Nearly 70% of US Prostate Cancers Could Be Watched

More than two-thirds (68%) of all prostate cancers in the US qualify for active surveillance (AS), according to a study published in the September issue of the Journal of Urology (Vol.194, pp. 680-684). And if a more stringent definition of AS eligibility is used, 44% of cases would be candidates for monitoring instead of immediate treatment, say senior author Ian M. Thompson III, MD, from the University of Texas Health Science Center at San Antonio, and colleagues.

These “target” figures are especially credible because they come from a population-based study funded by the National Cancer Institute, and the 3,828 participants from Texas undergo regular PSA testing. The authors explain that most previous reports of the actual rates of AS are biased because they come from patient series at centers where men are treated or are derived from tumors detected at urology practices. The Texas cohort provides “an opportunity to determine what could be a national target for rates of eligibility,” write the study authors.

Of the 320 men in the cohort who developed prostate cancer from 2000 to 2012, 281 had data that were sufficient to allow scoring on very detailed surveillance scorecard. Disease characteristics, such as a high Gleason score, rendered 131/320 men ineligible for AS. But 123 men met a conservative set of criteria and were eligible for AS. These “lowest-risk” men had a PSA density below 15%, fewer than three cores involved with cancer, a Gleason score of 6 or less, and cancer involving 50% of biopsy volume.

The FDA is requiring companies that make testosterone products to conduct a large clinical trial to determine the true risks and benefits of using the hormone, the agency said. In a New England Journal of Medicine perspective, Christine Nguyen, MD, of the FDA, and colleagues wrote that their agency is encouraging testosterone drug makers to work together on one large randomized controlled trial. FDA had called for such trials last March, but much of the reporting at that time focused on the immediate change, which was an updated label for all testosterone products, highlighting potential risks.

Researchers have recently noted the discrepancy between hormone therapy for men and women, noting that the Women’s Health Initiative answered important questions about hormone replacement — including its risks of heart attack and breast cancer. There has not been an equivalent trial for men, experts pointed out.

“The way testosterone is practiced is 20 years behind what we’ve learned about women and the use of hormone therapy,” Cynthia Stuenkel, MD, of the University of California San Diego, stated last March. “Until there are clinical trials that look at outcomes such as heart attack, stroke, and death, and other really big outcomes — not just some of the more subtle surrogate outcomes — we won’t be able to answer those questions.”

(Continued on page 4)
Ibodronate Similar to Radiation for Treating Prostate Cancer Bone Pain

When radiotherapy (RT) for metastatic prostate cancer bone pain is not available, ibandronate may be another option, UK researchers suggest. A single ibandronate infusion provided as much pain relief as a single dose of RT in a phase III noninferiority trial reported online August 4 in the Journal of the National Cancer Institute.

“Prostate cancer patients with localized pain from bone metastases should continue to be offered single-dose RT, which may give optimal pain relief in the first four weeks after treatment, but a third generation bisphosphonate such as ibandronate given as a single intravenous (IV) dose could also give effective overall pain relief,” concluded Dr. Peter Hoskin of the Mount Vernon Cancer Center in Northwood, Middlesex, UK and colleagues.

Their study involved 470 men from 58 medical centers in the UK. The men were mostly older than 65 and had a life expectancy of more than three months. Between 2003 and 2009, participants were randomly assigned to receive either one dose of RT (8 Gy) or one IV infusion of ibandronate (6 mg). Both groups were similar in baseline characteristics and representative of men seen in routine practice, according to the authors.

Pain was assessed with the Brief Pain Inventory using World Health Organization (WHO) criteria and the Effective Analgesic Score (EAS). The maximum allowable difference was plus-or-minus 15%. Patients who didn’t respond at four weeks were offered retreatment with the alternative therapy, although “there was no material difference in the crossover rates,” the authors said.

Overall, pain response was not statistically different for ibandronate at four or 12 weeks (WHO: -3.7% versus 6.7%, respectively). Using the EAS, corresponding differences were -7.5% and -3.5%, respectively. Similar results were seen at 26 and 52 weeks. The initial response with RT was quicker, but quality of life scores on the FACIT-G v4.0 were similar in the two groups at four and 12 weeks — including scores on the physical, social, emotional, and functional subscales.

Although each treatment has different side effects, the authors found no overall difference in toxicity. The median overall survival was 12.2 months for the RT group and 12.9 months for the ibandronate group.

Reuters Health Information 25 August 2015

Couples-based Interventions Following Prostate Cancer Treatment – A Narrative Review

Nelson CJ, Emanu JC, Avildsen I

Transl Androl Urol 2015; 4: 232-242

Background/Objective:
Sexual dysfunction following prostate cancer (PC) treatment often results in sexual avoidance and a loss of sexual intimacy, which can lead to relationship distress. This review aims to evaluate six studies intended to address relational and sexual intimacy following PC treatment and discuss methodological concerns which may help produce more effective interventions.

Methods:
Electronic databases used to conduct literature searches included Medline, PsychINFO, and Web of Science. Studies were included if they were: randomized controlled trials (RCTs) using samples of men diagnosed with PC of any stage, had a psychosocial intervention, and addressed at least one sexual and relational outcome.

Results:
As a whole, the literature has produced mixed results. While significant findings were reported, many of the primary hypotheses were not achieved. The six studies show that men with PC may benefit from education and support related to treatment options for erectile dysfunction (ED), whereas their partners may benefit more from interventions focused on relational issues. Important methodological limitations included: selection of general outcome measures as opposed to measures specific to sexuality or intimacy outcomes, lack of assessing distress or bother of the patient/couples as study entry criteria, heterogeneity of study populations, and lack of innovative intervention content as the current studies tested standard educational interventions, sex therapy approaches, and couples therapy strategies with only marginal success.

Conclusions:
Interventions based on innovative theoretical approaches as well as study designs that address the outlined methodological limitations are needed in this area.
Doc Moyad's What Works & What is Worthless Column, Also Known As "No Bogus Science" Column –
"Pomegranate=Not impressive in Latest/Past Placebo Clinical Trial(s). Drink Coffee?"
Mark A. Moyad, MD, MPH, University of Michigan Medical Center, Department of Urology
Editor's Note:
Us TOO invites certain physicians and others to provide information and commentary for the Hot SHEET to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and are not necessarily those of Us TOO International.

**Bottom Line:**
A major randomized, double-blind clinical trial of pomegranate extract failed to significantly prolong PSA doubling times (PSADT) versus placebo in men with rising PSA after primary therapy.\(^1\) BAM! OUCH! YIKES! However, coffee consumption still looks groovy!

First, I think it is commendable and impressive how pomegranate companies have supported a good deal of research (do you feel a “but” or “however” coming on?). However, the bad news is that despite 10+ years of excitement in this area there were few long-term of placebo comparative trials and this is what worried me. It was also worrisome that when someone ingested pomegranate supplements (juice, pills…) no significant beneficial changes in weight/waist size, blood sugar, blood pressure, or LDL cholesterol occurred (heart healthy= prostate healthy Moyad ~ 1999). For these and other reasons, I have for years said that pomegranate could be getting too much hype and might not do well in rigorous clinical trials. Many people/experts that will remain nameless until I see them (and remind them) pushed the pomegranate agenda aggressively and I do not believe this was helpful. Regardless, here is the issue — after three high quality trials, it seems that pomegranate works no better than a placebo for most men. One study was in men with advanced prostate cancer,\(^2\) another was for men having surgery for cancer,\(^3\) and the third and more recent trial was for men with rising PSA after primary therapy.\(^3\) I have nothing more to say on this topic. The results speak or shout for themselves but as you finish reading this column let me ask you five questions that are more important than any pomegranate or supplement product. Do you know exactly your weight/waist size? Do you know exactly your last LDL cholesterol value? Do you know your blood sugar value? Do you know your blood pressure numbers? Do you know why Coach Harbaugh at Michigan will win the national title in 2017? Okay, that last question was more rhetorical but the first four questions matter and everything else in this column don’t matter much!

Oh, and in my semi-humble opinion, I would get more excited about coffee for prostate health compared to other beverages. Stay tuned until next issue — this should ensure that you will continue to read my column because I am that desperate for attention, constant admiration and love.

**References:**

**PSMA Expression is Highly Homogenous in Primary Prostate Cancer**
Tsourakis MC, Klein F, Kluth M, et al
Appl Immunohistochem Mol Morphol 2015; 23: 449-455

**Background:** Prostate-specific membrane antigen (PSMA) is a suggested target for antibody-based therapy of prostate cancer, potentially involved in the regulation of cell migration. As heterogeneity may limit the applicability of targeted therapies, this study was undertaken to estimate the degree of heterogeneity of PSMA expression in prostate cancer.

**Methods:** For heterogeneity analysis, a prostate cancer heterogeneity TMA containing samples from 10 different tumor blocks of 189 consecutive prostate cancers was used. PSMA expression was analyzed by immunohistochemistry.

**Results:** PSMA expression was found in 97.6% of 1,171 interpretable tissue spots including 260 (22.2%) with weak, 345 (29.5%) with moderate, and 538 (45.9%) with strong positivity. On a patient level, a positive PSMA immunostaining was found in 172 of 173 analyzable patients (99.4%) with at least a weak staining reaction. PSMA immunostaining was homogenously positive in 161 prostate cancers (93.6%), whereas heterogeneous PSMA positivity was seen in 11 of 172 positive cases (6.4%). In these cases, heterogeneity was intrafocal in eight cases (72.7%) and interfocal in 27.3% cases. PSMA expression was completely absent in one patient.

**Conclusions:** Given the high frequency and high homogeneity of PSMA expression in prostate cancer, we conclude that increased PSMA expression may occur early in prostate cancer development. High homogeneity of PSMA expression is a strong argument for a high utility of PSMA as a prostate cancer drug target.

**How the ‘Heat’ Compound from Chili Peppers Could Help Kill Cancer Cells**
Capsaicin, the compound responsible for chilis’ heat, is used in creams sold to relieve pain, and recent research shows high doses kill prostate cancer cells. Now researchers are finding clues that help explain how the substance works. Their conclusions suggest that one day it could come in a new, therapeutic form. Their study appears in ACS’ The Journal of Physical Chemistry B.

About 10 years ago, researchers reported that capsaicin can kill prostate cancer (Continued on page 8)
Nerve-Sparing Technique Preserves Continence after Radical Prostatectomy

Preservation of the neurovascular bundles (NVBs) during radical prostatectomy (RP) preserves erectile function, but its effects on continence remain controversial. Some have argued that nerve-sparing techniques, not preservation of the neurovascular bundles (NVBs), are responsible for improved continence rates.

In an effort to resolve this question, Dr. Uwe Michl and colleagues, from University Hospital Hamburg-Eppendorf, Hamburg, Germany examined long-term continence rates of men who underwent primary non-nerve-sparing RP (NNS RP; 1,128 men), nerve-sparing RP with preservation of the NVBs (NS RP; 11,204 men), and initially nerve-sparing RP with secondary resection of the NVBs (secNNS; 201 men).

At 12 months after surgery, urinary continence rates (defined as zero or one safety pad daily) were 85.4% in the NS RP group, 87.0% in the secNNS group, and 70.5% in the NNS RP group. The 12-month continence rates did not differ significantly between the NS RP and secNNS groups (p=0.5), but continence rates were significantly higher in the secNNS group than in the NNS RP group (p=0.001).

Early continence rates (one week and three months) were higher in the NS group than in the secNNS group, but these differences were no longer evident at 12 months. Multivariable logistic regression analysis and propensity-matched analyses yielded similar results, according to the August 12 European Urology online report.

“Our results indicate that the meticulous apical dissection associated with the NS RP technique rather than the preservation of the NVBs itself may have a positive impact on long-term urinary continence rates,” researchers concluded. “We confirm that preservation of NVBs is important for early continence, and thus a NS approach should be attempted whenever safe oncologically.”

Dr. Gunnar Steineck, from Sahlgrenska Academy at the University of Gothenburg, Sweden, recently reported that the degree of preservation of the NVBs is important in determining continence after RP. He said, “We know it is better to preserve two bundles instead of one and do a partial preservation instead of none.”

He advised, “Consider carefully if it is necessary to injure each of the two neurovascular bundles. Take the time needed to preserve. Make those administering and financing surgery aware of the new data.”

“Not seldom prostate-cancer surgery implies a trade-off between preservation of some part of one or both bundles and possibilities to extirpate the tumor radically,” Dr. Steineck concluded. “We must improve our means to bring the patient into the decisional process for this trade-off. We know patient preferences vary greatly.”

Reuter Health Information
25 August 2015

Nationally Representative Trends and Geographic Variation in Treatment of Localized Prostate Cancer – The Urologic Diseases in America Project

Cary KC, Punnen S, Odisho AY, et al
Prostate Cancer Prostatic Dis 2015; 18: 149-54

Background: Several treatment options for clinically localized prostate cancer currently exist under the established guidelines. We aim to assess nationally representative trends in treatment over time and determine potential geographic variation using two large national claims registries.

Methods: Men with prostate cancer insured by Medicare (1998-2006) or a private insurer (Ingenix database, 2002-2006) were identified using International Classification of Diseases-9 and Current Procedural Terminology-4 codes. Geographic variation and trends in the type of treatment utilized over time were assessed. Geographic data were mapped using the GeoCommons online mapping platform. Predictors of any treatment were determined using a hierarchical generalized linear mixed model using the logit link function.

Results: The use of radical prostatectomy increased, 33-48%, in the privately insured i3 database while remaining stable at 12% in the Medicare population. There was a rapid uptake in the use of newer technologies over time in both the Medicare and i3 cohorts. The use of laparoscopic-assisted prostatectomy increased from 1% in 2002 to 41% in 2006 in i3 patients, whereas the incidence increased from 3% in 2002 to 35% in 2006 for Medicare patients. The use of neoadjuvant/adjuvant androgen deprivation therapy was lower in the i3 cohort and

FDA to ‘Low T’ Drug Makers: Prove It

(Continued from page 1)

Nguyen and colleagues re-capped the evidence base – or lack thereof – for testosterone products over the years. They noted in 2002 that an Institute of Medicine report said there was no definitive evidence that boosting testosterone levels in older men was beneficial or safe.

Recent studies have come to different conclusions, but the FDA issued the label changes last March after an advisory committee expressed concerns over the lack of evidence on safety and efficacy in the face of excessive direct-to-consumer marketing campaigns for “Low T.”

“Serum testosterone appears to decline as men age, and although this decline is usually modest, concentrations can fall below the normal range for healthy young men,” they wrote. “In these cases, it is unclear whether coexisting nonspecific signs and symptoms, such as decreases in energy and muscle mass, are a consequence of the age-related decline in endogenous testosterone or whether they are a result of other factors, such as coexisting conditions, concomitant medications, or perhaps aging itself.”

The FDA-required clinical trial – or trials, if the companies decide not to work together – will be conducted as several testosterone drug makers appear in court to face consolidated lawsuits from nearly 2,000 men who believe they suffered heart attacks and other adverse effects after taking the drugs.

The first of six so-called bellwether trials will begin in October 2016, and AbbVie, which makes the popular AndroGel®, will be the first company to go on trial.

MedPage Today
20 August 2015
New Drug-Like Compounds May Improve Odds of Men Battling Prostate Cancer

Researchers at Southern Methodist University, Dallas, have discovered three new drug-like compounds that could ultimately offer better odds of survival to prostate cancer patients. The drug-like compounds can be modified and developed into medicines that target a protein in the human body that is responsible for chemotherapy resistance in cancers, said biochemist Pia D. Vogel, lead author on the scientific paper reporting the discovery.

So far, there’s no approved drug on the market to reverse chemotherapy resistance caused by P-glycoprotein, or P-gp for short, said Vogel, a biochemistry professor at SMU. One potential drug, Tariquidar, is in clinical trials, but previous potential drugs have failed at that stage.

“The problem when a person has cancer is that the treatment itself is composed of cellular toxins -- the chemotherapy that prevents the cells from dividing. Usually upon the first chemo treatment the cancer responds well, and initially goes away. Ideally it doesn’t come back,” said Vogel, who is director of SMU’s Center for Drug Discovery, Design, and Delivery.

“Sometimes, however, the cancer returns,” she said. “The reason often is that some of the cancer cells “learn,” after the first rounds of chemotherapy, how to make a lot of this P-gp pump. The normal function of P-gp is to pump toxins from cells. After initial exposure, the cells surviving the chemo therapy make so much P-gp that it allows the cells to pump the chemotherapy drugs straight back out of the cells during subsequent rounds of treatment.” As a result, P-gp causes resistance of the diseased cells to a majority of drugs currently available for the treatment of cancer, as well as drugs used for treatment of infectious diseases like HIV/AIDS.

Using computer-generated model speeds up the drug discovery process. The new drug-like compounds discovered by Vogel and her co-authors offer hope that using a computer-generated P-gp model, explained here, developed to accurately mimic the physical, chemical and biological functions of the protein in the human body, will speed up the drug discovery process and work in real life as well.

“These are not drugs yet. We still have to develop them before they can go in the clinic,” Vogel said. “But what we know now is that they’re not toxic -- they have low toxicity to noncancerous cells, so that’s a pretty good predictor that they may be good candidates for drug development. But we need to do much more work.”

A pharmaceutical hit compound, like those discovered by Vogel and her co-authors, is a compound that is a promising candidate for chemical modification so it can eventually be delivered to patients as a therapeutic drug. The timeline from drug discovery to development to clinical trials and approval can take a decade or more.

Vogel and her co-authors, reported their findings online in the journal Pharmacology Research & Perspectives.

Study details

The SMU researchers discovered the three hit compounds after virtually screening more than 15 million small drug-like compounds made publically available in digital form from the phar-
Reversing Chemotherapy Resistance
(Continued from page 5)

macology database Zinc at the University of California, San Francisco.

Using SMU’s ManeFrame high performance computer, Wise ran the compounds through a computer-generated model of P-gp. The virtual model, designed and built by Wise, is the first computational microscope of its kind to simulate the actual behavior of P-gp in the human body, including interactions with drug-like compounds while taking on different shapes.

The ultra-high throughput computational searches by ManeFrame led the researchers to 300 compounds that looked like they may inhibit P-gp. The researchers then tested 38 of those in their physical lab and found four that inhibited the biochemical function of P-gp, stopping it in its action.

Each of the four compounds was then tested in the lab to see how it would affect a line of prostate cancer cells relatively sensitive to the chemotherapeutic Paclitaxel, commonly used to treat prostate cancer patients. Also, each was tested on a companion cell line already multi-drug resistant, as if the patient already had undergone chemotherapy using Paclitaxel.

Researchers found that with three of the four compounds, they were able to push back the sensitivity of the resistant cancer line to the level of the non-resistant one. “So the compounds re-sensitized the cancer cell lines to a really high degree, just as if the cancer was seeing the chemotherapy for the first time,” Vogel said.

Medical News Today 9 September 2015

Comparison of Continence Outcomes of Early Catheter Removal on Postoperative Day 2 and 4 after Laparoscopic Radical Prostatectomy – A Randomized Controlled Trial

BMC Urol 2015; 15, Epub

Background: The optimal timing of catheter removal following laparoscopic radical prostatectomy (LRP) has not yet been determined. This prospective study was designed to compare the efficacy and safety of catheter removal on postoperative day (POD) 2 vs. POD 4 after LRP and its impact on urinary continence outcomes.

Methods: One hundred and thirteen patients underwent LRP and were prospectively randomized into two groups: group 1 (n = 57) had the urinary catheter removed on POD 2 while group 2 (n = 56) had the catheter removed on POD 4. The urine loss ratio (ULR) was defined as the weight of urine loss in the pad divided by the daily micturition volume. Continence was defined as a pad-free status.

Results: No significant differences were observed in clinical features between groups 1 and 2. Acute urinary retention (AUR) after catheter removal occurred in 21 patients (18.6 %) (13 [22.8 %] in group 1 and 8 [14.3 %] in group 2 (p = 0.244). The first-day mean ULR values were 1.16 ± 4.95 in group 1 and 1.02 ± 3.27 in group 2 (p = 0.870). The last-day mean ULR was defined as the pad-free status.

(Continued on page 8)

Unaggressive Prostate Tumors
(Continued from page 1)

Those in the program were 24 times more likely to die from a cause other than prostate cancer over the 15-year follow-up, results showed.

For the study, urologists performed annual biopsies on all the men in the study group until the age of 75. This differs from today, where biopsies are only done in the riskier groups. When they are performed, doctors use MRI technology. Pathologists then check biopsy tissue for biomarkers of prostate cancer aggressiveness – proteins made by the PTEN gene.

The researchers reclassified 36% of the study participants to a more aggressive prostate cancer grade within two years of enrollment to the AS program. For men with very low-risk cancers – which would have usually precluded enrollment in the program – the cumulative risk of a grade reclassification was as follows:

- Over 5 years - 3%
- Over 10 years - 21%
- Over 15 years - 22%

For men with low-risk cancers, the risk of grade reclassification was:

- Over 5 years - 19%
- Over 10 years - 28%
- Over 15 years - 31%

The study reveals that the cumulative risk of a grade reclassification to a level that would be considered potentially lethal in most cases, but still curable, was no more than 5.9% for men with both very low and low-risk prostate cancers.

Despite the absence of significant change in their prostate cancer status, 109 men opted for surgical or radiation treatment. Among those whose cancers were reclassified, 361 opted to receive local treatment.

There is a careful balance, which is sometimes difficult to find,” Dr. Carter says, “between doing no harm without treatment and over-treating men, but our data should help. The ability to identify men with the most indolent cancers for whom surveillance is safe,” says Dr. Carter, “is likely to improve with better imaging techniques and biomarkers.”

Dr. Carter added “Our study should reassure men that carefully selected patients enrolled in AS programs for their low-risk prostate cancers are not likely to be harmed by their disease.”

Dr. Carter warns that the study outcomes may be confounded by two factors: the careful selection process for AS and the fact that no African-American men took part, who tend to have more aggressive cancers.

The study reveals that 30-40 percent of US men opt for AS compared with as many as 80% of men in Scandinavian countries. Dr. Carter says that the reasons for lower use of AS in the US may stem from fear of losing the opportunity for a cure.

The study concludes that a urology specialist should monitor men with low-risk prostate cancer in an AS program. Best practice guidelines for doctors, developed by the National Comprehensive Cancer Network (NCCN) – a group of the top cancer centers in the US – recommend AS.

Medical News Today 1 September 2015
Active surveillance (AS) again takes center stage in this month’s Hot SHEET with two interesting articles.

**a1p1c1** The first article is a large cohort study of nearly 1,300 men from Johns Hopkins Hospital. They found that over a 15 year period, only two men died and three developed metastatic disease when initially managed by AS. In contrast, 47 men died of other causes during this time. With careful monitoring, some men will have an increase in tumor grade, which for now remains one of the most widely used criteria for stopping AS. Whether or not that is the best one to use remains uncertain. One shortcoming of this study is that the median follow-up is only about five years so the long-term results may worsen as longer follow-up occurs. Also, this cohort contained no African-American men and uncertainty remains for that group. Still, it adds more strength to the belief that AS is not a death sentence and done properly, many men can safely delay therapy or avoid it altogether. Of note here is the large disparity between the risks of dying from prostate cancer vs. dying from other causes, which does not seem to get enough attention by the men who get diagnosed with the disease. Many of them obsess about their cancer while paying much less attention to their overall health and taking actions that could help prolong their life. Diet and exercise have proven health benefits for lowering cardiovascular risk, by far the greatest risk in the general population and yet few men make the lifestyle changes needed to reduce their chance of dying from non-cancer causes.

**a2p1c2** The second article is a population-based study from Texas. The authors followed nearly 4,000 men between 2000 and 2012 that had regular PSA exams. Sufficient data were available on 281 who were diagnosed with prostate cancer. Using Johns Hopkins criteria for low risk disease, 38% had low risk disease and another 24% met slightly higher risk criteria but were still considered candidates for AS. Since many of the men chose to undergo surgery, information was available to compare the initial and final pathology. Not surprisingly, about one-third of the cases had a higher Gleason score on the final reading. This continues to be a major issue for physicians concerned about the risks of AS who argue that biopsies underestimate the level of risk and is therefore jeopardizing those men if they do not have aggressive therapy. However, if that were a real concern then the death rate should have been much higher in the groups of men that chose long-term conservative therapy and that has not been the case. The authors acknowledge that their study was not used. That may be why the oral preparation was not used. That makes the lifestyle changes needed to reduce their chance of dying from non-cancer causes.

**a3p1c3** Growing concerns are occurring over the use of testosterone (T) replacement therapies. Extensive marketing around the country have led many men to get this treatment, often when they don’t even meet the criteria for low T. Now the FDA has indicated that the companies making these products need to conduct a large prospective study to define the risks and benefits, as has been done for hormone replacement therapies in women. The concerns about treating low T have escalated to the point that lawsuits have occurred. While these studies are ongoing, it will take several years for their completion. Any man who is told he should receive replacement T should be sure he meets the criteria of having a low T level and he should be made aware of the uncertainty regarding the risks.

**The Bottom Line:** Ibudronate appears to offer a similar reduction in bone pain for men with metastases and should be considered when men have significant symptoms.

**a5p2c2** Another important, but inadequately addressed problem is sexual dysfunction facing men treated for prostate cancer and its effect on their significant other. The article by Nelson, et al serves to illustrate the problem by reporting that not enough research is being done in this area. I personally think the problem often starts even before treatment is given because many doctors do not provide sufficient counseling about expectations or the correct odds that sexual dysfunction can occur. Clearly more work is needed in this area and doctors should spend more time communicating with their patients and partners about both initial and ongoing problems.

**The Bottom Line:** More work is needed to help men and their partners understand the risk of treatment-related sexual dysfunction.
Capsaicin (Continued from page 3)
cells in mice while leaving healthy cells unharmed. But translating that dose to humans would require them to eat a huge number of chili peppers per day. Figuring out how capsaicin works could help researchers transform it into an effective drug in the form of an injection or pill. It is known that the molecule binds to and affects the cell membrane. That prompted Ashok Kumar Mishra and Jitendriya Swain to investigate the mechanism of capsaicin’s effects so it might be harnessed in the future for new medicines.

By monitoring its natural fluorescence, they showed that capsaicin at a sufficiently high dose ruptures the cell membranes. With additional research, this insight could help lead to development of novel tools against cancer or other conditions.

Medical News Today
10 September 2015

Catheter Removal (Continued from page 6)
ULR values were 0.57 ± 1.60 in group 1 and 2.78 ± 15.49 in group 2 (p = 0.353). Continence rates at 3, 6, 9, and 12 months were 21.8, 41.1, 58.0, and 71.4 % in group 1 and 34.5, 66.0, 79.2, and 83.7 % in group 2 (p = 0.138, 0.009, 0.024, and 0.146, respectively). In AUR cases, continence rates at 3, 6, 9, and 12 months were 0, 23.1, 38.5, and 54.5 % in group 1 and 37.5, 75.0, 87.5, and 87.5 % in group 2 (p = 0.017, 0.020, 0.027, and 0.127, respectively). A multivariate analysis identified AUR after catheter removal on POD 2 as the only predictive factor for incontinence 6 and 9 months after LRP (p = 0.030 and 0.018, respectively).

Conclusions: Our results demonstrated that early catheter removal on POD 2 after LRP may increase the risk of incontinence.

Geographic Variation (Continued from page 4)
has decreased over time in both i3 and Medicare. Physician density had an impact on the type of primary treatment received in the New England region; however, this trend was not seen in the western or southern regions of the United States.

Conclusions: Using two large national claims registries, we have demonstrated trends over time and substantial geographic variation in the type of primary treatment used for localized prostate cancer. Specifically, there has been a large increase in the use of newer technologies (that is, laparoscopic-assisted prostatectomy and intensity-modulated radiation therapy). These results elucidate the need for improved data collection on prostate cancer treatment outcomes to reduce unwarranted variation in care.

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