 ng/mL (perfect on the Mark Moyad scale – if you have been reading this column in the past) before the study started!

What happened? Well, my friends the Butler Did It with the candlestick holder in the dining room! Wait – that is a line from a bad movie! I meant to say that the lifestyle group was the clear winner! The hip and spine bone mineral density increases were superior to any other groups. Now, this does not prove that exercise trumps dietary supplements because this was only an 18-month study. However, it does suggest that some men and women already getting 1000-1200 mg of calcium from diet

(milk, yogurt, kale, fish, etc. . .) and 800-1000 IU of vitamin D from food (fish, eggs, fortified foods. . .) may not need to always take these supplements. There are some men at higher risk of bone loss that should be careful and probably incorporate some supplementation, such as those on LHRH treatment.

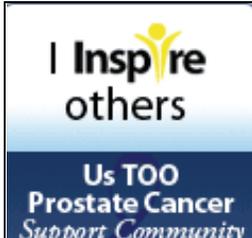
Still, if you meet with a nutritionist and she/he determines you are getting plenty of calcium and your blood level of vitamin D is adequate, do you really need these supplements? If you do not, please send any extra money you have saved to the Dr. Moyad Beer Fund and please note that this fund was established only for Dr. Moyad and was not intended to share with anyone even in case of an emergency or unusual circumstance (for example, if we were ever able to beat Ohio State in Football again, I will not and cannot share).

This is why Pints for Prostates was a good idea that Us TOO embraces because it not only raises money for prostate cancer, but allows us to share our beer if we want to with a friend (unlike the Moyad Beer Fund).

I think you get my PINT. . . I mean my point! See you next month when you can read the next DRAFT of my column and POUR over my material and TAP INTO more of my thoughts (all puns intended)!

### Reference:

Kukuljan S, Nowson CA, Sanders KM, et al. *J Clin Endocrinol Metab*, 5 January 2011 Epub ahead of print

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**DOCTOR CHODAK'S BOTTOM LINE** (Ref Key: article #, page #, column #)**Author:** *Winning The Battle Against Prostate Cancer, 2011*

PSA, PSA and more PSA – This month's *HotSheet* provides considerable new information about how to improve the way this test is used.

**a7p5c2** Despite its availability for more than 20 years, the best way to use PSA continues to evolve. Although initially a level above 4.0 ng/mL was thought to be abnormal, doctors eventually found out that cancer can be present even when with PSA level is only 1 ng/mL. Doctors continue to debate what PSA should be used to recommend a biopsy. Further analysis of the ERSPC screening study found few cancers in men with a PSA level below 3 ng/mL and few dying of cancer during a median follow-up of 11 years. One interpretation is that waiting until the PSA is greater than 3 ng/mL has little chance of leading to a bad survival result. For men with a PSA below 1 ng/mL, testing every 8 years may be reasonable.

**THE BOTTOM LINE:** Less frequent testing for men with a very low PSA and not doing a biopsy unless the PSA is above 3 ng/mL may lead to fewer men having unnecessary biopsies without leading to greater odds of dying from prostate cancer.

**a1p1c1** Another approach often used to diagnose prostate cancer is PSA velocity with values ranging from 0.35 to 0.75 ng/mL/year as a reason to do a biopsy. The study by Vickers and co-workers raises serious concern about the value of using PSAV. They found that this approach added little improvement over other indicators for finding potentially life-threatening cancers. It did, however, lead to many more biopsies and increased the chance of finding more men with non-life threatening cancers. Their conclusion is to not use PSAV as an indicator to perform a biopsy.

**THE BOTTOM LINE:** Until a better screening test becomes available, doctors always seek approaches that can detect life-threatening cancers when still curable but also avoid unnecessary biopsies and treatment for non-aggressive prostate cancers. These results from a well-done study provide good support for eliminating PSAV as a reason to perform a biopsy.

**a2p1c2** Once diagnosed, men are faced with knowing the extent of the cancer so

proper therapy can be selected. MRI, CT and PET scanning are tests that have the potential to determine if cancer is outside the prostate. Unfortunately, they have many false positives and rarely find extracapsular cancer in men with low and intermediate risk cancers. The study by Prasad found that these tests found extra capsular cancer in only 1% of the cases yet 36% of men with low-risk disease had the test and the rate was nearly 50% for intermediate risk cancers. They do recommend using these tests for high-grade cancer but no data is included in the abstract to permit a valid assessment. If these expensive tests yield so little useful information, one must question why they are being used so much.

**THE BOTTOM LINE:** Men who are diagnosed with a low or intermediate risk cancer should carefully question their doctor before undergoing the CT, MRI or PET scan unless they have decided to proceed with radiation treatment, in which case they are a necessary test for treatment planning.

**a3p1c3** Perhaps the most valuable use for PSA is in monitoring men following therapy to identify when disease progression has occurred and more therapy may be needed. The study by Loeb and co-workers presents interesting data addressing the question whether PSA testing is needed indefinitely after radical prostatectomy. Although they demonstrate that only a small percentage of recurrences occur beyond 10 years, the data as presented do not provide enough information to justify not performing PSA after that time. For example, it is unclear what the recurrence rate is beyond 10 years according to the initial PSA, the final Gleason score from the radical prostatectomy specimen and the pathological stage. To do that, the authors would need to divide up their population and only look at the information for the men with recurrences after 10 years. Unfortunately, only about 100 men with a biochemical recurrence have information beyond ten years, which is too few to make reasonable conclusions.

**THE BOTTOM LINE:** Until much more information is available, men should continue with at least annual PSA testing following radical prostatectomy because late recurrences do occur,

they are asymptomatic and may be easier to treat when discovered before symptoms develop.

**a6p4c3** For men who recur after radiation therapy, the optimal therapy is unclear. One option is salvage cryotherapy after radiotherapy but it has never been studied in a proper clinical trial. New data from a Canadian retrospective study found looks at overall survival in a group of men and the disease free survival at 10 years was only 39%. Nevertheless, the authors conclude that cryotherapy gives an acceptable result.

**THE BOTTOM LINE:** Unfortunately, no conclusions about the value of salvage cryotherapy can be made based on a study with this design. Did men do well because of the therapy or because their cancer would not have harmed them? How did the Gleason score, clinical stage or PSA affect the results? How will the results compare to other options? Without answers to these questions, the value of salvage cryotherapy cannot be determined.

**a11p8c2** Among the new treatments on the horizon, abiraterone has generated considerable excitement. It has been tested in men who progressed after docetaxel chemotherapy and, as previously reported, it improves survival. Another report now shows more detail about which men benefit from treatment and to what extent. The good news is that the drug improved survival in men failing either 1 or 2 types of chemotherapy and men with varying performance status.

**THE BOTTOM LINE:** When approved, abiraterone will be an important addition to the treatment options for men with advanced disease. Hopefully additional studies will be forthcoming in men with less advanced disease to see if even greater benefit occurs.

**MARK YOUR CALENDARS**

The dates have been selected for the 2011 Prostate Cancer Conference. Presented by the Prostate Cancer Research Institute (PCRI), their national annual Conference will be held in Los Angeles on September 9-11, 2011 at the Westin Los Angeles Airport Hotel. Visit <[www.pcri.org](http://www.pcri.org)> for more information.

**PSA TESTING DECLINES**

*(Continued from page 2)*

of the PLCO and ERSPC trial results. The trend was statistically significant when the final study period (period 6) was compared with the penultimate study period (period 5) among all 3 age groups (P <0.001), they say. But when the researchers compared the final study period with periods 1 to 5, they found that the decrease was only statistically significant for the younger (40 to 54 years) and oldest (75 years and older) groups (P <0.001 for both groups). Investigators also examined possible influence of the revised US Preventive Services Task Force (USPSTF) guidelines. In August 2008, USPSTF recommended limiting PSA screening in men 75 years and older because of the small likelihood of benefit at this advanced age. Dr. Zeliadt and colleagues noted decreased testing in the oldest age group, from 25.4% to 24.3% in the periods just before and just after the USPSTF update, respectively (P = 0.036). Men of other ages actually had a slight increase in PSA testing rates at this time, the study authors report.

*Medscape Medical News, 24 February 2011*

**DRUG WORKS IN MOST PROSTATE CANCER SUBGROUPS**

The investigational drug abiraterone acetate significantly improved outcomes in metastatic castrate-resistant prostate cancer in virtually every study-defined patient subgroup. Of 16 patient subgroups, a survival benefit with abiraterone was observed in 15.

Only in patients who had an Eastern Cooperative Oncology Group (ECOG) performance status of 2 did treatment with abiraterone fail to show a significant difference, Howard I. Scher, MD, chief of the genitourinary oncology service at Memorial Sloan-Kettering Cancer Center, in New York City, said at the 2011 ASCO Genitourinary Cancers Symposium.

Overall survival - the primary endpoint of the study - had been previously presented at the European Society for Medical Oncology in Milan last October.

The detailed subgroup analysis showed:

- 15.4-month overall survival among patients on abiraterone who had taken one previous line of chemotherapy, compared with 11.5 months for those on placebo, a 37% relative risk reduction (95% CI 0.51 to 0.78)

- 14.0-month overall survival among patients on abiraterone who had taken two previous lines of chemotherapy, compared with 10.3 months for those on placebo, a 26% relative risk reduction (95% CI 0.55 to 0.99)
- 15.3-month overall survival among patients on abiraterone with ECOG performance status of 0-1, compared with 11.7 months for those on placebo, a 36% relative risk reduction (95% CI 0.53 to 0.78)
- 7.3-month overall survival among patients on abiraterone who had an ECOG performance status of 2, compared with 7.0 months for those on placebo, a 19% relative risk reduction (95% CI 0.53 to 1.24).

He also reported significant differences in time to pain breakthrough, time to PSA progression, time to radiographic progression, and in PSA response.

While most of the data was presented in Europe, Oliver Sartor, MD, medical director of the Tulane Cancer Center in New Orleans and co-moderator of Scher's session stated that the new information on subgroups was encouraging.

*MedPage Today, 18 February 2011*

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