WRNMMC Us TOO, Inc.
A PROSTATE CANCER SUPPORT GROUP
SPONSORED BY
WALTER REED NATIONAL MILITARY MEDICAL CENTER
NEWSLETTER

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♦ New PCa SCREENING POLICY ♦

The U.S. Preventive Services Task Force (USPSTF) recently issued a draft recommendation that would modify its controversial opposition to routine screening for prostate cancer. The USPSTF recommendation in 2012 had concluded that any potential benefits from routine PSA testing were outweighed by the potential harms due a high percentage of false positives and aggressive treatment of slow-growing malignancies that might never pose a health threat. The task force had cited the facts that one in five men who had their prostates removed had suffered long-term problems with urinary incontinence and that two-thirds had long-term impotence.

The USPSTF cited new evidence that PSA testing shows a small benefit for men in ages 55 to 69. PSA testing within this group reduces the risk of dying from prostate cancer or developing advanced cancer that has spread beyond the prostate. The new data shows that PSA screening in this group prevents one to two deaths from prostate cancer over 13 years per thousand men screened. Men in this age category should discuss the PSA test's potential benefits and harms with their doctors and make decisions based on their own values and preferences. This new USPSTF recommendation retains its 2012 position that routine PSA testing is still inappropriate for men younger than 55 or older than 69.

The American Urological Association, which had denounced the USPSTF's 2012 recommendations, applauded this new recommendation, but continued to disagree with the task force's recommendation for men 70 or older.

The task force made no specific recommendations regarding African American men who are at greater risk for the disease, citing insufficient evidence. (Source: The Washington Post, April 12, 2017)

♦ *INSIDE THIS ISSUE* ♦

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♦ FROM THE EDITOR ♦

GOOD NEWS! At present, our quarterly speaker presents at WRNMMC with a video teleconference connection to viewers at the Fort Belvoir Community Hospital. We will soon be able to reverse the process - the speaker presents at Fort Belvoir with a video teleconference connection to viewers at WRNMMC. The primary location will be decided based on the proximity of the speaker to either location.

♦ SPEAKER'S REMARKS - FEBRUARY 2, 2017 ♦

Our speaker on Thursday, February 2, 2016, was Dr. James David, a psychotherapist in private practice treating individuals, couples and families. His topic was "**The ABCs of Self-Care**." A summary of his remarks was not available for this issue of the newsletter. It will be included in the August issue.

♦ MEETING SCHEDULE FOR MAY 4, 2017 ♦

Our speaker for Thursday, May 4, 2017, is **Dr. Robert Dean,** Department of Urology, WRNMMC whose topic is **Prostate Cancer Survivorship: Sexual Health Therapies.** Please join us at 7:00 PM in the America Building (Bldg 19), 2nd floor, Room 2525. Remember, your family and friends are also welcome.

(The presentation also may be viewed via video teleconference at the Fort Belvoir Community Hospital. Go to the Oaks Pavilion, 1st floor, Room 332, to participate.)

SEE THE BACK PAGE OF THIS NEWSLETTER FOR IMPORTANT INFORMATION ABOUT THIS MEETING.

♦ PROSTATE-SPECIFIC ISSUES ♦

Prostate Cancer Statistics for 2017. The American Cancer Society (ACS) recently published statistics regarding the estimated new cases and deaths for four major cancers during 2017 - colon and rectum, lung and bronchus, breast cancer, and prostate cancer by sex and age groups.

In the Prostate Cancer All Ages category there will be 161,360 new cases in 2017 of which 69,910 (43.3%) will be younger than 65 and 91,450 (56%) will be 65 and older. In comparison, there will be 71,420 new cases of male colon and rectal cancer of which 31,320 (44%) will be younger than 65 and 40,100 (56%) will be 65 and over. Lung cancer is a big cancer risk for men with 116,990 new cases in 2017 of which 37,890 (32%) will be younger than 65 and 79,100 (68%) will be 65 and over.

In the Prostate Cancer All Ages category for expected deaths during 2017 there will be 26,730 deaths of which 2,900 (10.8%) will be younger than 65 and 23,830 (89.1%) will be 65 or over.

In the Lifetime Probability of Developing and Dying from Prostate Cancer category 12.9 percent of men (I in 8) will develop prostate cancer and 2.5% of them will die from the disease (1 in 40). The AMS advises that this data cannot be compared with like data from previous years due to differing data base designs and other related issues. (Source: American Cancer Society Surveillance Research, 2017)

Prostate Cancer Treatment May Increase Colorectal Cancer Risk. Prostate cancer (PCa) patients who undergo bilateral orchiectomy, radical prostatectomy, or other treatments may be at increased risk of colorectal cancer, a new Swedish study suggests.

Yunxia Liu, MD, et al., Karolinska Institutet in Stockholm, used data from three national Swedish health registries to calculate the incidence of colorectal adenocarcinoma among 149,743 PCa patients, compared with the general Swedish male population. The investigators divided subjects into 4 groups: group 1, diagnosed between 1961 and 1980, historically received estrogen; whereas groups 2, 3, and 4, diagnosed between 1981 and 2008, underwent bilateral orchiectomy, prostatectomy, and other treatment (mainly gonadotropin-releasing hormone agonists, radiotherapy, or both). After 601,542 person-years of follow-up, 1,698 patients were diagnosed with colorectal adenocarcinomas.

Compared with the general male population, patients treated with bilateral orchiectomy,

prostatectomy, and other non-estrogen treatments had a 30%, 22%, and 37% increased incidence of colorectal cancer, respectively, according to an online report in *Cancer Control*.

No clear association was found among group 1 patients treated with estrogen. The researchers noted that previous studies in women have linked higher levels of estrogen and progesterone to lower risk of colorectal cancer.

“Treatment for prostate cancer diagnosed after 1980 may be associated with an increased risk of adenocarcinoma, implying a possible connection to ADT, one of the most common treatments in Sweden used after 1980,” the researchers stated. The increased risk among orchiectomy patients could be related to surgical androgen deprivation and the risk among non-surgery patients could be due to medically induced androgen deprivation.

Greater risks were observed in cases of adenocarcinoma of the distal colon and rectum than in the proximal colon. The investigators hypothesize that genetic and/or physiological mechanism may explain the differences because the gut originates from different parts of a developing embryo.

The researchers pointed out the strengths of the study, including its nationwide and population-based cohort design identified by from national registries, its large PCa cohort sizes, and long and complete follow-up times. They also acknowledged limitations, such as the absence of detailed information on hormonal treatments such as estrogen or anti-androgen medications. (Source: Lu, Y, et al. *Cancer Control*, April 2015 via. www.renalandurologynews.com/prostate-cancer/prostate-cancer-treatment-may-increase-colorectal-cancer-risk/article/421777/)

Prostate Cancer Mortality in Men With a Negative Initial Biopsy. "Hello. I am Dr Gerald Chodak from Medscape. Today I want to talk about the implications of having one negative prostate biopsy. Klemann and coworkers recently published an article based on the Danish Prostate Cancer Registry. They looked at more than 64,000 men who underwent a prostate biopsy between 1995 and 2011. They have follow-up through 2015, providing nearly 20 years of available data.

They found that for those men whose initial prostate biopsy was negative, only 2% eventually died from prostate cancer. The projected prostate cancer mortality in that group was about 5.2%. The odds of dying from other causes during that time was 23% in this group. Men who had a negative initial prostate biopsy were nearly 11 times more likely to die of causes other than prostate cancer.

About 11% of the men ultimately had a second biopsy. Even in that group, the mortality was low. The study also had data on about 22% of the men who had an initial PSA available. In the men whose PSA was 10 µg/mL or lower, the odds of dying from prostate cancer in that group, again, was only 1%.

Of the men who eventually underwent a second biopsy, the odds of being diagnosed with cancer and having a Gleason score of 8 were also extremely low, about 2+%. Some 19,000 men did not undergo a second biopsy, and the odds of dying from prostate cancer in this group was 1%.

These data are not based on men who underwent prostate cancer screening. Many of the men had only a six-core biopsy done at the time. When one looks at the European Randomized Study of Screening for Prostate Cancer (ERSPC), where patients had screening PSAs, the data are relatively consistent with those findings.

What does this information mean for the patient, going forward? The median age in this study was 67 and the median follow-up was only 5.9 years, even though there were up to 20 years of follow-up. If a man has a life expectancy of 25 or 30 years for example, it is hard to know how these data will help make a decision going forward.

Men who are 67 or older, or those with a life expectancy of, for example, 10-15 years or even up to 20 years, should realize that their risk of dying from prostate cancer after one negative biopsy is extremely low, especially compared with their risk for mortality from other causes.

Does this mean that men should not undergo a second biopsy or follow-up? Not necessarily. Certainly, continued PSA levels are reasonable to do. If a man's PSA goes above 10 µg/mL, then another biopsy may be warranted. In terms of whether we should be overly aggressive with this group, that question is reasonable to ask.

It would appear that the value of doing MRI-guided biopsies after one negative biopsy may help find more cancer, but it also may result in over-treating many of these men because the risk of dying from prostate cancer is still very low. Going forward, the debate is going to continue—whether ultrasound-guided, random biopsies, or MRI-guided biopsies are the way to proceed. For now, I think it is useful information to advise a patient who has had one negative biopsy core set that his risk of dying from prostate cancer, even without another biopsy, is extremely low." (Source: www.medscape.com/viewarticle/877243)

Prostate Biopsy May Be Avoidable if MRI Findings Are Negative. According to a recent study, a systematic biopsy detected clinically significant prostate cancer in only 3% of men with negative findings on MRI. Men who undergo multiparametric magnetic resonance imaging (mpMRI) for suspected prostate cancer (PCa) and have negative findings are highly unlikely to have clinically significant PCa found on subsequent systematic prostate biopsy

Sprenkle, MD, et al, Yale School of Medicine, found that men with no suspicious findings on prostate mpMRI had an approximately 3% chance of having clinically significant PCa—defined as Gleason grade 7 or higher—detected on systematic transrectal ultrasound (TRUS)-guided biopsy.

The study included 100 men who underwent mpMRI followed by TRUS-guided systematic prostate biopsy. Overall, 27 patients (27%) had PCa detected, including 10 (26.3%) of biopsy naïve men, 4 (12.1%) of 33 men who had a prior negative biopsy, and 13 (44.8%) of those previously on active surveillance. Gleason grade 7 or higher cancer was detected in 3 patients (3%) overall. The negative predictive value of a negative mpMRI was 73% for all PCa and 97% for Gleason grade 7 or higher cancer.

"Our results suggest that avoidance of systematic biopsy in patients with negative imaging results may be feasible," the investigators concluded. Multiparametric MRI doesn't yet replace standard-of-care biopsy techniques that use a large number of biopsies in a grid pattern to try to catch any cancerous areas. And it may turn out not to be useful or cost-effective for every man. "But stay tuned," the researchers said.

The investigators acknowledged some study limitations, including the relatively small sample size of the overall cohort. In addition, they noted that their institution is a tertiary care referral center, so their patient population may differ from that of general practice patients. (Source: *Urology* 2017; published online March 23, 2017 ahead of print) **(Editor's Note: See a related argument - next)**

Role of MRI Pre-Biopsy in Men at Risk for Prostate Cancer: Taking Off the Blindfold. This study review recent literature surrounding the use of the pre-biopsy prostate MRI and MRI-targeted biopsy in men at risk for prostate cancer.

Large series have strengthened the case for the use of MRI prior to prostate biopsy to maximize the detection of clinically significant disease, reduce the detection of clinically insignificant disease, and allow for tumor localization during targeted biopsy. Pre-biopsy MRI followed by targeted biopsy appears to have the ability to overcome the limitations of the standard 12-core template. Use of MRI and targeted biopsy in the setting of a prior negative biopsy is supported by the literature and a recent consensus statement by the American Urological Association and the Society of Abdominal Radiology's Prostate Cancer Disease-Focused Panel, but is contingent upon the availability and quality of multiparametric MRI acquisition and interpretation. In men with no previous biopsy, MRI and targeted biopsy appears to increase detection of clinically significant disease compared with systematic biopsy while reducing detection of indolent disease. The addition of prostate cancer biomarkers and predictive nomograms may further enhance pre-biopsy risk assessment.

Prostate MRI prior to biopsy may guide counseling regarding prostate cancer risk, allow for accurate tumor localization during targeted biopsy, and increase detection of clinically significant cancer while limiting detection of indolent disease. Its use prior to biopsy, in conjunction with biomarkers and predictive nomograms, may allow deferral of biopsy in select cases. (Source: Current Opinion in *Urology*, February 23, 2017 [Epub ahead of print] via http://www.ncbi.nlm.nih.gov/pubmed/28234749)

Bladder Cancer Risk Higher Following Prostate Radiotherapy. Prostate cancer patients who undergo radiation treatment, especially brachytherapy, are at increased relative risk of bladder cancer, according to study findings presented at the American Urological Association 2016 annual meeting. This increased relative risk occurs predominantly after 10 years. Bladder tumors found in men following prostate radiotherapy are generally lower stage, but higher grade than tumors found in patients without a history of prostate cancer, the study showed.

Keehn, MD, et al, at Albert Einstein College of Medicine, Bronx, NY, analyzed data from the 1973–2011 SEER database to ascertain the observed and expected number of bladder cancer cases after PCa radiotherapy. Bladder cancer developed in 6,401 of 346,429 men who underwent radiotherapy for PCa, which was 2.6 times the number of expected cases (2,464). All treatment modalities were associated with a higher relative risk of bladder cancer after 10 years, with the relative risk significantly higher following brachytherapy than after EBRT or EBRT plus brachytherapy.

Compared with men without a history of PCa, brachytherapy was associated with a 3.5-fold, 2.9-fold, and 5.5-fold increased risk of bladder cancer after 10 years in Caucasians, African Americans, and patients of other or unknown races, respectively, in adjusted analyses. (Source: http://www.renalandurologynews.com/aua-2016-bladderkidney-cancer/bladder-cancer-risk-higher-following-prostate-radiotherapy/article/495008)

Prostate Cancer Treatments Have Varying Side Effects, Study Shows. The long-term side effects of different prostate cancer treatments vary -- and knowing that may help men decide which one is right for them. That's the conclusion of two new studies published March 21, 2017, in the *Journal of the American Medical Association.*

Both studies followed men who had early stage prostate cancer treated with "modern" approaches -- including the latest surgical and radiation techniques. And both found that side effects sometimes persisted for up to three years.

The specifics, however, varied. Many men had surgery to remove the prostate. Overall, they tended to have greater declines in their sexual function, versus men who chose radiation or "active surveillance." They were also more prone to urinary incontinence.

On the other hand, men treated with radiation typically had more problems with bowel function. If they also received hormonal therapy, they were also at risk of hormone-related symptoms -- such as hot flashes and breast enlargement. On the brighter side, the issues with radiation were mainly limited to the first year after treatment.

Not surprisingly, both studies found, men who opted for surgery or radiation had more long-term symptoms than those who chose active surveillance. With that approach, men put off treatment in favor of having their cancer monitored with periodic blood tests and biopsies. Active surveillance is an option for prostate cancer because the disease is often slow-growing and may never progress to the point where it threatens a man's life.

But that doesn't necessarily mean active surveillance is the best option for any one man, according to the researchers. Much depends on whether the cancer is "low-risk" or not. Low-risk prostate cancers have characteristics that mark them as less aggressive. "If you're in that low-risk group," the researchers added, "active surveillance might be the best choice, to avoid treatment side effects."

But for men with more aggressive prostate tumors, treatment is typically advised to boost their long-term survival. For those patients, it's pretty clear that treatment is better than no treatment."

Dr. Freddie Hamdy, a professor of surgery at the University of Oxford in England, commented on the study. In general, he said, research suggests that when men with low-risk prostate cancer are carefully selected for active surveillance, they have "very low" death rates from the disease. For some men, active surveillance might be anxiety-provoking, but his own research has found that men on active surveillance do not have higher rates of anxiety or depression than prostate cancer patients who choose immediate treatment. "The anxiety generated in many of these patients is more likely to be related to the diagnosis of cancer, and the fact that [they] have to live with its consequences, irrespective of the treatment that they receive," Hamdy said.

For their study, Barocas, et al, Vanderbilt University, followed 2,550 men diagnosed with prostate cancer between 2011 and 2012. All had tumors that were confined to the prostate. Almost 60 percent had surgery; another 23.5 percent had external radiation; and 17 percent chose active surveillance.

Three years later, men who'd had surgery gave lower ratings to their sexual function, versus the two other groups. They also had more trouble with urinary incontinence: 14 percent said they had a "moderate or big problem" with urine leakage, compared with 5 to 6 percent of men in the other groups. Radiation, meanwhile, carried the biggest risks of bowel problems and hormonal side effects. But that faded by year three.

The second study -- of more than 1,100 men with early stage cancer -- had similar findings. Surgery carried higher risks of sexual dysfunction and urine leakage. For instance, of men with normal sexual function before surgery, 57 percent reported "poor" function two years later, the University of North Carolina researchers found.

External radiation, again, caused more short-term bowel problems. The study also included men who'd undergone brachytherapy -- a type of internal radiation that implants radioactive "seeds" in the prostate. Those patients had more issues with urinary tract obstruction and irritation.

So what's a man to do with that information? According to Dr. Barocas, patients can talk to their doctor about the types of side effects that might occur with each treatment -- then decide what they can personally live with. "If, for example, you already have poor sexual function -- as many patients in our study did -- that side effect might not mean as much to you," Barocas said. For a man with low-risk prostate cancer, he noted, the risk of any treatment side effect might not be "acceptable." Hamdy made another point:

While robot-assisted surgery has become the go-to approach, it has the same types of side effects that traditional open surgery always had. (Source: Daniel Barocas, M.D., M.P.H., associate professor, urologic surgery, Vanderbilt University, Nashville, Tenn.; Freddie Hamdy, M.D., professor, surgery, University of Oxford, England; March 21, 2017, *Journal of the American Medical Association* via HealthDay, Medline Plus, March 21, 2017)

Updated Guideline on Brachytherapy in Prostate Cancer. The American Society of Clinical Oncology (ASCO) and Cancer Care Ontario have issued a joint clinical practice guideline update on the use of brachytherapy for prostate cancer patients. According to an expert panel, brachytherapy is now the nonsurgical standard of care for the majority of patients with prostate cancer, either by itself or as part of a combination approach. The panel further asserted that brachytherapy is also more convenient than external-beam radiation [EBRT] and has a much higher chance of curing the disease. However, not every patient should have brachytherapy, and not all treatment centers are experienced in delivering high-quality brachytherapy.

The new guideline was online March 27, 2017, in the *Journal of Clinical Oncology*.

For urologists, who are most often the gatekeepers in terms of first contact with men with prostate cancer, this guideline update provides new information which they can incorporate into patient counseling and treatment decision making. By optimizing treatment selection, which may or may not be brachytherapy for a particular patient, outcomes should ultimately be improved. (Source: *J Clin Oncol*, published online March 27, 2017, via Uro today, March 28, 2017)

Earlier vs Later Prostate Cancer Recurrence Characterized. Men with earlier versus later biochemical recurrence of prostate cancer after radical prostatectomy have different etiologies for rising PSA levels, researchers concluded.

Llukani, MD, and Lepor, MD, et al, of New York University Langone Medical Center, studied 1597 men who underwent open retropubic radical prostatectomy (RP) from October 2000 to October 2009. The probabilities of developing biochemical recurrence (BCR) within 5 and 10 years were 12.3% and 18.4%.

The investigators defined BCR as 2 or more consecutive PSA measurements of 0.2 ng/mL or higher following RP. They defined earlier and later BCR as BCR occurring before and after 5 years.

Compared with patients who had earlier BCR, those who experienced later BCR had significantly lower biopsy Gleason scores, pathologic stage, pathologic Gleason score, positive surgical margin (PSM) rates, and preoperative PSA level, as well as significantly longer PSA doubling time (PSADT) and a greater likelihood of achieving an undetectable PSA nadir.

Men with later BCR had lower pathologic Gleason scores, lower PSM rates, and longer PSADT, suggesting that, overall, earlier BCR represents more aggressive disease.

Overall, 74.5%, 12.7%, and 12.7% of patients experiencing BCR underwent salvage radiation therapy (SRT), androgen-deprivation therapy (ADT), and active surveillance (AS), respectively. A significantly greater proportion of men in the earlier BCR group underwent SRT (80.8% vs 59%) and ADT (14.6% vs 8.2%), and a significantly greater

proportion of men in the later BCR group underwent AS (32.8% vs 4.6%), according to the investigators.

Men undergoing AS had a longer time to BCR and a longer PSA doubling time (PSADT) than those undergoing SRT. Compared with patients undergoing ADT, those undergoing SRT were younger, had a longer time to BCR and a longer PSA doubling time, and had lower biopsy and pathologic Gleason scores. They also had a greater likelihood of achieving a PSA nadir of 0.05 ng/mL or less. (Source: *BJU Int* 2017; published online ahead of print, April 5, 2017 via https://www.ncbi.nlm.nih.gov/pubmed/28220652)

Prostate Cancer Progression Risk in AS Not Linked to Family History. Family history of prostate cancer (PCa) is unlikely to be a reason to exclude men from active surveillance (AS) for low-risk PCa, researchers reported.

In a systematic review of 6 observational studies conducted before March 2016, Jim Dupree, MD, Jaya Marie Telang, and colleagues found no significant relationship between PCa progression risk and a family history of PCa among patients on AS or eligible for it. However, a study by Eugene Pietzak, MD, and colleagues published in *Urology*(2015;85:436-440) found that black men with a family history of PCa did have increased risks of aggressive pathology.

“Our results suggest that having a family history of prostate cancer should not automatically exclude men from being considered for active surveillance treatments, although some questions remain about risks for African American men with a family history of prostate cancer,” Dr Dupree, of the University of Michigan in Ann Arbor, told *Renal & Urology News*.

The studies varied in their definition of PCa progression, the authors acknowledged in a paper published online ahead of print in *BJU International*. Four studies relied on results from biopsy-detected pathology and two studies on serum biomarkers

Given the small numbers of patients, the investigators were unable to examine fully the role of race and genetic markers for PCa. “More research needs to be done to confirm these findings, especially among African American men," Dr Dupree stated. “Men obviously need to have thorough conversations with their doctors about risks, benefits, and options," he added. (Source: *BJUI.* DOI: 10.1111/bju.13862 [Epub] via Renal&Urology News, April 7, 2016)

♦ WRNMMC US TOO COUNSELORS ♦

For fifteen years or so the newsletter has provided the names and contact information for volunteers who were willing to share their prostate cancer experiences with newly diagnosed men and their partners.

We are discontinuing the counselor listing for several reasons. First, there have been remarkable developments in prostate cancer treatment options, processes and technology. Most of our volunteers have had their prostate cancer experiences prior to these developments. Furthermore, many hospitals now have procedures in place that provide newly diagnosed men with coordinated evaluations of their prostate cancer and the appropriate treatment option(s). Also, we are aware that most of our counselors are rarely contacted for advice of late.

On behalf of the WRNMMC UsTOO Chapter of Us TOO International, I want to express our gratitude to those listed below for their long and dedicated service in assisting newly diagnosed men and their families cope with the disease.

Dr. Jane Hudak, patient coordinator at WRNMMC, maintains a list of persons who can share their recent experiences with prostate cancer. Her contact information will be provided in all future editions of this newsletter.

WITH THANKS AND GRATITUDE TO:

TOM ASSENMACHER	KINSVALE, VA
TOM BAXTER	HAYMARKET, VA
JACK BEAVER	FALLS CHURCH, VA
LEROY BEIMEL	GLEN BURNIE, MD
BOB BUBEL	GRAND JUNCTION, CO
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NANCY WALLRATH	MCLEAN, VA

♦ MEETING ANNOUNCEMENT ♦

THURSDAY, MAY 4, 2017

7:00 - 8:30 PM

AMERICA BUILDING (BLDG 19, 2D FLOOR) ROOM 2525
(DIRECTLY ABOVE THE LAB/PHARMACY)

WALTER REED NATIONAL MILITARY MEDICAL CENTER

♦ SPEAKER ♦

ROBERT DEAN, MD

(DEPARTMENT OF UROLOGY, WRNMMC)

♦ TOPIC ♦

"PROSTATE CANCER SURVIVORSHIP: SEXUAL HEALTH THERAPIES"

Gate/Parking: If you enter the base through South Gate (Gate 2) off Rockville Pike/Wisconsin Avenue, take the first right (Palmer Road South). On your left will be the Emergency Room. Continue to follow signs to the America Building and the America parking garage.

Security: A military ID card is required to get on base. 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, 2016, to arrange entry. Have a photo ID card ready when arriving at the gate.