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NEWSLETTER

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♦ AGENT ORANGE AND THE BLUE WATER NAVY ♦

Service members who served in Vietnam between January 9,1962, and May 7,1975, are presumed to have been exposed to Agent Orange, the defoliant used extensively during the Vietnam War. Should they subsequently be diagnosed with prostate cancer or one of 12 other diseases associated with such exposure, their conditions are presumed due to that exposure. They need only provide evidence of such service and the appropriate medical diagnosis to receive tax-free compensation and other related benefits.

Large ocean-going naval vessels, the so-called "Blue Water Navy" and their crews are not presumed to have been exposed to Agent Orange or other herbicides, although some of these ships docked in harbors or otherwise operated in Vietnamese coastal waters. Consequently, the crew members are not entitled to the Agent Orange-related benefits provided by the Veterans Administration. An estimated 90,000 Vietnam veterans served off the coast of Vietnam during the prescribed period. They are not entirely without recourse.

These "Blue Water" veterans, who did **not** set foot in Vietnam or serve aboard ships that operated on the inland waterways of Vietnam anytime between January 9, 1962, and May 7, 1975, **must show on a factual basis** that they were exposed to herbicides during military service to receive disability compensation for diseases related to Agent Orange exposure. These claims are decided on a case-by-case basis.

The battle to obtain parity for "Blue Water Navy" veterans is not over. Veterans advocacy organizations have challenged the several VA decisions in federal court for decades. The case of *Gray vs. Secretary of Veterans Affairs,* No. 16-1782 is still before the U.S. Court of Appeals. (Source: Blue Water Navy and Agent Orange; *MILITARY OFFICER,* March, 2018, pp 94-96)

♦ *INSIDE THIS ISSUE* ♦

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♦ FROM THE EDITOR ♦

NEWSLETTER CONTENT

Our quarterly meetings have long had a guest speaker whose remarks were included in the subsequent newsletter. We no longer can provide a verbatim transcript of these presentations. Instead, we have relied on the speakers' slides to summarize their remarks. This method can affect the accuracy of the information presented. We regret that we will no longer include the speakers' presentations in the newsletter until such time we regain the capability to present a verbatim transcript.

Our quarterly meetings are linked by video teleconferencing between Walter Reed, Bethesda, and the Fort Belvoir Community Hospital. Unfortunately, technical difficulties forced the cancellation of our February 1 meeting. We regret the inconvenience it caused to those in attendance.

♦ MEETING SCHEDULE FOR MAY 3, 2018 ♦

Our speaker for Thursday, May 3, 2018, is Jennifer Cullen, PhD, MPH, Center for Prostate Disease Research, WRNMMC. Her topic is **"The Critical Role of Patient-Reported Outcomes in Improving Decision-Making for the Treatment of Prostate Cancer**." (Dr. Cullen was the scheduled speaker for the cancelled February meeting.)

Please join us at the America Building (Bldg 19), 2nd floor, Room 2525, WRNMMC (primary site) at 7:00 PM; or the Fort Belvoir Community Hospital, Oaks Pavilion, 1st floor, Library Lecture Room (S1.901) (via video teleconference).

Remember, your family members and friends are welcome to attend.

See the back page for information about getting access.

♦ PROSTATE SPECIFIC ISSUES ♦

FDA Warns Against Unapproved Erectile Dysfunction Products. Unapproved erectile dysfunction drugs are touted as a "healthy man alternative to the little blue pill." The FDA has issued a warning that unapproved erectile dysfunction (ED) drugs containing 100 mg sildenafil, the active ingredient in Viagra, are being advertised over broadcast and internet radio without a prescription.

The sildenafil dosage is particularly dangerous for the elderly and those with impaired liver or kidney function. When sildenafil interacts with nitrates, blood pressure can plummet.

The drugs are touted as a "healthy man alternative to the little blue pill,"or "healthy man," or "the power pill," according to the FDA. Acme Generics in India is the manufacturer, but the label also bears the name Sun Pharma. The seller may also be distributing unapproved tadalafil.

Although no adverse events have been reported, health care professionals are urged to report any adverse events to FDA's *MedWatch*. (Source: FDA News Release, March 16, 2018, via Renal and Urology News, March 20, 2018)

Therapeutic Sexual Aids are Scarce for Cancer Survivors. In contrast to other widely available cancer care products, sexual aids and resources are rarely available at cancer centers nationwide, according to a new study.

Treatment-related sexual dysfunction is a significant and distressing problem for many cancer survivors. National Comprehensive Cancer Network (NCCN) treatment guidelines recommend therapeutic aids for sexual health rehabilitation, such as vaginal dilators, moisturizers, and vacuum erection devices. However, cancer survivors are often uncomfortable or uninformed about how and where to obtain sexual aids.

Studies suggest that sexual dysfunction is one of the most common and distressing consequences of treatment, affecting between 50 percent and 90 percent of adult survivors, depending on type of treatment. A new study of 25 leading cancer centers found that 87 percent of the centers reported having no sexual aids available on site for men, and 72 percent reported having no aids for women, noted lead author Sharon Bober, PhD, a psychologist at the Dana-Farber Cancer Institute in Boston, during a presscast ahead of the 2018 Cancer Survivorship Symposium.

"There are many types of cancer treatments that can affect sexual health, for example, surgery or radiation to the pelvic region, which occur frequently with gynecologic or genitourinary cancers, or chemotherapy that causes sudden, premature menopause," Bober noted. "Guidelines advocate for doctors to inquire about sexual function, but unfortunately, that seldom happens."

The researchers contacted staff at 25 NCI-designated cancer centers/NCCN member institutions about the availability of sexual aids and resources for survivors. Potential sources of aids and resources at each center, such as custom boutiques and specialty retail shops, were identified using the phone and internet. Staff members at the boutiques was queried by phone to

see if they had sexual aids available for men and, in a separate call, for women. If the centers did not have sexual aids available, there was a follow-up call to see if they had recommendations for how survivors could access those resources.

Of the 25 centers contacted, 23 responded about aids for men, and 22 responded about aids for women. The majority of centers (72%) reported no therapeutic aids available for women. The staff was uncomfortable when asked about further resources, such as pamphlets. Results were similar for men—87 percent of centers had no sexual aids, and only one center had three or more products.

One center carried a vacuum device and two had penile support rings. Six centers had some aids for women, most commonly reported were personal lubricants, moisturizers, and dilators. One center stood out, having several types of aids for men and women. If a center had no aids, their recommendations were usually for people to do an internet search or visit a local pharmacy to obtain the aids.

“By and large, medical professionals do not regularly talk about sexual health, and we know that distressing problems are not consistently addressed,” Bober noted. “We need to normalize these conversations, and providing sexual aids is one step toward treating sexual health like any other aspect of survivorship care. It should be no different than providing wigs and head coverings to women who have lost their hair due to chemotherapy. It's important to give patients the message that regaining sexual health is a perfectly valid and life-affirming aspect of regaining overall quality of life.”

What to do? “What we really need to do is go to the centers that are successfully providing sexual health products and find out how they promote and provide resources to their patients. We can't keep the conversation at the 10,000-foot level—we need to talk concretely about how to partner with providers to make sexual health resources, including sexual health aids, available so cancer survivors can get the help that they need,” said Bober.

The one center that had an extensive list of products and resources for men and women could potentially serve as a model, she said. “The scarcity of sexual aids underscores the cultural taboos around cancer-related sexual dysfunction, as does the discomfort of responders. More availability of sexual aids at cancer centers would likely promote sexual rehabilitation. Providers may be more likely to recommend aids, and patients would have greater access,” Bober explained.

One observer commented that cancer can disrupt sex lives of patients. All too often, medical professionals don't take into account the sexual health of cancer survivors. This study illuminates how far we still have to go in this area. We have to be more diligent as physicians in helping our patients find the best tools and resources to be sexually healthy. (Source: *Oncology Times,* Volume 40, Number 6, March 20, 2018)

The Digital Rectal Examination at the Primary Care Level. The digital rectal examination (DRE) inadequately identifies risk for prostate cancer on a population level, according to a meta-analysis that compared DRE indications of elevated risk with biopsy outcomes. The DRE and prostate-specific antigen (PSA) measurement form the basis of population screening for

elevated risk for prostate cancer. Both procedures may be part of a well-care visit to a primary care provider.

Studies have suggested DREs are associated with a high rate of false-positives and no reduction in prostate cancer mortality, while subjecting patients to unnecessary and invasive follow-up procedures and perhaps over-diagnosis and over-treatment of prostate cancer. Despite questions about DRE benefits, a recent survey found that 81.0% of primary care physicians in Canada report using it in their clinics.

To better understand the effect of DRE, Leen Naji, MD, et al, Department of Family Medicine at McMaster University, Hamilton, Ontario, conducted a systematic review and meta-analysis of the diagnostic accuracy of DRE administered in the primary care setting as a screen for prostate cancer.

The researchers reviewed several databases for the terms "prostate cancer," "digital rectal examination," and "biopsy" in studies and systematic reviews that evaluated the effectiveness of DRE in screening for prostate cancer by primary care clinicians.

Their meta-analysis, published in the March/April issue of the *Annals of Family Medicine*, included 7 studies that enrolled a total of 9,241 patients who underwent a DRE. Diagnosis of prostate cancer was based on prostate biopsy.

The researchers concluded that a DRE as performed by primary care providers does not meet the World Health Organization criterion of benefits of a screening test outweighing harms.

"On the basis of the lack of evidence supporting its use, we do not recommend routinely using DRE as a screening tool for prostate cancer in primary care, unless it is proven effective in future studies. Additionally, although we did not study possible harms of DRE, its invasiveness and potential to lead to unnecessary biopsy, over-diagnosis, and over-treatment argue against its routine use," the researchers concluded. Limitations of the meta-analysis include the variability of the studies, in terms of who actually performed the DREs; absence of an accepted universal definition of abnormal DRE; and the lack of controls. Also, the false-negative rate could not be ascertained because men with negative results didn't progress to biopsy. (Source: Annals of Family Medicine; 2018;16:149-154)

Nine-Year Prostate Cancer Survival Differences Between Aggressive Versus Conservative Therapy in Men with Advanced and Metastatic Prostate Cancer. The survival benefit of local therapy in the setting of advanced prostate cancer remains unknown. The authors investigated whether prostate-directed treatment with either surgery or radiotherapy versus conservative treatment (androgen deprivation therapy) in the setting of locally advanced or metastatic disease was associated with improved survival.

Men diagnosed with locally advanced (cT3-T4 or N+ and M0) or metastatic prostate cancer were identified. The authors compared survival by treatment type, categorized as conservative (androgen deprivation therapy only) versus aggressive (radical prostatectomy or any type of radiotherapy). Nine-year overall survival and prostate cancer-specific survival were estimated using the Kaplan-Meier method. The Cox proportional hazards model was used to determine factors independently associated with 9-year prostate cancer-specific survival.

For men with advanced, nonmetastatic prostate cancer, conservative treatment alone was associated with a 4 times higher likelihood of prostate cancer mortality compared with men treated with surgery. In contrast, no difference was found between conservative versus aggressive treatment after adjusting for covariates for men with metastatic disease. The 9-year prostate cancer-specific survival rate was 27% for those receiving aggressive treatment versus 24% for men undergoing conservative treatment.

In summary, the authors did not observe a survival advantage with local therapy in addition to standard androgen deprivation therapy for men with metastatic prostate cancer. However, the results of the current study did affirm advantages in the setting of locally advanced disease. Aggressive local therapy in the setting of metastatic disease needs to be studied carefully before clinical adoption. (Source: *Cancer,* March 2, 2018, via www.ncbi.nlm.nih.gov.pubmed)

Routine Use Of Adjuvant Radiation After Positive Surgical Margins After Radical Prostatectomy: Not For All! Dr. Marc Dall'era gave a very interesting talk elaborating why not all patients with positive surgical margins (PSM) after radical prostatectomy (RP) should receive adjuvant radiation therapy. He began his talk with several important arguments why adjuvant treatment is nor for all. First, not all men with PSM recur, not all PSM are the same, early salvage may be just as good; next, the significant cost of adjuvant radiotherapy; and the argument that novel imaging and biomarkers will help identify men at risk who should be treated.

Dr. Dall'era mentioned the 3 prospective randomized trials assessing adjuvant radiotherapy after RP. These include the SWOG 87-94, EORTC 22911, and ARO 96-02. According to Dr. Dall'era, 30-35% of men in the SWOG and EORTC trials had persistent PSA after RP, making the treatment of radiation fall under the category of salvage and not adjuvant. Furthermore, only the ARO 96-02 required undetectable PSA at enrollment. Additionally, a substantial number of men in the control arm of these trials never recurred. Only the SWOG trial showed an overall survival advantage for adjuvant radiotherapy, and lastly, the patients in the control arms of all these trials generally received salvage radiotherapy later on.

Dr. Dall'era stated that these 3 randomized trials don't answer the question of whether all men with PSM need adjuvant radiotherapy. Some retrospective data show that up to 45% of men with PSM will not recur in a follow-up time of more than 10 years. Recent evidence also demonstrates that after 20 years of follow-up, no difference was seen in distant metastasis and overall survival in patients with PSM that received adjuvant radiotherapy, compared to those who didn't. There is a difference in the types of PSM, and it is also known that Gleason score of 4 and above at the margin has a much more substantial risk of prostate cancer-specific mortality than lower Gleason scores.

A description on the Decipher genomic classifier test was also given as a possible way to mark those patients at risk for recurrence which should be treated with adjuvant radiotherapy. Additionally, the usage of ultrasensitive PSA could be enlisted to help us decide who needs to be treated. Almost 100% of men with any postoperative ultra-sensitive PSA over 0.03 had eventual clinical biochemical recurrence (BCR).

Dr. Dall'era concluded his presentation by summarizing these points: Not all men with PSM recur, not all men with BCR progress to clinical recurrences or death. According to Dr. Dall'era, it is important to adopt a risk stratified approach and take into account the grade and length of

PSM, the value of ultrasensitive PSA at 3 months postoperatively, measure time to PSA recurrence, and use novel biomarkers and imaging to improve care and choose the appropriate patients for adjuvant radiotherapy. Lastly, it is important to note, that early salvage radiotherapy may work just as well with less overtreatment. (Source: Written by Hanan Goldberg, MD, Urologic Oncology Fellow, University of Toronto, Princess Margaret Cancer Center; Presented by Marc Dall'era at the 37th Congress of Société Internationale d'Urologie - October 19-22, 2017, Lisbon, Portugal)

Survival Outcomes of Younger Men (55 Years) Undergoing Radical Prostatectomy. While prostate cancer is typically a disease of older men with prevalence increases with each decade of life, it can and does occur in younger men. As these men are younger, treatment options are usually more easily accessible and more options are available. However, quality of life also plays an important role.

In this study, the authors focus on younger men (age < 55) diagnosed with prostate cancer to identify how they differ from their older counterparts. Specifically, they focused on the outcomes of men younger than 55 undergoing radical prostatectomy. Data was obtained from the Victorian Cancer registry, encompassing all patients with cancer diagnosis from 2004 to 2014. In that time period,109 were between 35 and 44 while 1,998 were between age 45 and 54. They were then compared against men between ages 55 and 74.

On univariate analysis, men under age 55 had higher rates of Gleason<= 7 disease and <= cT2 disease, while having similar median PSA values at the time of diagnosis. On multivariate analysis, adjusting for Gleason grade, T-stage and PSA, men between 45-54 had an improved overall survival, but this difference was not seen in men age 35-44. The 5- and10-year overall survival was higher for men 45-54 than men age 55-74. Unfortunately, the multivariate analysis was not listed, so these results could not be verified.

However, in terms of events and 5- and 10-year CSS, younger men had much fewer events and much better CSS.

There are many questions that need to be addressed. First, what was the median follow-up? Young patients are unlikely to die of other causes in that same time frame – hence overall survival may not be a very good outcome to measure. Additionally, much younger patients developing prostate cancer may have some genetic predisposition that was never assessed – those patients may affect the survival outcomes. Stage-matched survival also would have been more useful to present.

While important to understand, further analysis needs to be done to tease out the difference. (Source: Thenappan Chandrasekar, MD, Clinical Fellow, University of Toronto; at 37th Congress of Société Internationale d'Urologie - October 19-22, 2017- Lisbon, Portugal via UroToday, March 8, 2018)

Current PSA Monitoring Ignores Risk to Some Prostate Cancer Survivors. Prostate cancer survivors make up the largest group, 41 percent, of male cancer survivors. In these survivors, early detection of recurrence can lead to life-saving interventions, but in older men who

survived low-risk cancer and have limited life expectancy, those same interventions may do more harm than good.

However, when Walter, et al, University of California, San Francisco, analyzed current monitoring practices, they found that doctors use a one-size-fits-all approach to monitoring – performing the same frequency of testing regardless of a survivor's health and prognosis. In a new study, the researchers recommend that doctors individually tailor how often older prostate cancer survivors who have undergone curative treatment are monitored for disease recurrence.

This is the first study suggesting a need for guidelines to encourage prostate-specific antigen (PSA) monitoring that considers life expectancy, risk of recurrence, and the values and preferences of cancer survivors rather than a one-size-fits-all approach.

After surgery or radiation, some data suggest the interventions given just after early detection of recurrence based on elevated PSA levels may improve survival. But PSA monitoring may lead to complications from invasive diagnostics or treatment and may even be unnecessary in older men with a history of low-risk cancer or limited life expectancy.

In the study, the researchers examined the national VA and Medicare data of 13,397 men age 65 or older diagnosed with prostate cancer between January 1, 2003, and December 31, 2008, and treated with radiation or radical prostatectomy. All participants were followed for four years after their one-year treatment anniversary date.

Men with limited life expectancy treated for low-risk cancer are least likely to experience disease recurrence in their lifetime, making them the most likely to experience harms of PSA monitoring without benefit. However, these men received only marginally fewer PSA tests per year compared to men with longer life expectancy treated for high-risk cancer, the group most likely to benefit from monitoring.

The researchers note that the most consistent predictor of monitoring frequency was time since treatment, slightly decreasing every year, rather than any patient characteristic. The narrow range of PSA monitoring frequencies across patient and tumor characteristics indicates little individualization in how clinicians currently monitor for prostate cancer recurrence in older men.

Most of the men received approximately two PSA tests per year, which is consistent with current guidelines. The researchers hope their study will encourage new guidelines that take a more patient-focused approach to monitoring. (Source: *Journal of General Internal Medicine*),online , February 8, 2018)

Nocturia May Contribute to Sleep Problems in ADT. Sleep disturbances in men receiving androgen deprivation therapy for prostate cancer is associated with nocturia and hot flashes. Nocturia and hot flash interference may partly explain sleep disturbance among men receiving androgen-deprivation therapy (ADT) for prostate cancer (PCa), researchers concluded.

Gonzalez, PhD, et al, Moffitt Cancer Center Tampa, Florida, compared 78 men with PCa who were placed on ADT with matched groups of 99 men with PCa who underwent radical prostatectomy but not placed on ADT and 108 men with no history of cancer. Compared with con-

trols, ADT recipients spent more time awake after the onset of sleep and reported worse subjective sleep disturbance, more episodes of nocturia, and greater hot flash interference.

Throughout the 12-month study period, ADT recipients also were more likely than controls to report clinically significant sleep disturbance. At baseline and 6 and 12 months, 42%, 50%, and 59% of ADT recipients had clinically significant sleep disturbance. The proportions among the 2 control groups combined were 21%, 23%, and 26%, respectively, at the same time points.

After adjustment for comorbidities, education, and race, nocturia mediated the association between ADT and wake and after sleep onset, but not subjective sleep disturbance, whereas hot flash interference significantly mediated the association between ADT and subjective sleep disturbance, but not wake after sleep onset, Dr Gonzalez's team reported.

For the study, ADT recipients completed assessments before or within 1 month of starting ADT as well as 6 and 12 months later. The matched controls completed assessments at similar intervals. The investigators assessed comorbidities using a self-report version of the Charlson Comorbidity Index. They obtained information on baseline Gleason score, height, and weight from medical charts and assessed subjective sleep disturbance in the full sample using the Insomnia Severity Index. This scale assesses the subjective difficulty respondents have in falling asleep and staying asleep, and the impact sleep disturbance has on their daily functioning, the authors explained. They used the Hot Flash Related Daily Interference Scale to assess hot flash interference in the full sample. The scale is a 10-item measure that asks individuals to report the interference on various aspects of functioning associated with hot flashes. Each morning upon waking, participants recorded in a daily diary the number of times they urinated overnight. (Source: *Cancer* (2018;124:499-506).

Unethical: Cancer Bills Inflated 5 to 13 Times Higher: Patients with cancer can get a cruel surprise when they receive unexpected bills for costly "out-of-network" services provided in their ostensibly "in-network" hospital. Add in high monthly insurance premiums and deductibles, substantial copays, and the euphemistically named "coinsurance," and the unsuspecting patient can get a very nasty surprise indeed, says a team of physicians and healthcare analysts. The researchers found that wide variation in markups on outpatient oncology services in the United States can impose severe financial hardships on many patients.

"What we found in the marketplace is that over one quarter of the medical centers that provide cancer services are charging more than 5.1 times the Medicare allowable amount, and in some cases the centers are charging more than 15 times the Medicare allowable amount," said lead author, Martin A. Makary, MD, MPH, a cancer surgeon at Johns Hopkins Hospital in Baltimore, Maryland.

"Either this is a game that's gone awry, or it's just outright price gouging in the marketplace, and I think it's fair to ask, in a vulnerable time in someone's life, is it fair or reasonable to inflate a bill that much without their prior consent?" he added.

In their study, the researchers reviewed Medicare Part B physician reimbursement data from 2014 and found wide swings in markup of services by hospitals in many different oncologic specialties, including radiology, hematology/oncology, medical oncology, pathology, and radiation oncology.

Medical oncology services provided in for-profit cancer centers, and radiology and pathology services provided in "prestige" institutions, were associated with higher markups, they found.

And although insurers can haggle with hospitals to agree on reimbursement levels below prices on the hospital's "chargemaster" — a comprehensive list of billable goods and services — individual patients often get stuck paying full retail prices."On a moral level, we believe that it is unethical for a nonprofit medical center to put a patient with cancer into household bankruptcy because they cannot pay a bill inflated above what Medicare would pay for the identical service," they write.

Makary said in an interview with *Medscape Medical News* that "the poor bystanders in this system are the out-of-network patients — a growing group in the United States — the uninsured, and those who as a part of their religious faith pay their bills in full, such as the Amish and other faith-based communities."

He likened hospital pricing practices to the car sales game, where the dealer advertises manufacturer's suggested retail price as "the sticker price," in the knowledge that only the most uninformed and gullible of car shoppers will be willing to pay that amount rather than negotiate a fair price closer to the vehicle's actual cost.

But in healthcare, "the reality is that there are groups in the United States that pay that price, and they tend to be facing those inflated bills at a very vulnerable time in their life," he said.

Ted Okon, MBA, executive director of the Washington, DC-based Community Oncology Alliance (COA), who was not involved in the study, agrees that under the current pricing regime, it's difficult, if not impossible, for patients to know what they're getting into beforehand.

"Because there's a lack of transparency in that pricing, what happens is that patients go into the hospital, and they get their bills, and they are literally having sticker shock," he said in an interview.

The researchers looked at markup ratios — the charge billed divided by the Medicare allowable amount — for oncology services in hospitals throughout the United States, from humble community institutions to powerhouse academic medical centers considered the crème de la crème by their inclusion in the 2014 *US News & World Report* Hospital Honor Roll.

They found that markup ratios at individual hospitals varied widely, as shown in the table below.

Table. Markup Ratios for Oncology Services

Service	Markup Ratio (Median)	Interquartile Range
Radiology	3.7	3.1 - 4.5
Hematology/oncology	2.3	1.8 - 2.9
Medical oncology	2.4	1.8 - 3.0
Pathology	4.1	3.1 - 5.1
Radiation oncology	3.6	2.9 - 4.5

A multivariable analysis of markups by hospital size, profit or nonprofit status, urban vs suburban/rural location, academic vs nonteaching status, region, and prestige vs nonprestige reputation showed that for-profit institutions were associated with higher markups for medical oncology services, and that "prestige" hospitals were associated with higher-priced radiology and pathology services.

"Our findings contribute to emerging evidence that prestigious hospitals or large hospital chains use higher "chargemaster" pricing to anchor negotiations and gain higher reimbursement from insurers. In this way, price markups contribute to the inflation of medical costs in the healthcare system and can affect patients' treatment decisions as their out-of-pocket costs increase," the authors write.

The findings by Makary et al, are supported by a separate study, published online as a research letter on February 22. 2028, in *JAMA Oncology*. That study showed that chemotherapy provided in hospital outpatient departments is roughly twice as expensive as the same care provided in a physician's office.

The authors also found that the despite the cost differences, from 2004 to 2014 there was a distinct shift away from office-based chemotherapy to hospital-based infusions. For example, line-item spending for drugs in office-based chemotherapy settings was $1,466, compared with $3,799 for hospital outpatient chemotherapy.

Daily spending on patients was also substantially lower in offices, at $3,502 vs $7,973 for hospital-based chemotherapy. Aaron N. Winn, PhD, from the Pharmacy School at the Medical College of Wisconsin in Milwaukee, and colleagues from Harvard Medical School in Boston, Massachusetts, and the University of North Carolina at Chapel Hill, made this report: "Potential targets for reduction of excess spending and creation of a more efficient health care system can come from private insurers following Medicare's lead, which has started to equalize payments across sites of care," they write.

Equal payments regardless of the care site appears to be one of the few options available for addressing the markup disparity, commented COA's Okon.

Although prestige hospitals often justify higher prices by claiming higher overheads and greater severity of the patient case-mix, that argument falls apart when the price disparities are for charges imposed on different patients within the same institution.

"How can you literally charge different rates to a patient who may be on Medicare or a patient who may be on private insurance, and then somebody who comes in and doesn't have insurance is getting the chargemaster rate?" he said.

Consolidation of hospital systems gives the hospitals greater power to leverage prices to their advantage, Okon said.

And in some cases, the healthcare provider and the insurer are one and the same. For example, the Boston-based Partners HealthCare system owns Massachusetts General Hospital (MGH), Brigham & Women's Hospital, and other local hospitals, and also an insurer: Neighborhood Health Plan (NHP).

In this actual example, a Partners hospital (MGH) charges for chest computed tomography (CT), billed at $1131; NHP reimburses the hospital for $295; and the hospital then bills the NHP-insured patient for the remaining $836. Patients who have not met their $2,000 annual deductible (on top of $2,300 monthly premiums) are then on the hook for that $836, all of which trickles into Partners' (not-for-profit) coffers.

According to the Healthcare Bluebook, a website that publishes healthcare charges for specific procedures, chest CT with contrast can cost as low as $560, with $700 considered a "fair" price.

Okon said that he has read about some hospitals that now require patients to get bank approval before a procedure, akin to a house buyer getting preapproved for a mortgage loan. "The patient basically has to get, in essence, preauthorized by the bank, and the bank basically holds the bill. This is really troubling," he said.

How to change it? "It's very difficult," Okon acknowledged. "I think that Congress and in some cases individual states are realizing that this is a problem, and they are taking action."

He noted that the recent White House budget calls for site-payment parity for Medicare payments."But it's difficult, because patients who are paying a large deductible because of the chargemaster, get left holding the bag," Okon said. (Source: *The American Journal of Managed Care,* February 17, 2018, published online)

Testosterone Replacement Therapy Does Not Raise CV Risk. Middle-aged men who use testosterone replacement therapy (TRT) are not at elevated risk of cardiovascular events according to a new study. Men who take TRT are not more likely to experience cardiovascular events or thromboembolism, but they are at higher risk of obstructive sleep apnea (OSA), according to a new study.

In fact, the study of 6,844 male US military service members, retirees, and their dependents found that TRT was associated with a small but significant decrease in cardiovascular (CV) event risk, mainly due to a lower incidence of coronary artery disease (CAD), Alexander P. Cole, MD, of Brigham and Women's Hospital in Boston, and colleagues reported in a paper published online ahead of print in *BJU International*.

The 2-year absolute risk of cardiovascular events was 8.2% for TRT users compared with 10.5% among controls (men not using TRT and who had no history of prostate cancer, cardiovascular disease, thromboembolism, or OSA). When the investigators looked at congestive heart failure, stroke, and CAD separately, CAD was the only end point with significantly lower risk among TRT users.

The 2-year absolute risk of thromboembolic events was 2% in the TRT group and 1.4% among controls, a non-significant difference between groups.

The 2-year absolute risk of OSA was significantly greater among TRT than controls (16.5% vs 12.7%). “While previously demonstrated in small prospective studies, this association has not previously been shown in a large national study such as this,” Dr Cole's team noted.

Possible explanations for the association include morphologic and neuromuscular changes to the airways, changes in metabolic requirements, and changes to the physiologic response to hypoxemia and hypercapnia, the investigators noted.

The study population consisted of 3,422 TRT users and 3,422 controls matched by birth year, race, marital status, military rank, comorbid conditions, and residence region. Men in both groups had a median age of 51 years.

With regard to study limitations, the authors pointed out that their study population, although geographically diverse, may differ from the civilian population, thus limiting the generalizability of their findings. Another limitation may be the possibility of unmeasured confounders. These include patient characteristics not captured by diagnostic codes, such as the specific etiology of low testosterone levels. In addition, they explained that because the data source consisted of International Classification of Diseases diagnostic and procedure codes obtained from the TRICARE insurance program, they lacked granular information on how OSA was diagnosed. They also were unable to analyze TRT doses. “This latter point is certainly a limitation, given some evidence for a dose-dependent effect of TRT.”

In the past few years, TRT use has increased dramatically in relatively healthy men without definitive testicular or pituitary disease, but with testosterone levels below reference ranges for young men, Dr Cole told *Renal & Urology News*. “This has led to a lot of controversy, especially given that many of the symptoms of hypogonadism such as fatigue, decreased libido, and adiposity are sometimes considered part of the ‘natural' aging process, and also given some recent high-profile studies suggesting associations between testosterone replacement and medical side effects like heart disease.”

A problem with some of these studies, Dr Cole noted, is that they were disproportionately in older men, in some instances individuals with mobility impairments and other health problems.

“In terms of changing practice, I think that our results are probably consistent with a growing awareness that the cardiovascular and thrombotic risks of TRT may be less than once feared in younger, relatively healthy men,” Dr Cole said. “Regarding the modest increase in sleep apnea, this is important. The Endocrine Society Guidelines do include pre-existing OSA as a relative contraindication for TRT. Given our findings, I think that this may be an increasingly important topic for men considering TRT.” (Source: *BJU Int*. 2018; published online ahead of print.)

Increased Monitoring of Men with Metastatic Prostate Cancer at End of Life. In an evaluation of SEER-Medicare data, researchers sought to determine the benefits of extreme use of monitoring in patients with metastatic prostate cancer at the end of life on quality of care and survival outcomes.

More frequent disease monitoring did not improve survival or quality of care, but rather only substantially increased healthcare costs at end of life (EOL) among patients with metastatic prostate cancer (mPCa), according to a study published in *Cancer*.

Disease assessment with prostate-specific antigen (PSA) testing, bone scans, and cross-sectional imaging are regularly utilized among patients with mPCa, but due to a lack of universal guidelines for monitoring, the impact on health and economic outcomes warrant further study.

For this study, investigators identified 3,026 men with stage IV mPCa. Men with additional malignancies and who survived less than 6 months after diagnosis were excluded from the study. Researchers sought to evaluate the association between extreme use (more than 1 PSA testing/month; cross-sectional imaging or bone scans more frequently than every 2 months over 6 months), survival outcomes, cost, and quality of care at EOL.

Of the 3,026 men, 26% (791) were identified as extreme users. Extreme users were more likely to be young, married, more educated, higher earning, and of white/non-Hispanic race.

No statistically significant differences were observed in regards to any quality-of-care indicators at EOL between extreme and nonextreme users over the last month of life, including visits to the emergency department, more than 1 hospital admission, ICU admission, hospitalization for more than 14 days, or timing of hospice referral.

There were no statistically significant differences in overall mortality or prostate cancer-specific mortality between extreme and non-extreme users.

Compared with nonextreme users, extreme users had a 22.9% (mean cost, $35,454) and 35.1% (mean cost, $62,672) higher cost of health care within the first year of diagnosis and the last year of life, respectively.

Results showed that there were no associations with improvement in quality of care or survival with more frequent monitoring, only increased cost. The authors concluded that “physicians are encouraged to discuss treatment goals with patients and to devise appropriate monitoring plans based on these goals.” (Source: *Cancer,* doi: 10.1002;31297; published on line March 26, 2018; via Oncology Nurse Advisor, March 30, 2018)

Quality of PCa Screening Information on National Web Sites. The purpose of this study was to survey the accessibility and quality of prostate-specific antigen (PSA) screening information from National Cancer Institute (NCI) cancer center and public health organization web sites.

We surveyed the December 1, 2016, version of all 63 NCI-designated cancer center public web sites and 5 major online clearinghouses from allied public/private organizations. Web sites were analyzed according to a 50-item list of validated health care information quality measures. Web sites were graded by 2 blinded reviewers. Interrater agreement was confirmed by Cohen kappa coefficient.

Ninety percent of web sites addressed PSA screening. NCI cancer center sites covered 45% of topics surveyed, whereas organization web sites addressed 70%. All organizational web pages addressed the possibility of false-positive screening results; 41% of NCI cancer center web pages did not. Forty percent of NCI cancer center web pages also did not discuss next steps if a PSA test was positive. Only 6% of NCI cancer center web pages were rated by our reviewers as "superior" (e.g., addressing >75% of the surveyed topics) versus 20% of organizational web pages. Interrater agreement between our reviewers was high (kappa coefficient = 0.602).

NCI-designated cancer center web sites publish lower quality public information about PSA screening than sites run by major allied organizations. Nonetheless, information and communication deficiencies were observed across all surveyed sites. In an age of increasing patient consumerism, prospective prostate cancer patients would benefit from improved online PSA

screening information from provider and advocacy organizations. Validated cancer patient web educational standards remain an important, understudied priority. (Source: *Practical Radiation Oncology*; December 24, 2017 [Epub ahead of print]); via UroToday, February 20, 2018)

Comparative Toxicities and Cost of RTs for Prostate Cancer. A new study compares outcomes among younger men with prostate cancer who are treated with intensity-modulated radiotherapy (IMRT), which is the most commonly used form of radiotherapy (RT) in the United States, against outcomes with two less frequently used technologies, proton therapy and stereotactic body radiotherapy (SBRT).

The investigators report that men treated with proton radiation are less likely to experience adverse urinary effects and erectile dysfunction and more likely to have bowel toxicity at 2 years compared with men treated with IMRT.

The study also reports on cost. Proton therapy was nearly twice as expensive as IMRT, based on private insurance reimbursement costs. In contrast, the costs of administering SBRT and IMRT did not significantly differ, although SBRT treatment is associated with a modestly higher risk for urinary toxicity than IMRT.

To their knowledge, this study is unique in its assessment of the toxicity and cost of prostate radiation treatment options in the previously understudied, but significant patient population of younger men with private insurance, said the researchers. Hubert Pan, MD, Anderson Cancer Center, University of Texas, and colleagues write: "Men under age 65 years account for over 40% of all patients with prostate cancer. Our key findings, coupled with the real-world private insurance cost, will be useful for patients selecting the most appropriate treatment and for researchers designing cost-effectiveness models to guide treatment decisions in prostate cancer."

Using a large US commercial insurance database of men under age 65, the investigators matched 693 patients who had been treated with proton therapy to 3,465 patients who had been treated with IMRT. Another 310 men treated with SBRT were matched to 3,100 others treated with IMRT. Median follow-up for all groups ranged from 18 to 23 months.

One third of men who underwent proton radiotherapy experienced some form of urinary toxicity at 2 years compared with 42% of those who received IMRT. This urinary benefit with proton radiation was seen across multiple domains, including incontinence, bleeding/irritation, obstruction, and stricture, the study authors note. On the other hand, 20% of men who received proton therapy had some form of bowel toxicity at 2 years compared with 15% of IMRT patients — principally in the form of late bleeding or proctitis.

Erectile dysfunction was also less common among men who received proton treatment, at 21% at 2 years versus 28% for those treated with IMRT.

The mean cost of administering proton radiation to the payer was $115,501 compared with only $59,012 to administer IMRT. (Source: *Journal of Clinical Oncology* , published online March 21, 2018; via Medscape Medical News, March 29, 2018)

♦ MEETING ANNOUNCEMENT ♦

THURSDAY, MAY 3, 2018

7:00 - 8:30 PM

WRNMMC, AMERICA BUILDING (BLDG 19, 2D FLOOR) ROOM 2525

AND VIA VIDEO TELECONFERENCE AT FORT BELVOIR COMMUNITY HOSPITAL

(OAKS PAVILION, 1ST FLOOR, ROOM 332)

♦ SPEAKER ♦

JENNIFER CULLEN, PhD, MPH

DIRECTOR OF EPIDEMIOLOGIC RESEARCH

CENTER FOR PROOSTATE DISEASE RESEARCH

WALTER REED NATIONAL MILITARY MEDICAL CENTER

♦ TOPIC ♦

"THE CRITICAL ROLE OF PATIENT-REPORTED OUTCOMES IN IMPROVING OUTCOME IMPROVING DECISION-MAKING FOR THE TREATMENT OF PROSTATE CANCER"

Security: A military ID card is required to get on base at Walter Reed. Persons without a military-related ID card who are attending the meeting are required to register in advance in order to gain entry. To register, contact the CPDR front desk at 301-319-2900 at least four business days prior to Thursday, February 1, 2018, to arrange entry. Have a photo ID card ready when arriving at the gate.

Fort Belvoir: Persons without a military ID card should arrive at the entrance one hour before the presentation to complete the entrance procedure. Have a picture ID with you.