Urologists eye private equity partners

Firms offer economies of scale among other benefits, but there are drawbacks

Lisette Hilton / UT Correspondent

More urology practices are considering private equity partnerships as a way to thrive amid health care changes, and private equity firms increasingly see the value of investing in urology practices.

Could it be a match made in heaven?

Experts say private equity can mean big benefits to large urology groups and solo urologists alike. But the real impact of these partnerships on urologists, their patients, and health care in general remains unknown.

Today’s landscape

Private equity firms’ acquisition of physician practices has escalated in recent years. Historically, these firms have focused on dermatology practices but are increasingly eyeing urology, ophthalmology, and gastroenterology groups, according to a recently published article in Annals of Internal Medicine (Jan. 8, 2019 [Epub ahead of print]).

Urology is an attractive investment for private equity, hospital systems, and other investors because demand for services from an aging population is high and the supply of urologists is low. Also in play is the emerging landscape.

Please see PRIVATE EQUITY, on page 33

PRIVATE EQUITY PROS AND CONS

PROS

✓ Offers practices key organizational attributes: economic value in the purchase price, ability to influence the organization’s strategy post-transaction, and incentive/alignment mechanisms for physicians post-deal
✓ Provides resources to improve infrastructure, better negotiate with payers, and manage administrative/regulatory requirements
✓ Cost savings achieved with merging back office functions
✓ Upfront tax-advantaged cash payment may benefit physicians within 10 years of retirement
✓ Firms bring management experience, access to capital

CONS

✗ Physicians give up some control of the business
✗ Private equity firms work on an accelerated timetable, and decisions can be made with a short-term perspective
✗ Firm may be unfamiliar with regulatory/business aspects of health care
✗ Process of interviewing firms/due diligence is lengthy
✗ Data lacking on whether partnerships affect cost, quality of care

Inside

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Undetected kidney tumor leads to lawsuit

APPs play multifaceted role as urology team members

In this interview, Jim Kovarik, PA-C, of the University of Kansas Hospital, Kansas City, discusses the role of advanced-practice providers in a urology practice, how they are trained, and what procedures they can and should perform.

Q&A

Jim Kovarik, PA-C

UROLOGY WORK FORCE

For the full article, please turn to page 24
The UroLift System procedure is FDA-cleared for the treatment of symptoms due to urinary outflow obstruction secondary to BPH, including lateral and median lobe hyperplasia, in men 45 years of age or older. Results and patient experience may vary. Most common adverse events reported include hematuria, dysuria, micturition urgency, pelvic pain, and urge incontinence. Most symptoms were mild to moderate in severity and resolved within 2 to 4 weeks after the procedure. Consult the Instructions for Use (IFU) for more information.

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*Dr. Walter is UroLift faculty and a paid consultant for NeoTract|Teleflex
1. LIFT study showed an IPSS reduction of 47% at 1 year. Roehrborn, J Urology 2013
2. Roehrborn, J Urology 2013
3. No instances of new, sustained erectile or ejaculatory dysfunction: McVary, J Sex Med 2014

My IPSS went from 23 to 3, and I’m thoroughly satisfied with the results.

Peter J. Walter, M.D., F.A.C.S. Western New York Urology Associates and
UroLift® System Patient

The UroLift System procedure is FDA-cleared for the treatment of symptoms due to urinary outflow obstruction secondary to BPH, including lateral and median lobe hyperplasia, in men 45 years of age or older. Results and patient experience may vary. Most common adverse events reported include hematuria, dysuria, micturition urgency, pelvic pain, and urge incontinence. Most symptoms were mild to moderate in severity and resolved within 2 to 4 weeks after the procedure. Consult the Instructions for Use (IFU) for more information.

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To learn more about My Story, visit www.info.UroLift.com/UT
Check out the data at UroLift.com

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BRCA mutations increase risk of reclassification in AS

C urrent guidelines recommend active surveillance (AS) as the preferred management for most patients with low-risk prostate cancer (bit.ly/ProstateCaguide). Although its use has increased substantially over time, AS continues to be underutilized in the U.S. (JAMA 2015; 314:80-2). The reasons for this are multifactorial (BJU Int 2017; 120:32-9) and include uncertainty over the optimal patient selection and follow-up strategies.

There has been increasing recognition of the impact of germline mutations on prostate cancer risk and management decisions. In a study of men with metastatic disease, DNA repair gene mutations were identified in 18.1% (N Engl J Med 2016; 375:443-53). The 2018 NCCN prostate cancer guidelines recommend considering germline testing for all men with advanced and metastatic prostate cancer.

The prevalence of DNA repair mutations is lower in men with localized prostate cancer. For men with favorable-risk disease, the 2018 NCCN guidelines only recommend genetic testing if there is a strong family history (bit.ly/NCCNguides).

An important study by Carter et al (page 4) evaluated the prevalence of germline DNA repair mutations in men with favorable-risk prostate cancer and their association with grade reclassification during AS (Eur Urol Oct 8, 2018 [Epub ahead of print]). A total of 1,211 men on AS had a blood sample used for germline sequencing (three-gene panel). The overall frequency of germline mutations was low: BRCA1 in 11 patients (0.9%), BRCA2 in 11 (0.9%), and ATM in five (0.4%). Overall, 42% of men with mutations had grade reclassification vs. 23% of non-carriers (p=0.04).

How genetic results should influence patient management has already been discussed at several consensus conferences. At the 2017 Philadelphia Prostate Cancer Consensus Conference, 64% of participants voted that BRCA2 mutation status should be factored into management discussions for early-stage/localized prostate cancer (J Clin Oncol 2018; 36:314–24). At the Advanced Prostate Cancer Consensus Conference, when asked whether the presence of a germline BRCA1, BRCA2, or ATM mutation would influence their treatment decisions for low-risk prostate cancer, 45% of panel members voted against AS, 35% voted for standard treatment options (including AS), and 20% voted for another treatment option (Eur Urol 2018; 73:178-21).

The study by Carter et al provides important new data addressing this clinical question. Patients with favorable-risk disease who have a DNA repair mutation should be counseled that there is a significantly increased risk of reclassification with AS.
Germline mutations linked to grade reclassification during AS

Cheryl Guttman Krader
UT Contributing Editor

SAN FRANCISCO—Men with prostate cancer who are carriers of germline pathogenic mutations in the DNA repair genes BRCA1/2 and ATM are at increased risk for grade reclassification during active surveillance, according to research reported by H. Ballentine Carter, MD, at the 2018 AUA annual meeting in San Francisco.

“Active surveillance is often the preferred management option for men with favorable-risk prostate cancer, but some men on active surveillance have adverse outcomes,” said Dr. Carter, Bernard L. Schwartz Distinguished Professor of Urologic Oncology and professor of urology, Johns Hopkins University, Baltimore.

“Our findings suggest that active surveillance may not be the preferred management option for men with germline pathogenic mutations in these DNA repair genes.”

The study was published in European Urology (Oct. 8, 2018 [Epub ahead of print]) following its initial presentation at the AUA annual meeting.

The idea that germline pathogenic mutations in BRCA1/2 and ATM may independently identify men at risk for grade reclassification during active surveillance derived from recent evidence linking such mutations with metastatic and lethal prostate cancer.

To investigate the hypothesis, a study was conducted involving two independent cohorts of prostate cancer patients undergoing active surveillance. The study population comprised 882 men seen at Johns Hopkins and 329 men from the NorthShore University HealthSystem in suburban Chicago. All men had germline DNA samples that had been sequenced for 54 DNA repair genes, including BRCA1/2 and ATM. The sequencing was done at NorthShore using a targeted next-generation sequencing panel, and pathogenic mutations were defined according to American College of Medical Genetics guidelines.

At diagnosis, 97.6% of men were in grade group 1 (GG1, defined by a Gleason score of 3+3); 2.2% were in GG2 (Gleason score 3+4); and 0.2% were in GG3 (Gleason score 4+3). In surveillance biopsies obtained during a median follow-up of 3 years, 24% of men were reclassified (upgraded) from GG1 to a higher GG, and 8% were upgraded from GG1 to a GG ≥2.

Carrier rate for mutations higher in reclassified men

The carrier rate for pathogenic mutations in any of the three genes was significantly higher in men who were reclassified compared to those whose GG remained unchanged (3.8% vs. 1.6%), and the cumulative incidence of upgrading was significantly higher for mutation carriers versus noncarriers (41% vs. 22%). In a multivariable analysis adjusting for age, PSA density, number of cores with cancer, and Eigenvalues (genetic background), mutation carriers had a statistically significant, twofold higher risk for upgrading than noncarriers, Dr. Carter reported.

Analyses considering the three genes individually showed that men with a pathogenic mutation in BRCA2 had the greatest risk for reclassification. Fifty percent of men carrying a pathogenic mutation in BRCA2 were reclassified during follow-up compared with 22% of men without a pathogenic BRCA2 mutation. In the adjusted analysis, carrying a BRCA2 pathogenic mutation increased the risk of upgrading by 2.74-fold.

The cumulative incidence of upgrading from GG1 to GG ≥3 was also significantly higher for men with a pathogenic mutation in any of the three genes compared with noncarriers (20% vs. 8%), and in the adjusted analysis, mutation carriers had a 2.4-fold increased risk of upgrading from GG1 to GG ≥3.

A pathogenic mutation in BRCA2 was also associated with the strongest risk for upgrading from GG1 to GG ≥3. The incidence of upgrading from GG1 to GG ≥3 was 36% among men with a pathogenic mutation in BRCA2 and 8% in noncarriers. In the multivariable analysis, carriers of a pathogenic mutation in BRCA2 had a 5-fold increased risk for upgrading from GG1 to GG ≥3.

In Brief / For up-to-date news, visit urologytimes.com

NSD2 GENE LINKED WITH SPREAD OF PROSTATE CANCER

A recent study has found that a specific gene in cancerous prostate tumors indicates when patients are at high risk for the cancer to spread.

The study, which was published in Nature Communications (2018; 9:5201), identified the NSD2 gene through a computer algorithm developed to determine which cancer genes that spread in a mouse model were most relevant to humans. The authors, led by Antonina Mitrofanova, PhD, of Rutgers School of Health Professions and Rutgers Cancer Institute of New Jersey, New Brunswick, were able to turn off the gene in the mice tumor cells, which significantly decreased the cancer’s spread.

CLINICAL UPDATES

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8 ■ PAIN CONTROL
11 ■ KIDNEY CANCER
Radiation oncology consult linked to active therapy

Patients seeing radiation oncologist more likely to receive RT vs. seeing only urologist

Cheryl Guttman Krader
UT Contributing Editor

SAN FRANCISCO—Patients who receive a radiation oncology consultation after being diagnosed with localized prostate cancer are much more likely to receive active therapy than men managed only by a urologist, and the men seen by a radiation oncologist are particularly likely to be treated with radiation therapy, according to a Canadian population-based, retrospective cohort study.

The research raises several questions that deserve further investigation, said Robert K. Nam, MD, who presented the findings at the 2018 AUA annual meeting in San Francisco and is senior author of the published paper (Br J Cancer 2018; 118:1399-05).

“The findings also raise concerns about whether patients are being overtreated by radiation oncologists or not educated appropriately.”

ROBERT K. NAM, MD

“Chamie et al reported that seeing a radiation oncologist increased the likelihood that patients with indolent prostate cancer would receive radiation treatment, but that study was limited to men >65 years of age who were diagnosed at a time when active surveillance was less accepted than currently. To our knowledge, ours is the first study evaluating the impact of a radiation oncology consultation on treatment patterns for a population including all men diagnosed with localized prostate cancer in the contemporary era,” said Dr. Nam, Ajmera Family Chair in Urologic Oncology and professor of surgery, Edmond Odette Cancer Centre Sunnybrook Health Sciences Centre, University of Toronto.

“As multidisciplinary assessment is being advocated for men with prostate cancer, it is important to consider potential referral biases. It is possible that patients referred to a radiation oncologist may be more likely to receive radiation therapy because they perceive that their urologist believes they need radiation. Perhaps our findings also reflect the intent of multidisciplinary assessments where patients desiring treatment provided with informed choices are more likely to choose patient-centered care. However, the findings also raise concerns about whether patients are being overtreated by radiation oncologists or not educated appropriately.”

The study conducted by Dr. Nam and colleagues identified 16,666 men diagnosed with non-metastatic prostate cancer in Ontario between 2010 and 2013. A total of 11,416 men were included in a matched pair analysis that compared treatment patterns for men who saw a radiation oncologist within 90 days of diagnosis and those without a radiation oncology consultation.

Results showed that men who received a radiation oncology consult were 5.7 times more likely to undergo active therapy in the year following diagnosis compared with those who saw a urologist alone. Among men who saw a radiation oncologist, 25% underwent radical prostatectomy (RP), 60% had radiation therapy (RT), and 15% had active surveillance/watchful waiting (AS/WW). In contrast, among the men who saw only a urologist, 45% underwent RP, only 7% received RT, and 48% were managed with AS/WW.

Active treatment trend holds regardless of risk category

Further analyses explored issues that might affect treatment decisions and found that receipt of active treatment remained higher among men seen by a radiation oncologist regardless of risk category and patient age/comorbidity. Among men with intermediate-/high-risk disease (Gleason score ≥7, stage 2, or PSA >10.0 ng/mL), 34% of patients seeing a urologist did not receive active treatment compared with just 11% who had a radiation oncology consultation. In the group referred to a radiation oncologist, more than twice as many men were managed with RT compared with RP (61% vs. 28%).

“A lot of patients seen by the urologist only may have been undergoing monotherapy with androgen deprivation therapy, and we will be analyzing that in the future,” Dr. Nam said.

Among men with low-risk disease (Gleason stage 6, stage 1, and PSA <10.0 ng/mL), 87% of those seen by a urologist alone were managed with AS/WW compared with 44% of those who had a radiation oncology consult. When men with the “lowest of low risk” disease (Gleason stage 6, stage 1, PSA <10.0, and two or fewer positive cores) saw a radiation oncologist, they were more likely to be managed with AS/WW, but still 26% received RT and 11% underwent RP.

Interestingly, an analysis that stratified men into four subgroups based on age and comorbidity showed that increasing age and comorbidity increased the likelihood that men seen by a radiation oncologist would receive active treatment. Men in the oldest age/highest comorbidity subgroup were 20 times more likely to receive active treatment if they saw a radiation oncologist than men seen by a urologist alone, Dr. Nam reported.

Men diagnosed at an academic center where biopsies are reviewed by specialized genitourinary pathologists were 4.5 times more likely to receive active treatment than their counterparts whose cancer was diagnosed by a community practitioner.

Treatment patterns for men seen by a urologist alone were influenced by time as the rate of AS/WW rose from 85% for men diagnosed in 2010 to 93% for those diagnosed in the last 2 years of the study. However, the proportion of men undergoing AS/WW after seeing a radiation oncologist remained steady throughout the 4 years of the study. UT

TABLE

<table>
<thead>
<tr>
<th>Management choice</th>
<th>Men who saw a radiation oncologist</th>
<th>Men who saw only a urologist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radical prostatectomy</td>
<td>25%</td>
<td>45%</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td>60%</td>
<td>7%</td>
</tr>
<tr>
<td>Active surveillance/watchful waiting</td>
<td>15%</td>
<td>48%</td>
</tr>
</tbody>
</table>

Source: Robert K. Nam, MD
Findings question validity of large PCa trial

PIVOT results put value of RP in doubt, but analysis points to sampling bias

Cheryl Guttman Krader
UT Contributing Editor

SAN FRANCISCO—According to the updated report from the Prostate Cancer Intervention versus Observation Trial (PIVOT), radical prostatectomy had no significant benefit over observation for reducing mortality among men with clinically localized disease. The appropriateness of applying those findings to patients seen in daily practice is questionable, however, considering information from an analysis assessing the external validity of PIVOT, said Firas Abdollah, MD, at the 2018 AUA annual meeting in San Francisco. To evaluate the generalizability of the PIVOT results, Dr. Abdollah and colleagues compared the characteristics of its patient population with those of prostate cancer patients within three nationwide databases—the Surveillance, Epidemiology, and End-Results (SEER) population-based registry, the National Cancer Database (NCDB) hospital-based registry, and the Prostate, Lung, Colorectal and Ovarian (PLCO) trial.

Relative to all three external populations, men in PIVOT were older and had more comorbidities, the authors found. The differences between cohorts in age and general health might explain why the all-cause mortality rate was also much higher in PIVOT compared with the other prospective observational studies (56% vs. 96.4% and 94%, respectively). Higher mortality rate in PIVOT cohort

The overall mortality rates in the PIVOT, SEER, NCDB, and PLCO cohorts were 64%, 23%, 9%, and 8.1%, respectively. Dr. Abdollah noted that the median follow-up in PIVOT, which was 12.7 years, is similar to that for the SEER database (12.3 years), whereas the median follow-up for men in the PLCO trial and NCDB was only 7.5 and 9 years, respectively.

“Interestingly, the overall mortality rate for a subgroup of men from SEER that we excluded from our comparative analysis because they had not been given a recommendation for surgery was 50%. Presumably, these individuals were not recommended definitive treatment because of pre-existing conditions, and yet their mortality rate was still lower than that reported in PIVOT.” UT

“Our findings point to a sampling bias in PIVOT and indicate that the men who enrolled in PIVOT are not representative of those we are seeing in clinical practice.”

FIRAS ABDOLLAH, MD

Patients on AS still undergo unnecessary biopsies

Half of patients switch from surveillance to active treatment within 10 years

Cheryl Guttman Krader
UT Contributing Editor

SAN FRANCISCO—Active surveillance is only moderately able to reduce the harmful effects of prostate cancer overdiagnosis from PSA testing, according to an analysis of the long-term outcomes of men enrolled in the Prostate Cancer Research International Active Surveillance (PRIAS) program, a prospective observational study assessing active surveillance in real-world practice.

The results, which were published in *Translational Andrology and Urology* (2018; 7:98-105) and presented at the 2018 AUA annual meeting in San Francisco, considered the first 500 men entered into PRIAS. At enrollment, all of the men had very low-risk or low-risk disease with a Gleason score (GS) 3+3.

During a median follow-up of 6.5 years, the 500 men underwent a total of 838 biopsies, and the vast majority of those (79% or 90%) did not lead to risk reclassification. Nevertheless, 249 men (50%) switched from active surveillance to invasive treatment within 10 years of follow-up.
and 18% of the switches were for reasons other than reclassification per PRIAS protocol criteria. Furthermore, a review of pathology findings available from 99 men who underwent radical prostatectomy showed that 34% had low-risk disease (GS 3+3 and ≤cT2), 33% had “low” intermediate-risk disease (GS 3+4 and ≤cT2), 7% had intermediate-risk prostate cancer (GS 4+3 and ≤cT2), and 25% had high-risk or locally advanced prostate cancer (GS ≥4+4 or ≥T3), reported first author Frank-Jan H. Drost, MD.

Surveillance does not solve overtreatment problem

“The current U.S. Preventive Services Task Force recommendation to counsel men on PSA screening for prostate cancer is based in part on the idea that active surveillance for men with low-risk prostate cancer can prevent direct overtreatment and reduce the harms associated with overdiagnosis. But our study showed that active surveillance can still lead to many unnecessary, potentially harmful biopsies. In addition, it does not solve the problem of overtreatment, which occurred in at least one-third of men. Furthermore, it should be stressed that half of patients eventually do switch to active treatment, of which 18% does so without an indication of risk reclassification (eg, for anxiety),” said Dr. Drost, PhD candidate, departments of urology and radiology and nuclear medicine, Erasmus University Medical Center, Rotterdam, the Netherlands.

“Therefore, we believe that the ability of active surveillance to reduce the risk of harms from PSA testing might be overstated. Although it can prevent overtreatment in the beginning, it does not give carte blanche to perform PSA screening in all men. Rather, clinicians should be selective when counseling patients about PSA screening and aim to avoid overdiagnosis of prostate cancer in the first place.”

The analysis of outcomes from PRIAS included men enrolled at 30 centers across eight countries from the time of the study launch in December 2006 through July 2008. During that period, the PRIAS protocol recommended PSA testing every 6 months, annual digital rectal examination, and biopsy at planned timepoints of 1, 4, 7, and 10 years and every 5 years thereafter or yearly if PSA doubling time was 0 to 10 years. The protocol also recommended a switch to active treatment for grade reclassification, two or more positive cores, and stage ≥cT2. At enrollment, the 500 men included in the outcomes study had a median age of 65.9 years and median PSA of 5.3 ng/mL; 80% had ≤cT1c disease and 69% had one positive biopsy core.

Biopsy reclassification was identified using two sets of criteria. Based on upgrading alone to GS ≥3+4, only 10% of the 838 biopsies led to reclassification. When the definition considered criteria of GS ≥3+4 or two or more cores positive, 21% of biopsies led to reclassification.
Prophylactic antibiotic use increasing for prostate Bx

Quinolones remain most prescribed oral Tx, but their use has dropped

Andrew D. Bowser / UT Correspondent

In men undergoing prostate biopsy, use of prophylactic antibiotics has been increasing appropriately over time, and fluoroquinolones still dominate, results of an insurance claims database analysis show.

There was a marked increase in regimens that incorporate parenteral administration in the analysis of private insurance claims filed between 2009 and 2015, which was presented at the 2018 American College of Surgeons clinical congress in Boston.

Although fluoroquinolones remained the most prescribed oral therapy, their usage significantly decreased over the time period evaluated, said investigator Mark Henry, MD, a urology resident with Emory University School of Medicine, Atlanta, working with Christopher P. Filson, MD, MS, and colleagues.

“Moving forward, we hope to look to see if this is going to impact outcomes specifically with infections,” said Dr. Henry, who noted increased concerns about fluoroquinolone side effects and emerging antibiotic resistance in a podium presentation of the results.

To evaluate trends in antibiotic use for prostate biopsies, Dr. Henry and colleagues queried the Truven Health MarketScan Database for exposures to prophylactic antibiotics. “They looked in the 30-day pre-procedure window for oral antibiotics, and in the 24-hour pre-procedure window for parenteral antibiotics.”

Fluoroquinolones were the most frequently used oral antibiotics, though use decreased significantly over time, from 76.8% in 2009 to 71.7% in 2015 (p<0.001), Dr. Henry reported.

Use of augmented regimens increased from about 6.5% in 2009 to about 25% in 2015, he added.

“Odds of receiving prophylactic antibiotics increased significantly over time, results of multivariable logistic regression analysis suggested.”

Compared to 2009, the odds ratio for prophylactic antibiotics in 2010 was 1.15 (95% CI: 1.12-1.18; p<0.001), increasing in a stepwise fashion for each successive year, up to an odds ratio of 3.61 (95% CI: 3.48-3.74; p<0.001) in 2015, Dr. Henry reported.

“Charlson comorbidity score linked with receipt of antibiotics”

Increasing Charlson comorbidity score was also notably and significantly associated with receipt of antibiotics, Dr. Henry told meeting attendees.

“AUA guidelines recommend prophylactic antibiotics for patients undergoing transrectal ultrasound-guided prostate biopsy, with fluoroquinolones and cephalosporins as the first-line choice, Dr. Henry noted.

“However, there is a growing concern for the side effects of fluoroquinolones, as well as the potential resistance of E. coli, which is the main target of these antibiotics,” he said.

In parallel, there’s been increasing support and interest in augmented regimens that utilize intravenous or intramuscular antibiotics as well at the time of prostatectomy, he said.

That’s why the authors sought to evaluate trends over time in both fluoroquinolone use and parenteral antibiotics using this insurance database, he told attendees.

Some urology RVUs do not track with complexity, outcomes

Disparity seen with RPLND, cystectomy with bilateral LND

Andrew D. Bowser

UT Correspondent

While the relative value units (RVUs) associated with urologic procedures are generally in line with the surgical complexity and outcomes associated with them, there are four outliers that may warrant a closer look, results of a recent investigation show.

Two procedures that had work RVUs lower than expected based on the combination of operating time, morbidity, and length of stay were retroperitoneal lymph node dissection and cystectomy with bilateral pelvic lymph node dissection, according to the analysis, which was presented at the 2018 American College of Surgeons clinical congress in Boston.

By contrast, laparoscopic partial nephrectomy and laparoscopic ureteral reimplantation had work RVUs that could be adjusted downward, based on a model including three variables, said investigator Case Wood, MD, a urology resident with the University of North Carolina, Chapel Hill.

Table: RVU adjustment after applying multivariable model

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Actual RVU</th>
<th>Change from model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retroperitoneal lymph node dissection</td>
<td>17.7</td>
<td>+10.6</td>
</tr>
<tr>
<td>Cystectomy with bilateral pelvic lymph node dissection</td>
<td>34.1</td>
<td>+6.5</td>
</tr>
<tr>
<td>Laparoscopic partial nephrectomy</td>
<td>27.4</td>
<td>-6.8</td>
</tr>
<tr>
<td>Laparoscopic ureteral reimplantation</td>
<td>25.7</td>
<td>-6.7</td>
</tr>
</tbody>
</table>

Source: Case Wood, MD
Northwestern Medicine is proud to introduce the Polsky Urologic Cancer Institute of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University at Northwestern Memorial Hospital. Led by extraordinary physicians and scientists, we offer innovative, multidisciplinary treatment of all genitourinary cancers. Learn more at nm.org/polsky.
75% of urologic surgery patients have unused opioids

Andrew D. Bowser / UT Correspondent

Current prescribing practices after urologic procedures may be leading to a substantial overupply of opioids in the community, amounting to millions of unused pills every year, results of a recent survey suggest.

Three-quarters of patients reported unused opioids from their initial postoperative prescription, and on average, the patients had only used about half of the pills they received, according to the survey data.

That translates into tens of millions of excess pills unused if extrapolated to the broader urology community, said researcher Kathryn E. Hacker, MD, PhD, a urology resident at the University of North Carolina at Chapel Hill, working with Matthew E. Nielsen, MD, MS, and colleagues.

Reducing the oversupply of opioids related to urologic procedures could have a substantial impact on the nation’s current opioid crisis, suggested Dr. Hacker, who presented the survey findings in a presentation at the 2018 American College of Surgeons clinical congress in Boston.

“I think one specific way we can practice opioid stewardship is just to be aware of what we’re prescribing, and work on prescribing what patients need versus what we have historically prescribed, which a lot of studies—including this one—show is in excess,” Dr. Hacker said in an interview.

Results of the survey are consistent with those of another telephone survey-based study, published in Urology (2018; 123–101–7), showing that 60% of prescribed opioids went unused among 155 patients who had undergone major prostate or kidney operations.

In that study, conducted by researchers at the University of Pittsburgh Medical Center, over-prescribing just in those 155 individuals led to an estimated 2,622 excess pills in the community.

Since conducting their own survey, Dr. Hacker and colleagues have put together a list of appropriate prescribing amounts for urologic procedures to share with colleagues.

“For each procedure, we now have a standard amount that we prescribe,” Dr. Hacker said. “We vary that if someone has shown increased pain postoperatively and we know they’ll need more, but I think having a set amount and setting patient expectations has been a big change for us that we’re really working on.”

55% of prescriptions used on average

In the present study, Dr. Hacker and colleagues conducted a telephone survey of 606 patients who had undergone urologic procedures over a 6-month period spanning 2017–2018. They were able to contact 264 of those patients, approximately 2 weeks after their procedures to ask about their postoperative opioid usage, storage, and disposal.

Of those patients, 75% reported they had unused opioids. The average amount of the prescription used was just 55%, survey results show.

Reported usage ranged from 20% to 60%, meaning that in some cases, up to 80% of the prescription went unused, Dr. Hacker told Urology Times.

That translated into about 2,800 unused opioid pills just for this group of 264 patients. However, if that’s extrapolated to the 11,703 practicing urologists listed in the AUA’s 2015 census, there are about 24 million excess opioid pills going out into the community each year related to urologic procedures, Dr. Hacker and colleagues reported.

One other notable finding from the survey was that only 13% of patients used locked storage locations for their opioid prescriptions.

“That’s now something that we can target in order to make sure that these medications aren’t sitting out on the kitchen counter, available for diversion by other family members,” Dr. Hacker said. UT

Reported usage ranged from 20% to 60%, meaning that up to 80% of the prescription sometimes went unused.

RVUs

continued from page 8

codes for a wide range of urologic surgery procedures. They identified more than 190,000 non-emergent urologic procedures performed between 2012 and 2016.

Work RVUs for those procedures ranged from a low of 4.64 for transurethral resection of small bladder tumor, up to 44.26 for radical cystectomy with neobladder.

Lymph node dissection should be more than 10 units higher

Retroperitoneal lymph node dissection had an RVU value of 17.7, but should actually be around 10.6 units higher, going by a multivariable model the authors built based on three variables, including length of stay, operating time, and length of hospitalization.

Lymph node dissection had an RVU value of 17.7, but should actually be 10.6 units higher, going by a multivariable model the authors built based on three variables, including length of stay, operating time, and patient morbidity.

Likewise, cystectomy with bilateral pelvic lymph node dissection was 34.1 RVUs, which could be increased by 6.5 units, based on the modeling.

By contrast, laparoscopic partial nephrectomy had an RVU value of 27.4 that would be decreased by 6.8 based on this model, while laparoscopic ureteral reimplantation would go from an RVU value of 25.7 that would be revised downward by 6.7. That’s a net increase of about 3.5 RVUs, just looking at this set of four procedures, according to Dr. Wood.

“Certainly, our outcomes are limited by the variables that we’ve defined to represent complexity and workload, but we were surprised to see as good of a correlation as we did,” he said.

Length of stay, operative time, and morbidity were used to create the multivariable model because they had strong correlations with RVUs at the individual variable level, with R2 values of 0.80, 0.87, and 0.75, respectively, Dr. Wood said.

Based on these findings, RVUs for individual CPT codes should be reassigned using a “data-driven approach,” he said. UT
The mutation status of three genes—BAP1, PBRM1, and TP53—had independent prognostic value for patients with advanced or metastatic renal cell carcinoma (RCC) treated with first-line tyrosine kinase inhibitors, and was a useful addition to a risk model that stratifies patients with the disease, a new study indicated.

When mutation status of these three genes was added to the Memorial Sloan Kettering Cancer Center (MSKCC) risk model, there was improved risk stratification of patients with RCC about to initiate first-line therapy.

“Compared with the original MSKCC risk model, our genomically annotated tool altered risk grouping for about half of participants analyzed from two independent cohorts,” Martin H. Voss, MD, medical oncologist at Memorial Sloan Kettering Cancer Center, New York and colleagues wrote in *Lancet Oncol* (2018; 19:1688-98).

Currently, the MSKCC risk model integrates clinical and laboratory data as a prognostic tool for patients with RCC. In this analysis, Dr. Voss and colleagues tested if several mutations had any prognostic value in RCC.

The authors conducted a retrospective study using tissue and outcome data from patients with metastatic disease assigned to TKIs in the COMPARZ trial (357 patients) and RECORD-3 trial (258 patients). In the training cohort, they used next-generation sequencing to evaluate associations between cancer-specific outcomes and the mutation status of six genes (BAP1, PBRM1, TP53, TERT, KDM5C, and SETD2). Using the original MSKCC risk model, 24% of patients were favorable risk; 61% were intermediate risk, and 15% were poor risk.

Samples with any mutation in BAP1 or TP53, or both (odds ratio [OR], 1.57; 95% CI, 1.21–2.04; *p*=.0008), and the absence of a mutation in PBRM1 (OR, 1.58; 95% CI, 1.16–2.14; *p*=.0035) were prognostic for overall survival. For progression-free survival, PBRM1 status had prognostic effect.

In the validation model, BAP1, TP53, and PBRM1 were added to the MSKCC model and the model was tested for prognostic value against the original MSKCC risk model. One point was added for the presence of one or more mutations in BAP1, TP53, or both. In addition, one point was added if BAP1, TP53, and PBRM1 had concurrent mutations or if PBRM1 was wild type.

Overall, patients could score between zero and seven points and the number of risk groups increased from three to four. Favorable risk was zero points, good risk, one point, intermediate risk, two points, and poor risk, three or more points.

**Genetic information improves performance of model**

Using the updated model, 10% of patients were favorable risk; 22%, good risk; 30%, intermediate risk; and 38%, poor risk. “The addition of the genomic information improved the performance of the model for predicting overall survival and progression-free survival, according to the study. “Future work could include extending our investigations to include the IMDC model, the second of the two most commonly applied tools for prognostication and stratification in the metastatic space,” the authors wrote.

Commenting in an accompanying editorial Neeraj Agarwal, MD, and Roberto Nussenzveig, of Huntsman Cancer Institute, Salt Lake City, UT and Sumanta K. Pal, MD, of City of Hope Comprehensive Cancer Center, Duarte, CA noted that although this study shows the value of genomic information on prognostic models, it comes at a time “when the MSKCC stratification tool is being phased out.”

“Allocation to novel regimens such as cabozantinib [Cabometyx] or nivolumab [Opdivo] plus ipilimumab [Yervoy] is predicated on intermediate-risk or poor-risk classification on the basis of IMDC criteria, not MSKCC criteria,” they wrote.

“This development in mind, the genomic markers assessed by Voss and colleagues could warrant reassessment in the context of the studies that are leading to approval of these regimens. Until this happens, clinical implementation of the IMDC criteria (without genomic markers) will most likely prevail,” UT

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**FOUR-YEAR DATA PUBLISHED FOR BPH THERAPY**

Data from a randomized clinical trial demonstrate that Rezum Water Vapor Therapy, a minimally invasive treatment for BPH, provides durable results and preserves sexual function four years after treatment.

The study, published online ahead of print in *Urology* (Jan. 21, 2019), found that patients continued to experience significant and sustained improvement in their symptoms and quality of life over this period.

“This 4-year study supports the use of the... Rezum System as a minimally invasive alternative for men with moderate-to-severe BPH who do not want to rely on pharmaceutical management of their symptoms,” said Kevin T. McVary, MD, lead author and co-principal investigator of the Rezum II Trial.

*Compared with the original MSKCC risk model, our genomically annotated tool altered risk grouping for about half of participants analyzed from two independent cohorts.*

**MARTIN H. VOSS, MD, ET AL.**

*Lancet Oncol* 2018; 19:1688-98

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“With this development in mind, the genomic markers assessed by Voss and colleagues could warrant reassessment in the context of the studies that are leading to approval of these regimens. Until this happens, clinical implementation of the IMDC criteria (without genomic markers) will most likely prevail.” UT

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“Data from a randomized clinical trial demonstrate that Rezum Water Vapor Therapy, a minimally invasive treatment for BPH, provides durable results and preserves sexual function four years after treatment.”

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“The data demonstrate that this advanced technology can empower urologists to achieve significant clinical improvements and deliver an impactful, durable response for their patients,” added Dr. McVary, professor of urology at Loyola University Medical Center, Maywood, IL. Over the 4 years, the trial showed a surgical retreatment rate of 4.4% and no new adverse events noted between years three and four.

The clinical results also highlighted continued preservation of sexual function in patients, including no de novo erectile dysfunction reported at 4 years.

The study was funded by NxThera, Inc.

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Data from a randomized clinical trial demonstrate that Rezum Water Vapor Therapy, a minimally invasive treatment for BPH, provides durable results and preserves sexual function four years after treatment.

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METS? NO METS? START XTANDI.

Regardless of metastatic status, XTANDI offers your patients with castration-resistant prostate cancer (CRPC) the confidence of proven efficacy when PSA is rising* during LHRH therapy.11

* PSA level ≥ 2 ng/mL with at least 2 consecutive rises despite castrate testosterone levels (≤ 50 ng/dL).2-4

Indication and Important Safety Information

**Indication**
XTANDI (enzalutamide) is indicated for the treatment of patients with castration-resistant prostate cancer (CRPC).

**Important Safety Information**

**Warnings and Precautions**

**Seizure**
occurred in 0.4% of patients receiving XTANDI in clinical studies. In a study of patients with predisposing factors for seizure, 2.2% of XTANDI-treated patients experienced a seizure. Patients in the study had one or more of the following pre-disposing factors: use of medications that may lower the seizure threshold; history of traumatic brain or head injury, cerebrovascular accident or transient ischemic attack; Alzheimer’s disease, meningioma, or leptomeningeal disease from prostate cancer; unexplained loss of consciousness within the last 12 months; history of seizures, presence of a space occupying lesion of the brain, history of arteriovenous malformation, or history of brain infection. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. Advise patients of the risk of developing a seizure while taking XTANDI and of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

**Posterior Reversible Encephalopathy Syndrome (PRES)**
In post approval use, there have been reports of PRES in patients receiving XTANDI. PRES is a neurological disorder which can present with rapidly evolving symptoms including seizure, headache, lethargy, confusion, blindness, and other visual and neurological disturbances, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably MRI. Discontinue XTANDI in patients who develop PRES.

**Hypersensitivity**
reactions, including edema of the face (0.5%), tongue (0.1%), or lip (0.1%) have been observed with XTANDI in clinical trials. Pharyngeal edema has been reported in post-marketing cases.

**Adverse Reactions**
The most common adverse reactions (≥ 10%) that occurred more frequently (≥ 2% over placebo) in the XTANDI patients from the randomized placebo-controlled trials were asthenia/fatigue, decreased appetite, hot flush, arthralgia, dizziness/vertigo, hypertension, headache and weight decreased. In the bicalutamide-controlled study, the most common adverse reactions (≥ 10%) reported in XTANDI patients

**Embryo-Fetal Toxicity**
XTANDI can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment with XTANDI and for 3 months after the last dose of XTANDI.

**Ischemic Heart Disease**
In the placebo-controlled clinical studies, ischemic heart disease occurred more commonly in patients on the XTANDI arm compared to patients on the placebo arm (2.7% vs 1.2%). Grade 3-4 ischemic events occurred in 1.2% of patients on XTANDI versus 0.5% on placebo. Ischemic events led to death in 0.4% of patients on XTANDI compared to 0.1% on placebo. Monitor for signs and symptoms of ischemic heart disease. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Discontinue XTANDI for Grade 3-4 ischemic heart disease.

**Falls and Fractures**
In the placebo-controlled clinical studies, falls occurred in 10% of patients treated with XTANDI compared to 4% of patients treated with placebo. Fractures occurred in 8% of patients treated with XTANDI and in 3% of patients treated with placebo. Evaluate patients for fracture and fall risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents.

**Hypersensitivity Reactions**
Permanently discontinue XTANDI for serious hypersensitivity reactions.

**Falls**
In the placebo-controlled clinical studies, falls occurred in 10% of patients treated with XTANDI compared to 4% of patients treated with placebo.

**Fractures**
In the placebo-controlled clinical studies, falls occurred in 10% of patients treated with XTANDI compared to 4% of patients treated with placebo. Fractures occurred in 8% of patients treated with XTANDI and in 3% of patients treated with placebo. Consider use of bone-targeted agents.

**Embryo-Fetal Toxicity**
Safety and efficacy of XTANDI have not been established in females. XTANDI can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment with XTANDI and for 3 months after the last dose of XTANDI.

**Adverse Reactions**
The most common adverse reactions (≥ 10%) that occurred more frequently (≥ 2% over placebo) in the XTANDI patients from the randomized placebo-controlled trials were asthenia/fatigue, decreased appetite, hot flush, arthralgia, dizziness/vertigo, hypertension, headache and weight decreased. In the bicalutamide-controlled study, the most common adverse reactions (≥ 10%) reported in XTANDI patients.
XTANDI significantly prolonged metastasis-free survival\(^6\) in patients with nonmetastatic CRPC and significantly extended overall survival and radiographic progression-free survival in patients with metastatic CRPC\(^7\).

**Nonmetastatic CRPC:** Median metastasis-free survival was 3 years (36.6 months [95% CI, 33.1-\(\infty\)]) with XTANDI + LHRH therapy\(^1\) vs 14.7 months (95% CI, 14.2-15.0) with placebo + LHRH therapy\(^1\) (HR = 0.29 [95% CI, 0.24-0.35]; P < 0.0001).\(^3\)

- As seen in the PROSPER trial: a multinational, randomized, double-blind phase 3 trial that enrolled 1401 patients with nonmetastatic CRPC who progressed on LHRH therapy\(^1\). Eligibility criteria included PSA doubling time ≤ 10 months and no prior chemotherapy\(^1,14\).

**Metastatic CRPC:** 23% reduction in the risk of death with XTANDI + LHRH therapy\(^1\) vs placebo + LHRH therapy\(^1\) (HR = 0.77 [95% CI, 0.67-0.88]) and 83% reduction in the risk of radiographic progression or death vs placebo + LHRH therapy\(^1\) (HR = 0.17 [95% CI, 0.14-0.21]; P < 0.0001).\(^1\)

- As seen in the PREVAIL trial: a multinational, randomized, double-blind phase 3 trial that enrolled 1717 patients with metastatic CRPC who progressed on LHRH therapy\(^1\). Eligibility criteria included no prior chemotherapy\(^1\).

**Drug Interactions**

**Effect of Other Drugs on XTANDI** Avoid strong CYP2C8 inhibitors, as they can increase the plasma exposure to XTANDI. If co-administration is necessary, reduce the dose of XTANDI.

Avoid strong CYP3A4 inducers as they can decrease the plasma exposure to XTANDI. If co-administration is necessary, increase the dose of XTANDI.

**Effect of XTANDI on Other Drugs**

Avoid CYP3A4, CYP2C9, and CYP2C19 substrates with a narrow therapeutic index, as XTANDI may decrease the plasma exposures of these drugs. If XTANDI is co-administered with warfarin (CYP2C9 substrate), conduct additional INR monitoring.

Please see adjacent pages for Brief Summary of Full Prescribing Information.

**References:**

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Printed in USA. 076-4062-PM 1/19

XTANDI, Astellas, and the flying star logo are registered trademarks of Astellas Pharma Inc.
XTANDI® (enzalutamide) capsules for oral use

Initial U.S. Approval: 2012

BRIEF SUMMARY OF PRESCRIBING INFORMATION

The following is a brief summary. Please see the package insert for full prescribing information.

INDICATIONS AND USAGE
XTANDI is an androgen receptor inhibitor indicated for the treatment of patients with castration-resistant prostate cancer.

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
Seizure
Seizure occurred in 0.4% of patients receiving XTANDI in clinical studies. In these trials, patients with predisposing factors for seizure were generally excluded. Seizure occurred from 13 to 604 days after initiation of XTANDI. Patients experiencing seizure were permanently discontinued from therapy and all seizure events resolved.

In a single-arm trial designed to assess the risk of seizure in patients with pre-disposing factors for seizure, 8 of 366 (2.2%) XTANDI-treated patients experienced a seizure. Three of the 8 patients experienced a second seizure during continued treatment with XTANDI after their first seizure resolved. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. Patients in the study had one or more of the following pre-disposing factors: the use of medications that may lower the seizure threshold (~54%), history of traumatic brain or head injury (~28%), history of cerebrovascular accident or transient ischemic attack (~24%), and Alzheimer’s disease, meningoia, or leptomeningeal disease from prostate cancer, unexplained loss of consciousness within the last 12 months, past history of seizure, presence of a space occupying lesion of the brain, history of arteriovenous malformation, or history of brain infection (all <5%). Approximately 17% of patients had more than one risk factor.

Advise patients of the risk of developing a seizure while receiving XTANDI and of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

Posterior Reversible Encephalopathy Syndrome (PRES)
There have been reports of posterior reversible encephalopathy syndrome (PRES) in patients receiving XTANDI. PRES is a neurological disorder which can present with rapidly evolving symptoms including seizure, headache, lethargy, confusion, blindness, and other visual and neurological disturbances, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably magnetic resonance imaging (MRI). Discontinue XTANDI in patients who develop PRES.

Hypersensitivity
Hypersensitivity reactions, including edema of the face (0.5%), tongue (0.1%), or lip (0.1%) have been observed with enzalutamide in four randomized clinical trials. Pharyngol edema has been reported in post-marketing cases. Advise patients who experience any symptoms of hypersensitivity to temporarily discontinue XTANDI and promptly seek medical care. Permanently discontinue XTANDI for serious hypersensitivity reactions.

Ischemic Heart Disease
In the combined data of three randomized, placebo-controlled clinical studies, ischemic heart disease occurred more commonly in patients on the XTANDI arm compared to patients on the placebo arm (2.7% vs 1.2%). Grade 3-4 ischemic events occurred in 1.2% of patients in the XTANDI arm compared to 0.5% in the placebo arm. Ischemic events led to death in 0.4% of patients in the XTANDI arm compared to 0.1% in the placebo arm. Monitor for signs and symptoms of ischemic heart disease. Optimize cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Discontinue XTANDI for Grade 3-4 ischemic heart disease.

Falls and Fractures
Falls and fractures occurred in patients receiving XTANDI. Evaluate patients for fracture and fall risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents.

In the combined data of three randomized, placebo-controlled clinical studies, falls occurred in 10% of patients treated with XTANDI compared to 4% of patients treated with placebo. Falls were not associated with loss of consciousness or seizure. Fractures occurred in 8% of patients treated with XTANDI and in 3% of patients treated with placebo. Grade 3-4 fractures occurred in 2% of patients treated with XTANDI and in <1% of patients treated with placebo. The median time to onset of fracture was 337 days (range: 2 to 996 days) for patients treated with XTANDI. Routine bone density assessment and treatment of osteoporosis with bone-targeted agents were not performed in the studies.

Embryo-Fetal Toxicity
The safety and efficacy of XTANDI have not been established in females. Based on animal reproductive studies and mechanism of action, XTANDI can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment with XTANDI.

Falls occurred from 13 to 604 days after the last dose of XTANDI. XTANDI should not be handled by females who are or may become pregnant.

ADVERSE REACTIONS
Clinical Trial Experience
Because clinical trials are conducted under predetermined treatment guidelines and consider use of bone-targeted agents.

Table 1. Adverse Reactions in AFFIRM

<table>
<thead>
<tr>
<th>Reaction</th>
<th>XTANDI N = 800</th>
<th>Placebo N = 389</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 (%)</td>
<td>Grade 2 (%)</td>
<td>Grade 3 (%)</td>
</tr>
<tr>
<td>N = 800</td>
<td>N = 389</td>
<td></td>
</tr>
<tr>
<td>Adverse Reactions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>22</td>
<td>1.1</td>
</tr>
<tr>
<td>Vascular Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot flush</td>
<td>20</td>
<td>0.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6.4</td>
<td>2.1</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>12</td>
<td>0.9</td>
</tr>
<tr>
<td>Dizziness</td>
<td>9.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Spinal Cord Compression</td>
<td>7.4</td>
<td>6.6</td>
</tr>
<tr>
<td>Posterior Reversible</td>
<td>6.6</td>
<td>0.0</td>
</tr>
<tr>
<td>Impairment Disorders</td>
<td>4.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4.0</td>
<td>0.3</td>
</tr>
<tr>
<td>Infections and Infestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper Respiratory Tract</td>
<td>11</td>
<td>0.0</td>
</tr>
<tr>
<td>Infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower Respiratory Tract</td>
<td>8.5</td>
<td>2.4</td>
</tr>
<tr>
<td>Infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>8.8</td>
<td>0.0</td>
</tr>
<tr>
<td>Anxiety</td>
<td>6.5</td>
<td>0.3</td>
</tr>
<tr>
<td>Renal and Urinary Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematuria</td>
<td>6.9</td>
<td>1.8</td>
</tr>
<tr>
<td>Pollakiuria</td>
<td>4.8</td>
<td>0.0</td>
</tr>
<tr>
<td>Injury, Poisoning and Procedural Complications</td>
<td>4.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td>3.8</td>
<td>0.0</td>
</tr>
<tr>
<td>Dry Skin</td>
<td>3.5</td>
<td>0.0</td>
</tr>
<tr>
<td>Respiratory Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epistaxis</td>
<td>3.3</td>
<td>0.1</td>
</tr>
</tbody>
</table>

1. Grade 4 includes Grade 3 with a change in medical condition. Grade 4 includes Grade 3 with a change in medical condition.

2. Includes hypertension, diabetes, or dyslipidemia.

3. Includes amnesia, memory impairment, cognitive disorder, and disturbance in attention.

4. Includes postural hypotension, upper respiratory tract infection, sinusitis, rhinitis, pharyngitis, and laryngitis.

5. Includes pneumonia, lower respiratory tract infection, bronchitis, and lung infection.
PREVAIL (NCT01212991): XTANDI versus Placebo in Chemotherapy-naive Metastatic CRPC

PREVAIL enrolled 1717 patients with metastatic CRPC who had not received prior cytotoxic chemotherapy, of whom 1715 received at least one dose of study drug. The median duration of treatment was 17.5 months with XTANDI and 4.6 months with placebo. Grade 3-4 adverse reactions were reported in 44% of XTANDI-treated patients and 37% of placebo-treated patients. Discontinuations due to adverse events were reported for 6% of XTANDI-treated patients and 6% of placebo-treated patients. The most common adverse reaction leading to treatment discontinuation was fatigue/asthenia, which occurred in 1% of patients on each treatment arm. Table 2 includes adverse reactions reported in PREVAIL that occurred at ≥ 2% higher frequency in the XTANDI arm compared to the placebo arm.

### Table 2. Adverse Reactions in PREVAIL

<table>
<thead>
<tr>
<th>Disorder</th>
<th>XTANDI (N = 183)</th>
<th>Placebo (N = 189)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthenic Conditions</td>
<td>32.6%</td>
<td>16.1%</td>
<td>0.00</td>
</tr>
<tr>
<td>Peripheral Edema</td>
<td>1.6%</td>
<td>0.4%</td>
<td></td>
</tr>
<tr>
<td><strong>Musculoskeletal and Connective Tissue Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back Pain</td>
<td>29.7%</td>
<td>22.0%</td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>21.6%</td>
<td>11.1%</td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>7.7%</td>
<td>4.2%</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10.8%</td>
<td>14.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Vascular Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot flush</td>
<td>18.0%</td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>14.2%</td>
<td>1.3%</td>
<td></td>
</tr>
<tr>
<td><strong>Nervous System Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>11.0%</td>
<td>7.1%</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>11.2%</td>
<td>7.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Reproductive System and Breast Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysuria</td>
<td>5.9%</td>
<td>0.2%</td>
<td></td>
</tr>
<tr>
<td><strong>Infections and infestations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection</td>
<td>16.0%</td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>Lower Respiratory Tract and Lung Infection</td>
<td>7.9%</td>
<td>5.7%</td>
<td></td>
</tr>
<tr>
<td><strong>Psychiatric Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>8.2%</td>
<td>0.1%</td>
<td></td>
</tr>
<tr>
<td>Renal and Urinary Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematuria</td>
<td>8.8%</td>
<td>1.3%</td>
<td></td>
</tr>
<tr>
<td>Injury, Poisoning and Procedural Complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>13.6%</td>
<td>5.3%</td>
<td></td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>19.3%</td>
<td>16.7%</td>
<td></td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight Decreased</td>
<td>12.8%</td>
<td>6.5%</td>
<td></td>
</tr>
<tr>
<td>Reproductive System and Breast Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Synecomastosis</td>
<td>3.4%</td>
<td>0.0%</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Adverse Reactions in PREVAIL (Continued)

3. Includes all osseous fractures from all sites.
4. Includes dizziness and vertigo.
5. Includes dyspnea, exertional dyspnea, and dyspnea at rest.
6. Includes nasopharyngitis, upper respiratory tract infection, sinusitis, rhinitis, pharyngitis, and laryngitis.
7. Includes pneumonia, lower respiratory tract infection, sinusitis, rhinitis, pharyngitis, and laryngitis.

### Table 3. Adverse Reactions in TERRAIN

TERRAIN enrolled 375 patients with metastatic CRPC who had not received prior cytotoxic chemotherapy, of whom 372 received at least one dose of study drug. The median duration of treatment was 11.6 months with XTANDI and 8.3 months with bicalutamide. Discontinuations with an adverse event as the primary reason were reported for 7.6% of XTANDI-treated patients and 6.3% of bicalutamide-treated patients. The most common adverse reactions leading to treatment discontinuation were back pain and pathological fracture, which occurred in 3.8% of XTANDI-treated patients for each event and in 2.1% and 1.0% of bicalutamide-treated patients, respectively. Table 3 shows overall and common adverse reactions (> 10%) in XTANDI-treated patients.

### Table 3. Adverse Reactions in TERRAIN

<table>
<thead>
<tr>
<th>Disorder</th>
<th>XTANDI (N = 183)</th>
<th>Placebo (N = 228)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthenic Conditions</td>
<td>32.6%</td>
<td>16.1%</td>
<td>0.00</td>
</tr>
<tr>
<td><strong>Musculoskeletal and Connective Tissue Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back Pain</td>
<td>29.7%</td>
<td>22.0%</td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>21.6%</td>
<td>11.1%</td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>7.7%</td>
<td>4.2%</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10.8%</td>
<td>14.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Vascular Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot flush</td>
<td>18.0%</td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>14.2%</td>
<td>1.3%</td>
<td></td>
</tr>
<tr>
<td><strong>Nervous System Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>11.0%</td>
<td>7.1%</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>11.2%</td>
<td>7.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Psychiatric Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>8.2%</td>
<td>0.1%</td>
<td></td>
</tr>
<tr>
<td>Renal and Urinary Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematuria</td>
<td>8.8%</td>
<td>1.3%</td>
<td></td>
</tr>
<tr>
<td>Injury, Poisoning and Procedural Complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>13.6%</td>
<td>5.3%</td>
<td></td>
</tr>
<tr>
<td><strong>Metabolism and Nutrition Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>19.3%</td>
<td>16.7%</td>
<td></td>
</tr>
<tr>
<td><strong>Infections and infestations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection</td>
<td>16.0%</td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>Lower Respiratory Tract and Lung Infection</td>
<td>7.9%</td>
<td>5.7%</td>
<td></td>
</tr>
<tr>
<td><strong>Psychiatric Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>8.2%</td>
<td>0.1%</td>
<td></td>
</tr>
</tbody>
</table>

### PROSPER (NCT02003924): XTANDI versus Bicalutamide in Chemotherapy-naive Metastatic CRPC

PROSPER enrolled 1401 patients with non-metastatic CRPC, of whom 1395 received at least one dose of study drug. Patients were randomized 2:1 and received either XTANDI at a dose of 160 mg once daily (N = 930) or placebo (N = 465). The median duration of treatment at the time of analysis was 18.4 months (range: 0.0 to 42 months) with XTANDI and 11.1 months (range: 0.0 to 43 months) with placebo. Overall, 32 patients (2.3%) receiving XTANDI died of cardiac arrest (n = 1), left ventricular failure (n = 1), and pancreatic carcinoma (n = 1). Grade 3 or higher adverse reactions were reported among 31% of XTANDI-treated patients and 23% of placebo-treated patients. Discontinuations with an adverse event as the primary reason were reported for 8% of XTANDI-treated patients and 6% of placebo-treated patients. Of these, the most common adverse event leading to treatment discontinuation was fatigue, which occurred in 1.8% of the XTANDI-treated patients compared to none of the placebo-treated patients. Table 4 shows adverse reactions reported in PROSPER that occurred at ≥ 2% higher frequency in the XTANDI arm than in the placebo arm.

### Table 4. Adverse Reactions in PROSPER

<table>
<thead>
<tr>
<th>Disorder</th>
<th>XTANDI (N = 930)</th>
<th>Placebo (N = 465)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metabolism and Nutrition Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>9.6%</td>
<td>3.9%</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>Nervous System Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>12.0%</td>
<td>0.5%</td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>11.0%</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td><strong>Vascular Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot flush</td>
<td>13.0%</td>
<td>7.7%</td>
<td></td>
</tr>
<tr>
<td><strong>Psychiatric Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>2.8%</td>
<td>0.2%</td>
<td></td>
</tr>
</tbody>
</table>

### Laboratory Abnormalities

In the AFFIRM and PREVAIL studies in metastatic CRPC, Grade 1-4 neuropenia occurred in 15% of patients receiving XTANDI (1% Grade 3-4) and in 6% of patients receiving placebo (0.5% Grade 3-4).

Table 5 shows laboratory abnormalities that occurred in ≥ 5% of patients, and more frequently (> 2%) in the XTANDI arm compared to placebo in the PROSPER study.

### Table 5. Laboratory Abnormalities in PROSPER

<table>
<thead>
<tr>
<th>Disorder</th>
<th>XTANDI (N = 930)</th>
<th>Placebo (N = 465)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hematology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>8.2%</td>
<td>0.5%</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>Chemistry</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>16.3%</td>
<td>8.8%</td>
<td>1.5</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>78.2%</td>
<td>27.0%</td>
<td>1.3</td>
</tr>
<tr>
<td>Hypomagnesemia</td>
<td>26.0%</td>
<td>21.0%</td>
<td></td>
</tr>
</tbody>
</table>
**Hypertension**

In the AFFIRM and PREVAIL studies in metastatic CRPC, hypertension was reported in 11% of patients receiving XTANDI and 4% of patients receiving placebo. Medical history of hypertension was balanced between arms. Hypertension led to study discontinuation in 1% of patients in each arm. In the PROSPER study in non-metastatic CRPC, hypertension was reported in 12% of patients receiving XTANDI and 5% of patients receiving placebo.

**Post-Marketing Experience**

The following additional adverse reactions have been identified during post-approval use of XTANDI. Because these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate the frequency or establish a causal relationship to drug exposure. Body as a Whole: hypersensitivity (edema of the face, tongue, lip, or pharynx)

**Gastrointestinal Disorders:** vomiting

**Neurological Disorders:** posterior reversible encephalopathy syndrome (PRES)

**DRUG INTERACTIONS**

**Drugs that Inhibit CYP2C8**

Co-administration of a strong CYP2C8 inhibitor (gemfibrozil) increased the composite area under the curve (AUC) of enzalutamide plus N-desmethyl enzalutamide by 2.2-fold. Co-administration of XTANDI with strong CYP2C8 inhibitors should be avoided if possible. If co-administration of XTANDI with a strong CYP2C8 inhibitor cannot be avoided, reduce the dose of XTANDI.

**Drugs that Induce CYP3A4**

Co-administration of rifampin (strong CYP3A4 inducer and moderate CYP2C8 inducer) decreased the composite AUC of enzalutamide plus N-desmethyl enzalutamide by 37%. Coadministration of strong CYP3A4 inducers (e.g., carbamazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine) with XTANDI should be avoided if possible. St John’s wort may decrease enzalutamide exposure and should be avoided. If co-administration of a strong CYP3A4 inducer with XTANDI cannot be avoided, increase the dose of XTANDI.

**Effect of XTANDI on Drug Metabolizing Enzymes**

Enzalutamide is a strong CYP3A4 inducer and a moderate CYP2C9 and CYP2C19 inducer in humans. At steady-state, XTANDI reduced the plasma exposure to midazolam (CYP3A4 substrate), warfarin (CYP2C9 substrate), and omeprazole (CYP2C19 substrate). Concomitant use of XTANDI with narrow therapeutic index drugs that are metabolized by CYP3A4 (e.g., alfentanil, cyclosporine, diltiazem, digoxin, ergotamine, fentanyl, imatinib, ketoconazole, sirolimus, and tacrolimus), CYP2C9 (e.g., phenytoin, warfarin) and CYP2C19 (e.g., S-mephentoin, clopidogrel) should be avoided, as enzalutamide may decrease the exposure of these drugs. If co-administration with warfarin cannot be avoided, conduct additional INR monitoring.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

**Risk Summary**

The safety and efficacy of XTANDI have not been established in females. Based on animal reproductive studies and mechanism of action, XTANDI can cause fetal harm and loss of pregnancy. There are no human data on the use of XTANDI in pregnant females. In animal reproduction studies, oral administration of enzalutamide in pregnant mice during organogenesis caused adverse developmental effects at doses lower than the maximum recommended human dose (see Data). XTANDI should not be handled by females who are or may become pregnant.

**Animal Data**

In an embryo-fetal developmental toxicity study in mice, enzalutamide caused developmental toxicity when administered at oral doses of 10 or 30 mg/kg/day throughout the period of organogenesis (gestational days 6-15). Findings included embryo-fetal lethality (increased post-implantation loss and resorptions) and decreased anogenital distance at ≥ 10 mg/kg/day, and cleft palate and absent patellae bone at 30 mg/kg/day. Doses of 30 mg/kg/day caused maternal toxicity. The doses tested in mice (1, 10 and 30 mg/kg/day) resulted in systemic exposures (AUC) approximately 0.04, 0.4 and 1.1 times, respectively, the exposures in patients. Enzalutamide did not cause developmental toxicity in rabbits when administered throughout the period of organogenesis (gestational days 6-18) at doses levels up to 10 mg/kg/day (approximately 0.4 times the exposures in patients based on AUC).

In a pharmacokinetic study in pregnant rats with a single oral 30 mg/kg enzalutamide administration on gestation day 14, enzalutamide and/or its metabolites were present in the fetuses at a Cmax that was approximately 0.3 times the concentration found in maternal plasma and occurred 4 hours after administration.

**Lactation**

**Risk Summary**

The safety and efficacy of XTANDI have not been established in females. There is no information available on the possibility of XTANDI in human milk, the effects of the drug on the breastfeeding infant, or the effects of the drug on the breastfed infant. Enzalutamide and/or its metabolites were present in milk in lactating rats (see Data). Data Following a single oral administration in lactating rats on postnatal day 14, enzalutamide and/or its metabolites were present in milk at a Cmax that was 4 times higher than concentrations in the plasma and occurred 4 hours after administration.

**Females and Males of Reproductive Potential**

**Contraception**

Males Based on findings in animal reproduction studies, advise male patients with female partners of reproductive potential to use effective contraception.

**Pediatric Use**

Safety and effectiveness of XTANDI in pediatric patients have not been established.

**Geriatric Use**

Of 2784 patients who received XTANDI in four clinical trials, 6% were 65 and over, whereas 3% were 75 and over. No overall differences in safety or effectiveness were observed between these patients and younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

**Patients with Renal Impairment**

A dedicated renal impairment trial for XTANDI has not been conducted. Based on the population pharmacokinetic analysis using data from clinical trials in patients with metastatic CRPC and healthy volunteers, no significant difference in enzalutamide clearance was observed in patients with pre-existing mild to moderate renal impairment (30 mL/min ≤ creatinine clearance [CrCl] < 60 mL/min) compared to patients and volunteers with baseline normal renal function (CrCl ≥ 90 mL/min). No initial dosage adjustment is necessary for patients with mild to moderate renal impairment. Severe renal impairment (CrCl < 30 mL/min) and end-stage renal disease have not been assessed.

**Patients with Hepatic Impairment**

Dedicated hepatic impairment trials compared the composite systemic exposure of enzalutamide plus N-desmethyl enzalutamide in volunteers with baseline mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, or C, respectively) versus healthy controls with normal hepatic function. The composite AUC of enzalutamide plus N-desmethyl enzalutamide was similar in volunteers with mild, moderate, or severe baseline hepatic impairment compared to volunteers with normal hepatic function. No initial dosage adjustment is necessary for patients with baseline mild, moderate, or severe hepatic impairment.

**OVERDOSAGE**

In the event of an overdose, stop treatment with XTANDI and initiate general supportive measures taking into consideration the half-life of 5.8 days. In a dose escalation study, no seizures were reported at < 240 mg daily, whereas 3 seizures were reported, 1 each at 360 mg, 480 mg, and 600 mg daily. Patients may be at increased risk of seizure following an overdose.

**NONCLINICAL TOXICOLOGY**

Carcinogenesis, Mutagenesis, Impairment of Fertility

Administration of enzalutamide to male and female rasH2 transgenic mice by oral gavage daily for 26 weeks did not result in increased incidence of neoplasms at doses up to 20 mg/kg/day. Enzalutamide did not induce mutations in the bacterial reverse mutation (Ames) assay and was not genotoxic in either the in vitro mouse lymphoma thymidine kinase (Tk) gene mutation assay or the in vivo mouse micronucleus assay.

Based on nonclinical findings in repeat-dose toxicology studies, which were consistent with the pharmacological activity of enzalutamide, male fertility may be impaired by treatment with XTANDI. In a 26-week study in rats, atrophy of the prostate and seminal vesicles was observed at ≥ 30 mg/kg/day (equal to the human exposure based on AUC). In 4-, 13-, and 39-week studies in dogs, hypospermatogenesis and atrophy of the prostate and epididymides were observed at > 4 mg/kg/day (0.3 times the human exposure based on AUC).

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Astellas Pharma US, Inc., Northbrook, IL 60062

Pfizer Inc., New York, NY 10017

**Revised:** July 2018

198511-XTA-USA

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076-3717-PM
Preoperative variables may be predictive of post-cystectomy complication risk

Researchers hope to create prediction calculator for preoperative patient counseling

Andrew Bowser
UT Correspondent

The risk of high-grade postoperative complications after radical cystectomy for bladder cancer might be predicted using a model that incorporates several routinely collected preoperative variables, a researcher reported at the 2018 Society of Urologic Oncology annual meeting in Phoenix.

Using data collected during the course of preoperative history, physical examination, and staging, Sida Niu, MD, and colleagues at the University of Kansas Medical Center, Kansas City developed a series of prediction models using a cohort of patients who underwent radical cystectomy for bladder cancer at their institution.

The best performing prediction model utilized four variables—body mass index, creatinine, preoperative chemotherapy, and robotic approach, said Dr. Niu, urology resident at the University of Kansas, working with Eugene Lee, MD, and colleagues.

Although further study is needed, the current data suggest these models might help identify certain patients who can benefit from further patient education, counseling, and development of risk reduction strategies, Dr. Niu said in an interview with Urology Times.

“We tried to include mostly modifiable variables, but some non-modifiable variables are also included because they provide information in helping patients understand their postoperative risks, which can be informative when counseling patients contemplating radical cystectomy,” he said.

Their retrospective study included 508 patients, of whom 336 (66%) had at least one complication of any grade. In looking at 28 preoperative variables collected for those patients, they identified 14 that were associated with increased risks of high-grade postoperative complications.

Out of those 14 variables, they chose 11 to design a series of prediction models, the accuracy of which they assessed using area under the receiver operating characteristic curve (AUROC) and a cross-validation procedure.

BMI among variables with highest predictive accuracy

The variables with the highest prediction accuracy in univariable analysis were BMI (AUROC 0.643; odds ratio, 1.09), creatinine (0.609, 2.43), preoperative chemotheraphy (0.597, 1.22), and robotic approach (0.590, 2.33), Dr. Niu reported.

The authors described a total of 20 prediction models, the best performing of which utilized those four variables and had an AUROC of 0.727.

The complication rates in this retrospective cohort were in line with previous studies showing that up to 60% of patients undergoing radical cystectomy will experience complications, such as postoperative ileus or infections, within 90 days of the procedure, according to Dr. Niu.

“Many of these complications will prolong the hospital stay, increase total cost of the treatment, and decrease the overall quality of life for these patients,” he said.

While this predictive model is not ready for use on a wide scale, Dr. Niu said investigators hope that with further evaluation of interactions between individual variables, they’ll be able to further improve the accuracy of their prediction models and eventually create a prediction calculator that could be used to counsel patients in the preoperative setting.

“That might be a substantial improvement over current practice, he added.

“When we identify patients who may be candidates for radical cystectomy, we often use a vague picture of their health that we get from their charts—do they have comorbidities like heart conditions or lung conditions? Have they had previous abdominal surgeries or radiation therapy?” he said. “While these questions help us assess the patient as a surgical candidate, the process can certainly be improved to include a feedback component that allow patients to make lifestyle changes and potentially decrease their risk of postoperative complications.”

The authors reported on complications from 31- to 90-days post-procedure in part because their earlier investigations showed risk models in this window performed better than in the 30-day postoperative period, Dr. Niu said.

The authors hypothesized that complications in that earlier 30-day time frame may be more related to the surgery itself, rather than due to individual characteristics or preoperative factors, he added. UT

TRIAL TO PAIR KIDNEY CA IMMUNOTHERAPY WITH PERSONALIZED VACCINE

By pairing a novel personalized cancer vaccine with a more established immunotherapy drug that is administered to patients in an innovative fashion, scientists at Dana-Farber Cancer Institute, Boston, are testing a first-of-its-kind strategy aimed at improving outcomes for kidney cancer patients who are at high risk of recurrence following surgery.

This two-pronged approach to mobilizing a patient’s immune response against cancer cells that remain in the body after surgery is being evaluated in a phase I clinical trial that aims to enroll 15 to 20 patients. It is the first trial to evaluate a personalized cancer vaccine in patients with kidney cancer.

“These are patients who have high-risk disease, and have had it all surgically removed,” said David Braun, MD, PhD, who is leading the trial together with Toni Choueiri, MD, and Patrick Ott, MD, PhD, and in a collaboration with the Broad Institute of MIT and Harvard. “There is no clear evidence of disease left in their body, but we know that up to half of them will eventually have disease recurrence” resulting from undetected residual tumor cells. “Currently, there are no good treatment options available for these patients” to decrease the chances of recurrence.

The new approach is aimed at improving the success of immunotherapy for these patients by combining ipilimumab (Yervoy) with a personalized vaccine designed to recognize neoantigens. The vaccine, known as NeoVax, is based on research at Dana-Farber led by Catherine Wu, MD, Dr. Braun said that such a vaccine could “steer” the immune response—after being freed by the checkpoint blocker drug—to focus tightly on the cancer cells.
When addressing the treatment for high-risk prostate cancer, all of the guidelines recommend either surgery or radiation therapy as a valid option for initial treatment. In a recent analysis of Surveillance, Epidemiology, and End Results data, Huang et al report that prostatectomy was associated with improved cancer-specific and overall mortality when compared to primary radiation therapy in men age <60 years (J Urol 2019; 201:120-8).

The authors analyzed data from the most recent SEER registry, focusing on younger men (<60 years) who had Gleason score 8-10 prostate cancer, without nodal or distant metastases. After excluding men with metastases or without initial surgery or radiation or short follow-up (<2 years), 2,228 men met the study criteria. The median age was 56 years and the median follow-up was 44 months.

Of these 2,228 men, 1,459 (65.5%) underwent surgery and 769 (34.5%) were treated with radiation therapy. Within the radiation therapy cohort, external beam alone was used in 583 (75.8%) and external beam plus brachytherapy was used in 186 (24.2%). Among the men treated with initial surgery, 266 (18.2%) required adjuvant radiation therapy. The surgery cohort was more likely to be somewhat younger, Caucasian, and with PSA <20 ng/mL.

The estimated 7-year cancer-specific mortality was lower in the surgery cohort compared to the radiation group—8.2% and 12.1% (p=.001), respectively. The 7-year overall mortality was similarly reduced in the surgery group—10.2% versus 21.2%, respectively. On multivariable analysis, prostatectomy was associated with a significant decrease in cancer-specific mortality and overall mortality, after controlling for age, Gleason score, clinical T stage, and PSA level (p=.001). In men undergoing surgery, there was a 16.5% decrease in cancer-specific mortality and a 40.6% decrease in overall mortality compared to initial radiation. On multivariable analysis, prostatectomy was associated with a significant decrease in cancer-specific mortality and overall mortality compared to initial radiation.

While a number of important clinical variables were included in the analysis, some of the most pertinent data were not available: comorbidities, use and duration of hormonal therapy, and the dose of radiation. It is possible that the lower mortality from surgery noted in this analysis may be due to selection of healthier patients for surgery.

Effects of hormonal therapy must be taken into account
Hormonal therapy, which has long been used in combination with radiation therapy of high-risk cancer, is associated with both short-term and long-term systemic toxicity. The adverse effects of hormonal therapy may be a significant contributing factor for the higher overall mortality noted with radiation therapy.

If history is our guide, it’s unlikely that a large, randomized controlled trial will be successfully conducted in the space of localized prostate cancer. We are then left to make the best use of available data from various sources such as SEER or other larger registries or single-institution experience. When counseling our younger patients about potential advantages of surgery, it’s essential to be cognizant of the limitations and confounding factors listed above.

### TABLE COMPARISON OF RP, RT FOR HIGH-RISK PROSTATE CA: KEY FINDINGS

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated 7-year cancer-specific mortality was lower in the surgery cohort compared to the radiation group</td>
<td>8.2% and 12.1% (p&lt;.001), respectively</td>
</tr>
<tr>
<td>7-year overall mortality was also lower in the surgery group</td>
<td>10.2% versus 21.2%, respectively</td>
</tr>
<tr>
<td>On multivariable analysis, prostatectomy was associated with a significant decrease in cancer-specific mortality and overall mortality</td>
<td></td>
</tr>
<tr>
<td>In men undergoing surgery, there was a 16.5% decrease in cancer-specific mortality and a 40.6% decrease in overall mortality compared to initial radiation</td>
<td></td>
</tr>
</tbody>
</table>

Source: J Urol 2019; 201:120-8
Persistent disparities in outcomes between men and women with bladder cancer highlight areas of needed improvement in the delivery of oncologic care. There were approximately 81,190 new cases of bladder cancer in the United States in 2018, and the majority of these cases were in men. While males are three to four times more likely to develop the disease, women tend to present with advanced stage, experience differences in quality of life following treatment, and suffer worse cancer-specific mortality (Surveillance, Epidemiology, and End Results (SEER) Program Populations [1992-2018], www.seer.cancer.gov, released 2018).

Based on Surveillance, Epidemiology, and End Results (SEER) data, women appear to have better cancer-specific mortality for most malignancies; however, this does not appear to be the case for bladder cancer (Cancer Epidemiol Biomarkers Prev 2011; 20:1629–37). Epidemiologic and biologic explanations have been offered, but our incomplete understanding of the issue suggests numerous contributing factors.

In this article, we examine these factors, with a focus on current research that elucidates their role in the bladder cancer gender disparity. The table provides a summary of these research findings.

**Disparities in evaluation and diagnosis**

Perhaps the most evident disparity confronting female patients with bladder cancer relates to timely evaluation and diagnosis. The reasons for this are multifaceted and reflect differences in how female patients with hematuria progress through the health care system. Interpretation of hematuria in the female patient can be challenging for primary care physicians. While hematuria is certainly concerning for malignancy, it is also present in a number of benign conditions, including urinary tract infections, which are common in postmenopausal females.

In a large population study performed by Cohn and colleagues, women presenting with hematuria who were ultimately diagnosed with bladder cancer were far more likely to be treated for a suspected urinary tract infection during initial evaluation than males (Cancer 2014; 120:555-560). Similarly, evaluation of practice patterns of primary care physicians by Buteau and colleagues demonstrated that women presenting with hematuria often underwent three or more pre-referral consultations with their primary care provider for the same complaint before referral for urologic evaluation (OR: 2.31, 95% CI: 1.98–2.69) (Urol Oncol 2014; 32:128-14).

It is possible that these barriers are the result of conflicting guidelines regarding the evaluation of asymptomatic microscopic hematuria. While the AUA defines microscopic hematuria as greater than 3 red blood cells per high powered field as the trigger for further diagnostic evaluation, 2017 guidelines from the American College of Obstetricians and Gynecologists favor a cutoff of 25 red blood cells per high powered field for non-smoking women under 50 years of age. This may lead to confusion for primary care physicians as to when referral is appropriate. Similarly, women who present to their gynecologist for evaluation of microscopic hematuria may experience delays in urologic referral.

While individually, these factors likely play only a small role in the overall delay in evaluation, the effect is notable. Cohn and colleagues demonstrated that women were more likely to experience a delay in time to diagnosis when compared to men (85.4 days vs. 73.6 days; *p<.001) and a higher rate of >6-month delay in diagnosis (17.3% vs. 14.1%; *p<.001) (Cancer 2014; 120:555-61). It has been well documented that delays in diagnosis translate to poorer cancer-specific outcomes (J Urol 2003; 169:110-5).

**Differences in cancer-specific outcomes**

Even after diagnosis, female patients with bladder cancer continue to suffer worse outcomes than males following definitive treatment. While it has been proposed that advanced stage presentation in women may be to blame, this does not fully explain differences in overall survival. An analysis of 5-year survival between men and women with bladder cancer found that women fared worse across all stages (J Urol 2000; 163:687-71). This would suggest that gender continues to play a role even after diagnosis.

The evidence for nonmuscle-invasive bladder cancer is mixed and somewhat limited. One single-institution series suggests that women were less likely to receive intravesical therapy for nonmuscle-invasive disease, but larger population cohorts have failed to demonstrate this (Urol Oncol 2014; 32:23.e1-9; Br J Cancer 2013; 108:1514-40).

Several studies have examined the use of treatment modalities and associated outcomes in women with muscle-invasive bladder cancer. An analysis of SEER data that examined the use of radical cystectomy or radiotherapy in patients with muscle-invasive bladder cancer revealed that while men were more likely to receive radiotherapy, there were no differences in the use of radical cystectomy between men and women (J Urol 2003; 170:1765-71).

Similarly, it has been demonstrated that female patients do not experience significant differences in surgical margin status and lymph node count at the time of cystectomy (Eur Urol 2014; Please see BLADDER Ca, page 20).
Differences in urinary diversion utilization and HRQoL

Despite equivalent use of radical cystectomy between men and women, the use of continent diversions is underutilized in the female population. A recent review of radical cystectomies performed in the United States revealed that while the use of continent urinary diversions has declined, male patients still received continent diversions at more than twice the rate of female patients (Bladder Cancer 2018; 4:113-20). It has been demonstrated that women suffer worse health-related quality of life outcomes following ileal conduit when compared to men (In Vivo 2018; 32:139-43).

While patient perception of body image and the results of surgery impact a number of quality of life measures in all patients, several studies have suggested this may be improved with the use of continent diversion. In a meta-analysis performed by Cerruto et al, 65% of men who had an orthotopic neobladder following radical cystectomy showed improved quality of life measures when compared to those who received an ileal conduit (Eur J Surg Oncol 2016; 42:343-60).

Few studies have compared health-related quality of life measures in men and women following cystectomy. In one study of 73 female patients who underwent radical cystectomy, those who received an orthotopic neobladder were more likely to experience improvements in future perspective of their illness, perceptions of body image, and sexual function than those who received an ileal conduit (Eur J Surg Oncol 2018 [In press]). The factors driving the underutilization of orthotopic neobladder use in females are unclear, but may be related to gender-specific complications and adverse outcomes following urinary diversion. A study of urinary functional outcomes in women receiving an orthotopic neobladder revealed that hypercontinence rates may be as high as 44.6% in female patients (World J Urol 2014; 32:221-8).

There is a paucity of data comparing men to women in terms of daytime incontinence, nighttime incontinence, hypercontinence, and sexual function following orthotopic diversion. Lack of standardization of questionnaires, varying definitions of continence, under-sampling of female patients, and variable assessments of sexual function are mostly to blame. Further assessment of gender differences in this area is needed.

Potential biologic differences

The role of sex steroids and the hormonal axis has been investigated as a potential biologic explanation for the gender divide in bladder cancer. Population analyses have shown that bladder cancer is more common in postmenopausal vs. premenopausal women. Loss of AR and ERα and increases in ERβ were associated with an increase in tumor grade and stage. Raloxifene inhibited growth of urothelial cell carcinoma in an in vivo model (J Urol 2007; 69:1221-6).

In a study conducted by Sonpavde and colleagues, raloxifene (Evista), an estrogen receptor modulator, was found to inhibit the growth of urothelial cell carcinoma in an in vivo model (J Urol 2007; 69:1221-6). The implications of androgen and estrogen receptors as drivers of tumorigenesis are profound. The role of tamoxifen (Nolvadex), a selective estrogen receptor modulator (SERM), is currently under investigation for the treatment of low- and intermediate-risk bladder cancer (NCT02197897). Further study is needed to determine the role of androgens in the treatment of bladder cancer.

Summary

Gender disparity in bladder cancer is a complex issue that likely stems from diagnostic delays, therapeutic differences, and possibly biologic factors. Each of these areas provides opportunities for improvement and for the eventual elimination of the gender divide. Partnerships with primary care providers and gynecologists should remain a priority to improve education and understanding of the importance of timely evaluation of hematuria in the female patient. Hopefully, continued understanding of the biologic drivers of urothelial carcinoma will provide novel therapeutic targets for both male and female patients with bladder cancer.
Filling the Gap in BPH CARE

Last year, the AUA updated its guidelines for benign prostatic hyperplasia (BPH). The update includes a recommendation for urologists to consider prostatic urethral lift (PUL) for the treatment of some patients with BPH.

Six experienced providers of PUL joined a panel to examine the AUA’s new guidelines, the current status of the UroLift System® within the standard of care for BPH, and how to improve the care pathway for BPH.

read this supplement at urologytimes.com/bphcare
Endoscopic robotic platforms: What the future holds

Novel systems offer new opportunities in transurethral bladder resection, URS

Since its first documented use in the early 1800s, endoscopy has evolved to be an essential part of the urologist’s toolkit. The subsequent century saw multiple engineering and clinical use advancements that led to the evolution of modern endoscopes. These changes have revolutionized the way clinicians diagnose and treat a variety of urologic pathologies. Combined with an increased interest and accessibility of surgical robots, multiple novel endoscopic robotic platforms are being developed to potentially improve outcomes, ease performance and learning challenges, and improve surgical ergonomics.

This article highlights some of the emerging endoscopic robotic systems in urology.

Current challenges of endoscopic surgery

Despite being fundamental to the diagnosis and treatment of many urologic diseases, some challenges exist during endoscopic surgeries. Adequate visibility stands as a central pillar of endoscopy. Although fiberoptic scopes have improved significantly since their first documented use in the 1960s, their “honeycomb”-like image, as well as fiber deterioration over time, can lead to impaired visibility. Camera systems have continued to evolve, incorporating advances in image capture and display.

Recent advances have favored imaging chips at the scope tip over traditional fiberoptic bundles. Though digital scopes provide a clearer image, the imaging chip requires a larger scope tip, with most being 7.7F to 9.7F. This increase in size in flexible scopes, however, exemplifies another challenge of endoscopic surgery: endoscopic accessibility. The caliber of the working instrument, the number of previous scope usages, and the patient’s upper tract anatomy can complicate maneuverability during flexible ureteroscopy. In the lower urinary tract, anatomic variability (ie, capacious bladders or significant intravesical lobes) can impede routine cystoscopic evaluations or transurethral procedures.

An automated, ultrathin scanning-fiber endoscope of small diameter (1.5 mm) for bladder cancer surveillance has been developed. The system allows for machine-controlled surveillance and uses a spiral cam motion to map the entire surface of the bladder.

These factors, which can affect endoscopic accessibility and the time length of increasingly complex procedures, highlight another challenge of endoscopic surgery: surgeon ergonomics. Factors leading to surgeon fatigue and potential injury are multifactorial, variable, and dependent on the procedure being performed. However, they are further compounded by decreased visibility and maneuverability when performing endoscopic cases, increasing surgeon discomfort, and decreasing intraoperative efficiency, likely impacting physician dexterity over time. Though surgical experience can certainly help overcome difficulties when performing endoscopic procedures, new endoscopic robotic systems attempt to improve on these challenges.

Transurethral systems

Urologists developed the first transurethral robotic system to perform transurethral resection of the prostate in the 1980s, but this did not meet with commercial development (Proc Inst Mech Eng H 1991; 205:35-8). With the increased acceptance of surgical robotics for laparoscopy over the last two decades, multiple engineering groups and companies have been developing new transurethral robots.

Noting some of resource and time limitations of bladder cancer surveillance, Soper et al developed an automated, ultrathin scanning-fiber endoscope of small diameter (1.5 mm) for bladder cancer surveillance. The system allows for machine-controlled surveillance and uses a spiral cam motion to map the entire surface of the bladder, which they demonstrated ex vivo in a pig bladder (IEEE Trans Biomed Eng 2012; 59:1670-80). Given the small size of the scanning fiber as well as the automated nature of the motion, the potential advantages of this technology could be increased patient comfort, performance by ancillary clinic staff, and improved detection by use of image analysis and confirmation of full surface scanning.

More recently, our engineering-based research team at Vanderbilt has been developing a transurethral robot platform (ie, TURBot) for bladder tumor resection (J Endourol 2018; 32:516-22). Transurethral resection of bladder tumor can be a technically challenging procedure given anatomic constraints using rigid instruments, as well as difficulty monitoring resection depth to minimize risk of perforation while ensuring adequate tissue for treatment and staging. The TURBot system uses a flexible, multi-backbone continuum robot, fitted with three 1.8-mm working channels, allowing...
for visualization and laser ablation or resection across the entire bladder surface (figure 1).

The technology has successfully been evaluated in vivo in porcine experiments. Though en bloc tumor laser resection was achieved in these models, it was complicated by lack of depth perception and limited degrees of freedom of the working components (figure 2). Current efforts are aimed at improving these limitations in future prototype systems.

An additional rigid endoscopic system using bendable, concentric tube robotic platform tools is being developed to perform prostate and endoscopic surgery including holmium laser enucleation of the prostate (HoLEP) (J Endourol 2016; 30:692–6). Although this procedure has been shown to be durable with good patient outcomes, the learning curve has limited its wide acceptance. The robotic platform comprises a user interface and computer control to manipulate the concentric tube tools and allows for two-plus tools to dexterously interact through a 27F scope (figure 3).

The platform has shown to have 65% improvement in accessible areas compared to rigid endoscopes in simulations and has successfully been demonstrated in a cadaveric model. The potential of complex surgical maneuvers including retraction and enhanced tissue manipulation is part of the ongoing development of this system.

**URETEROSCOPIC SYSTEMS**

Several investigational robotic flexible endoscopic systems have been developed with the intention to potentially treat urolithiasis and perform upper tract endoscopy. The initial foray into robotic control was use of the Sensei and the Magellan systems by Hansen Medical. These systems utilized robotically controlled catheters that were actively manipulated to passively maneuver the shaft of the ureteroscope. The passive manipulation of the scope lead to limited maneuverability in the upper tract, however (Urolithiasis 2018; 46:69–77). Auris Health ultimately acquired Hansen Medical in 2016 and has been developing the Monarch robotic system for bronchoscopy. Given the size similarity to ureteroscopes, such a system may be applicable to upper tract urologic endoscopy.

The Avicenna Roboflex system from ELMED Medical Systems has been developed and clinically evaluated since 2010. The system comprises multiple features, including a finely tuned robotic platform designed to control insertion, rotation, and flexion of a standard ureteroscope in the field. The system has a surgeon control console where the surgeon is seated outside of the radiation field and allows for adjustment of seat and arm height for comfort. The console adds a touch screen-activated irrigation pump, touch screen laser-fiber control, and pedals to control fluoroscopy; laser activation is integrated into the system.

Currently, any commercially available ureteroscope can be used with the Avicenna Roboflex, as well as any laser type. There is, however, no integration of a basket or grasper, although these can be controlled by a bedside assistant. Multiple clinical studies have evaluated the system in Europe. Most recently, a multicenter phase II study was performed by Klein et al (J Urol 2016; 195[suppl]:e406–7 [abs. PD18–08]). The group was able to demonstrate the safety and efficacy of the platform in 266 patients with a mean stone size of 1.4 cm. They were able to successfully perform fragmentation, dusting, and extraction of stone fragments. Total operative time was 96 minutes, with mean console and robotic docking times of 65 minutes and 4 minutes, respectively. FDA approval of the device is still pending.

**CONCLUSIONS**

The field of urology has been at the forefront of the scientific evolution of surgical robotics and minimally invasive surgery. Novel endoscopic robotic systems open the door for a new set of diagnostic and therapeutic possibilities to offer patients. Further studies on improvements in patient and disease outcomes, as well as cost considerations, will ultimately drive how these robotic systems are integrated into clinical practice.
APPs play multifaceted role as urology team members

When properly trained and working as part of the clinical team, physician assistants and nurse practitioners can take on a wide range of responsibilities, according to Jim Kovarik, PA-C. In this interview, Kovarik discusses the role of advanced-practice providers in a urology practice, how they are trained, and what procedures they can and should perform.

Q: There are manpower issues in urology, and we have a huge aging population. We have a lot of patients to see and not enough urologists to see them. With our current throughput, that’s not going to change; I think residency programs are set. This leads to the question, how should advanced-practice providers (APPs) be used in urology practice?

A: APPs can really be utilized almost anywhere in a urology practice. They can be utilized in clinic to help see more patients, whether they’re routine follow-up patients, post-op and pre-op patients, or new patients. They can assist in the OR as first assistants, including robotic cases with appropriate training. They can help out with hospital rounds, hospital consults, and even ER consults. APPs assist with evening or weekend call to take some of the pressure off physicians or to spread the workload among providers in the practice.

Q: In your practice, what is your role within the department of urology? How do you fit into the workflow?

A: In general, APPs need to be allowed to work at the top of their licensure, competency, and level of experience. In my current role, I act as an adjunct to the faculty. I work in their clinics part of the time. The other 50% of the time, I have my own clinical practice and see my own template of patients, thus helping improve the efficiency of the practice to make sure patients are getting seen in a timely manner.

Q: You received specialty-specific training in urology and, in fact, you have procedures under your belt. Do you think doing procedures within a scope of practice is important for the use of an APP?

A: Absolutely, it is within the scope of practice for APPs to perform urologic procedures such as complex catheter placements with or without cystoscope assistance. Given the appropriate training and experience, APPs can perform cystoscopic stent removal and even diagnostic cystoscopies. Some APPs perform transrectal ultrasound and prostate biopsies, urodynamics studies, penile injection, testosterone pellet implants, and shock wave lithotripsy.

Q: You’re very good about making sure that you’re under supervision, for example, by taking pictures at the time of cystoscopy. Do you consider it important to work side by side with your attending and your supervisor?

A: Absolutely. One of the most important aspects of being an APP in a urology-specific practice is to work as a team. I think it is appropriate and essential to make sure you are communicating well with your supervising/collaborating physician or colleague physicians. Communication includes taking relevant cystoscopic pictures so if something is questionable, you can not only document it for the medical record, but also take it back to your supervising physician to ask his or her opinion, if necessary.

Q: Some hospitals or practices do APP training in their clinics, so it’s on-the-job training as it were. There are also courses available. What do you think is the optimal training—within a practice so that you can fit it to the needs of the practice, or is it something that should be done on a national level?

A: This is a controversial issue in the urology world right now. Currently, most urology APPs receive on-the-job urology-specific training and procedure training. There are a few urology PA and APP postgraduate training programs. Regarding performing cystoscopy, the Society of Urologic Nurses and Associates (SUNA) and Urological Association of Physician Assistants (UAPA) provide cystoscopy workshops and hands-on opportunities to expose APPs to cystoscopic procedure possibilities.

I know the AUA is evaluating how to appropriately provide cystoscopy and procedure education and possibly training to make sure those who go through a course are truly qualified to do what they need to do. Ultimately, I do not believe that a single course will allow an APP to immediately perform completely unsupervised cystoscopies or prostate biopsies.

JIM KOVARIK, PA-C

Kovarik is a urology-trained physician assistant at the University of Kansas Hospital, Kansas City. He is the current president of the Urological Association of Physician Assistants (UAPA) and a member of the AUA Advanced Practice Providers Education Committee.

Kovarik was interviewed by J. Brantley Thrasher, MD, professor of urology at the University of Kansas Medical Center, Kansas City.

Do you think doing procedures within a scope of practice is important for the use of an APP?

J. BRANTLEY THRASHER, MD

Absolutely, it is within the scope of practice for APPs to perform urologic procedures such as complex catheter placements with or without cystoscope assistance.

JIM KOVARIK, PA-C

If the APPs have been appropriately trained, they can take on some of those procedures and improve patient satisfaction by improving patient access and decreasing wait times.
But just like with residency training, the more procedures someone performs, the more proficient and knowledgeable he or she becomes at performing the procedure. They must also know what is expected and know their own limitations—that’s where having the supervising physician’s support and knowledge is critically important.

Q: What resources do you think are needed for an APP to be successful in practice?
A: I would answer the same way if you were hiring a new physician to the practice. It sounds simple, but they essentially need all the same tools and resources, including some form of administrative assistant or someone to help with scheduling and a nurse or medical assistant for rooming patients and doing ancillary tasks in clinic. They need an appropriate number of clinic rooms to see patients, depending on how many patients they are expected to see in the course of a day.

They possibly need some administration time to get through the paperwork that goes along with a clinical practice. They need some place to work—at minimum, a desk, a computer, and phone. Again, it sounds simple but others have told me that’s not always a given. I would argue they also need a CME budget to attend courses from the AUA, UAPA, and SUNA to gain specialty-specific urology education and training.

Q: What specific training courses are offered right now that you would recommend?
A: There are great resources out there. The AUA Urology Core Curriculum and AUA University APP Education curriculum are fantastic resources. Both are available online. The AUA annual meetings have an APP track with numerous options for APPs to attend, including instructional courses throughout the meeting and the current two-day course, Urologic Care for the Advanced Practice Provider.

Q: How do you see APPs being best utilized in a urology practice?
A: APPs are best integrated in a team-based approach. I do not believe urology APPs should be independent providers, although we should be working autonomously.

JIM KOVARIK, PA-C

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J. BRANTLEY THRASHER, MD

she can continue that quality of care in the same manner as the physician.

Q: What do you consider inappropriate uses of an APP? What do you see as a waste of time, energy, training, or beyond scope of practice?
A: APPs should practice at the top of their license. They should be treated as providers and be given that expectation. They should not be used as scribes. They should see patients on their own, whether that’s triaging the patient for the supervising physician or seeing patients autonomously in their own clinic.

Q: Do you have any other take-homes for the readership regarding APPs and what procedures they might perform to best utilize their specialty-specific expertise?
A: I think it’s helpful to find out what the APP is passionate about and what he or she is good at doing. Some people are passionate about men’s health or women’s urologic health, while some are more comfortable dealing with oncology issues, erectile dysfunction, pelvic pain, or stone medical management. Some APPs prefer to be in the operating room and may be best utilized as first assists. Some APPs are interested in research. Some are interested in managing inpatients and hospital consults. Some APPs want to take call. All of those are certainly available options.

As far as procedures go, APPs may perform a multitude of procedures, including but not limited to complicated catheter placements, performing and interpreting urodynamic studies, transrectal ultrasonography, and prostate biopsies. MRI fusion-guided biopsies are certainly reasonable, as are cystoscopies for stent removals or diagnostic cystoscopies—with the appropriate training and initial supervision—and minor office procedures such as penile injections and testosterone pellet implants. Performing these types of procedures expands the services of the practice and allows physicians to see more complex patients who are better suited for their training and expertise.

RECORD PERCENTAGE OF WOMEN MATCH WITH PROGRAMS

The 2019 Urology Residency Match results released recently by the Society of Academic Urologists (SAU) and the AUA show a record-high 83% of women participating in the process have matched to urology residency positions, an increase from 75% in 2018.

More than 430 aspiring urologists registered for the SAU/AUA Urology Residency Match. Of those who registered, 90% submitted preference lists, competing for a record 339 available positions across the country.

The AUA uses a computerized mathematical algorithm to match applicants with programs using the preferences expressed on their ranked lists. When the matching algorithm was processed, 85%—the highest rate in nearly a decade—matched to a vacancy within 136 registered and accredited training programs in the United States, leaving just nine vacancies unmatched, according to a press release from the AUA.

“We are extremely proud of the success of the Urology Residency Match and welcome the continued growth in program participation and applicants,” said SAU Past President Byron D. Joyner, MD. “In the past 5 years alone, we have seen an increase of nearly 20% in the number of urology positions offered and a rise in the match rates for nearly every applicant group.”

“We are honored to play a small role each year in moving forward the careers of these young physicians and wish each of the talented men and women nothing but success as they begin their journey toward becoming urologists,” said AUA President Robert C. Fisigan, MD.

How to get reimbursed when using –22 modifier

Documentation should include reason procedure required extra time

We continue to see a high percentage of errors in the hundreds of audits we perform each year. Fortunately, in the last few years, we have performed more audits to assist practices in billing accurately to improve income than to assist them in decreasing “take backs.”

In a series of articles, we plan to address in detail the documentation and communication that needs to occur in order to bill for different services, such as the procedure that was much more difficult and took a lot longer than the average procedure. How should you bill for services on the same day or during the global period? Many services have specific codes for specific variations of the procedure; how do you know you’ve picked the correct code? We’ll cover most of the problematic issues that we have seen that stem from problems with documentation, communication, and/or coding.

For this first installment, we will focus on the –22 modifier. (Note: We will target these articles to those who have at least some knowledge. If you need some more basic knowledge to understand this article, please feel free to contact us and we can provide you with options.)

The use of the –22 modifier, even with excellent supporting documentation, does not guarantee increased payment.

Stating a case is difficult not sufficient for applying modifier

We will start with the complicated surgical case that took you a lot longer to perform than usual; for example, a cystectomy on an obese patient who had previous radiation and has lots of adhesions. Dictating that it was a tough case that was much more difficult than usual is not adequate documentation to satisfy the requirements for using the –22 modifier, the most accurate way to request and receive increased payment in most cases.

This is the CPT definition of the –22 modifier: Increased Procedural Services. When the work required to provide a service is substantially greater than typically required, it may be identified by adding modifier 22 to the usual procedure code. Documentation must support the substantial additional work and the reason for the additional work (ie, increased intensity, time, technical difficulty of procedure, severity of patient’s condition, physical and mental effort required). Note: This modifier should not be appended to an evaluation/management service.

The appropriate documentation should include:

• the reason it required extra time (patient was obese, multiple adhesions from prior surgery/radiation, etc.). This information should be included in the body of the operative note relating to the performance of the procedure.
• the increased degree of difficulty for that surgery. This information is more subjective and should be included in a summary or the “findings” section.

• the extra amount of time that the procedure required in relation to an average procedure (such as twice the amount of time it usually takes). This should also be included in the summary of the procedure or “findings” section of the procedure note. It can also be included in the body of the operative note in a more granular notation.

• any additional information that would inform a medical director or an auditor as to the difficulty and the extra time required. This should also be included in the summary or “findings” section of the operative note. You can also include non-clinical but relevant issues that complicated the performance of the case. Documenting that you were up all night, had a hangover, or equipment malfunctioned would not qualify for extra payments.

The –22 modifier requires medical review by the payer in nearly all cases. The process of

GET CREATIVE WITH PATIENT PAYMENT OPTIONS

The new year brings new health plans, often with higher deductibles, and old bills that patients may be struggling to pay. According to 2018 data compiled by MedData, 83% of physician practices with fewer than five practitioners reported that their top collection challenge was slow payment among high-deductible plan patients. In this landscape, physicians may have to get creative in order to increase their revenue. Technology has made paying for goods and services incredibly convenient, with options such as digital wallets, e-statements, and text reminders to pay balances owed, but it’s also increasing consumer demand for a variety of payment options, says Deirdre Ruttle, vice president of strategy for InstaMed, a health care payments network in Philadelphia. To read more, see the full article from Urology Times sister brand Medical Economics at bit.ly/flexiblepay.
Review will slow payment of the claim. Additionally, the modifier is by definition for services that are substantially greater than what is required normally. It should also be said that the use of the –22 modifier, even with excellent supporting documentation, does not guarantee increased payment. Therefore, the modifier should not be added to a procedure unless the extra work and time were significant and the documentation supports the work.

Payments for each procedure are considered to be based on the average procedure. As “average” represents a range of time and effort, also consider placing a threshold on when to report the modifier. As a general guideline, we have seen mention of a 25% variation up and down as still considered.

For example, a procedure noted as more difficult than average but completed within 145 minutes compared to the normal 120 minutes (120% of normal time) may not warrant extra payment consideration and the modifier is not used. On the other end, a very difficult case requiring 170 minutes for the same procedure (142% of the normal time) should warrant extra payment consideration and the use of the –22 modifier.

Submitting operative note recommended

Finally, we have found through the Physician Reimbursement Services outsourced billing service and through discussion with other practices that submission of the operative note with the claim when first sent to the payer saves time and significantly improves your chances of being paid at a higher rate. Your billing staff should monitor all claims. Monitoring claims for which the –22 modifier requires extra attention, and if claims are denied, they should be appealed with additional documentation. In short, if you are hoping to be paid more with the –22 modifier, make sure you are committed to both the documentation and the follow-up.

In the second installment of this series, we plan to discuss the proper documentation to support payment for E/M services on the same day as a procedure.

We have found that submission of the operative note with the claim when first sent to the payer saves time and significantly improves your chances of being paid at a higher rate.

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**ACCURATE BILLING STARTS WITH DOCUMENTATION, COMMUNICATION**

One of the most common complaints we hear at Physician Reimbursement Systems is, “I am working harder and making less.” Even if you were perfect in billing and collections, this would be true. With few exceptions, Medicare and private payers have been holding reimbursement rates steady or decreasing payments per service for the past decade. Meanwhile, costs have increased.

What is worse, most of you are not being paid for all services that you provide. That means there is money on the table. You should claim your share. We are not suggesting that you overbill, add modifiers that should not be added, bill for services twice, unbundle, game the system, etc. We are only suggesting that you bill correctly for all the services provided and start working smarter.

For more about the fundamentals of accurate billing, including recent Comprehensive Error Rate Testing data regarding claims, go to [www.urologytimes.com/accurate-billing](http://www.urologytimes.com/accurate-billing).
2019 ‘to-do list’: Reduce debt, contribute to retirement plans

Include disability insurance, estate planning on your financial checklist

Q: My New Year’s resolution was to get my financial house in better order. Where is a good starting point?
A: While not comprehensive, here is a checklist to get you started. There are certain to be other items you will want to address, but getting these financial items in place is a good start.

Set short- and long-term financial goals. Whether you want to be debt-free in 10 years or own a home in 5, you are more inclined to save if you have specific goals. Factor these goals into a budget and figure out where you can squeeze the extra money from to make these goals realities.

Budgeting. Every effective financial plan starts with a budget. Identify necessary spending and savings items. Give yourself a little leeeway but stick close to the guidelines you’ve created throughout 2019.

Emergency funds. We have seen clients saved by their emergency funds numerous times. A sudden job loss, major surprise expense, or unexpected health issue can change your financial picture quickly. The general rule of thumb is to maintain an emergency fund equal to three to six times your monthly living expenses.

Debt reduction. Some forms of debt such as a mortgage on a house may be perfectly acceptable due to the tax deductibility of the interest. However, you should do your best to reduce your other debt, especially if you are paying interest at relatively high rates such as those on credit cards.

Retirement plan contributions. If you already contribute to an employer plan such as a 401(k) or 403(b), keep it going. The IRS increased the contribution amount for 2019 to $19,000 ($25,000 if over age 50). 401(k)s and 403(b)s should be maxed out before utilizing other tax-advantaged retirement accounts because they are protected by federal law from malpractice lawsuits and creditors. If you own your practice, determine if you are utilizing the best type of retirement plan for your specific situation.

Traditional and Roth IRAs. If you are already maxing out employer provided retirement accounts and wish to save additional amounts toward retirement, consider contributing to a traditional or Roth IRA. These accounts also offer excellent tax-advantaged growth and are protected in most states from malpractice lawsuits. The contribution limit increased to $6,000 per year for 2019 ($7,000 if over age 50).

Disability and life insurance. Often overlooked, disability and life insurance are actually very important components of financial security. Disability insurance supplements a portion of your income in the event you are sick or disabled and unable to work. In the event of a long-term disability, it could ensure you stay in your home and/or are still able to save for financial goals like retirement. All eligible physicians should have comprehensive disability coverage.

Life insurance is slightly more situational, but if you own a home with a mortgage or have any other debts that would not be absorbed by your death, have children whose college educations you would want to guarantee, or have an individual or organization you would want to provide for in the event of your death, then life insurance should be considered.

Estate planning. The complexity of an estate plan may vary based on your assets and needs, but having basic estate planning strategies in place is important. Work with an estate planning attorney to review whether you need wills, powers of attorney, trusts, etc.

These are important items to have in place and will give you a good foundation to start moving toward a financially secure future. I recommend speaking with your financial adviser about other areas that could use improvement.

Q: Is there anything I can do at the beginning of the year to prepare my investments for the year ahead?
A: Assuming you have an investment strategy in place that includes an asset allocation mix that is appropriate based on your risk and return objectives and you have investments that fit into these asset classes, then a good item to review at the beginning of the year is portfolio rebalancing. Over the course of the past year, certain asset classes will have outperformed, and others will have underperformed, so rebalancing the portfolio and getting it back in line to start the year may be a good idea.

FINANCIAL TIPS

When contributing to retirement plans, 401(k)s and 403(b)s should be maxed out before utilizing other tax-advantaged retirement accounts because they are protected by federal law from malpractice lawsuits and creditors.

Traditional and Roth IRAs offer excellent tax-advantaged growth and are protected in most states from malpractice lawsuits.

Over the course of the past year, certain asset classes will have outperformed, and others will have underperformed, so rebalancing the portfolio and getting it back in line to start the year may be a good idea.

Mr. Witz is educational program director at MEDIQUIS Asset Advisors, Inc. in Chicago. He welcomes readers’ questions and can be reached at 800-883-8555 or witz@mediquis.com.

The information in this column is designed to be authoritative. The publisher is not engaged in rendering legal, investment, or tax advice.
Cybersecurity: How to safeguard your practice against threats

HHS toolkit outlines basic practices to combat phishing, ransomware attacks

The U.S. Department of Health and Human Services Office for Civil Rights, as of this writing, has 412 cases of breaches of unsecured protected health information involving more than 500 individuals who are under investigation (bit.ly/OCRbreachportal). Most of these involve health care providers, mostly involving hacking or an IT incident, and most involve information in email. These statistics serve as a sobering reminder that medical practices remain an attractive target for hackers, possibly because many are small businesses with no dedicated IT professionals on staff.

On Dec. 28, 2018, HHS released a set of publications intended to help medical practices of all sizes confront this very real threat (bit.ly/HHS-cybersecurity). In this article, I will summarize the threats and recommended practices for cybersecurity in your practice.

According to HHS, the five most common cybersecurity threats in health care are:

**Email phishing attacks.** These consist of attempts to deceive someone into giving out sensitive information via email. A common scenario might involve an employee who appears to come from a legitimate source, and directs the employee to enter their login credentials. Those credentials are then hijacked to access other systems. This is the most common threat in medical practices leading to reported breaches.

**Ransomware attacks.** According to HHS, “Ransomware is a type of malware (malicious software) distinct from other malware; its defining characteristic is that it attempts to deny access to a user’s data, usually by encrypting the data with a key known only to the hacker who deployed the malware, until a ransom is paid. After the user’s data is encrypted, the ransomware directs the user to pay the ransom to the hacker (usually in a cryptocurrency, such as Bitcoin) in order to receive a decryption key.” (bit.ly/ransomwarefactsheet).

**Loss or theft of equipment or data.** The concern here is that the stolen equipment may contain unencrypted, unsecured protected health information. This is the third most common cause of data breaches reported to HHS.

**Insider, accidental, or intentional data loss**

Attacks against connected medical devices that may affect patient safety. Connected devices in a urology practice may include x-ray equipment, urodynamic machines, and other lab equipment. These interfaced devices typically contain protected health information and are vulnerable.

The HHS report, “Health Industry Cybersecurity Practices: Managing Threats and Protecting Patients,” (bit.ly/10cybersecuritypractices) recommends 10 cybersecurity practices to address these five threats, and the recommendations are tailored to the size of the practice (small, medium, and large). The report is accompanied by technical “how-to” volumes (bit.ly/managingthreats and bit.ly/cybersecuritysmallpractice) that facilitate the implementation of these practices. I highly recommend that every practice download the section of the volume pertinent to your practice size and implement these best practices. For example, the table below, from the technical volume for small practices (bit.ly/cybersecuritysmallpractice), provides recommendations for safeguarding your practice from phishing attacks.

**TABLE SAFEGUARDING AGAINST PHISHING TECHNIQUES**

<table>
<thead>
<tr>
<th>Phishing technique</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Check embedded links</td>
<td>Validate that the URL of the link matches the text of the link itself. This can be achieved by hovering (not clicking) your mouse cursor over the link to view the URL of the website to be accessed.</td>
</tr>
<tr>
<td>Look for suspicious From: addresses</td>
<td>Check received emails for spoofed or misspelled From: addresses. For example, if your organization is “ACME” and you receive an email from <a href="mailto:user@AMCE.com">user@AMCE.com</a>, do not open the email without verifying that it is legitimate.</td>
</tr>
<tr>
<td>Be cautious with “urgent” messages</td>
<td>If the email message requires immediate action, especially if it includes a request to access your email or any other account, do not open the email or take any action without verifying that it is legitimate.</td>
</tr>
<tr>
<td>Be cautious with “too good to be true” messages</td>
<td>If you receive an unexpected message about winning money or gift cards, do not open the email or take any action without verifying that it is legitimate.</td>
</tr>
</tbody>
</table>

Source: U.S. Department of Health and Human Services

Bottom line: Cybersecurity threats in a urology practice are real and can result in harm to patients—and your business. HHS has released a valuable toolkit that can be adopted by practices of any size with minimal effort. Follow these 10 basic practices and put your practice on the best cybersecurity footing for 2019.
Tools urologists need to thrive in a value-based world

Practices must embark on a journey that goes beyond new technology

Urology practices were unanimous in looking to add predictive capabilities to their analytics, so they could anticipate outliers or adverse events before they happened, design appropriate interventions, and ultimately improve their value-based performance in terms of outcomes and cost.

Data and analytics at the center

If the EHR was a technology linchpin for fee-for-service billing models, it is transitioning to become just one component—albeit a critical one—sitting atop a new data foundation needed to power value-based care success. The ability to support cross-functional, team-based care across settings and venues, during and in between office visits, with access to rich clinical and financial patient data, requires the integration and harmonization of data from disparate sources that have not traditionally talked to one another. This may take the form of a practice-level health information exchange that can aggregate, integrate, and exchange population-based information, including medical claims, clinical, lab, prescriptions, sociodemographic and bio-genomic data.

Value-based care also necessitates a redoubled focus on the quality and consistency of all data. We recently studied the data requirements for a selection of urology-specific MIPS measures and found that while most inputs resided in the EHR, more than two-thirds were unstructured—for example, captured in narrative notes with an elevated risk of errors, duplication, or even omission. Many practices found that they needed to manually abstract and curate charts in order to submit measures properly.

Practices are looking for this investment in new technology capabilities and protocols to pay off in the form of a new generation of analytics that can drive both insights and action for MIPS and future APMs. Urology groups told us their wish list includes new clinical, financial, and population health analytics:

• Clinical analytics. When asked for the top capabilities they needed on the clinical side, urology practices pointed to gaps in clinical care and care continuity (38%), patient identification for clinical action and/or research (23%), and the ability to track and analyze a patient’s entire care journey (19%). Most importantly, urology practices were unanimous in looking to add predictive capabilities to their analytics, so they could anticipate outliers or adverse events before they happened, design appropriate interventions, and ultimately improve their value-based performance in terms of outcomes and cost. Nearly 90%

Please see VALUE-BASED WORLD, page 31

With 2018 behind us, it is a natural time to reflect on the major developments that took place in health care in general and urology specifically. For many, it will be remembered as the year that value-based care became a reality. Just over a year ago, Urology Times reported that only one-fourth of urologists understood the choices available to them as part of the Merit-based Incentive Payment System (MIPS) and alternative payment model (APM) programs created by CMS (Dec. 2017, page 1).

Fortunately, some of that confusion has since dissipated. With only a couple of urology practices participating in an APM—the Oncology Care Model—and no urology-specific candidates yet approved, most urologists are experiencing value-based care through MIPS.

With the first MIPS results released last November, urologists began to better understand the clinical, financial, and operational inputs that would positively or negatively affect their MIPS performance. One area of focus: the suitability of the technology tools and infrastructure on which their offices depend. Around the same time, we sat down with the leadership of 25 prominent urology practices nationwide to talk about the tools they were looking for in a value-based world.

A new job for urology EHRs

During the fee-for-service era, the electronic health record established itself as the central technology of many urology practices, and with good reason. It was designed specifically to document patient encounters in the office setting, with an eye on the billing and collections workflow to follow. However, as MIPS has evolved—specifically, with the introduction of cost as 10% of the overall MIPS score for performance year 2018—it has become increasingly important for urologists to manage their patients more holistically, across all care settings and comorbidities.

The urology practices in our group said they need access at the point of care to information and insights that draw from an array of clinical and financial inputs, across entire care teams. Legacy EHRs, with their notoriously closed architectures and difficult data access, were simply not built for these value-based requirements.

As a result, more than half of the practices in our group said that in the next year they either will change their EHR (19%) or are actively looking to change it (35%). Interestingly, nearly all of those wanting a new EHR solution espoused the need for new requirements, driven by value-based considerations. They specifically want to take the opportunity of an EHR replacement to help them positively change their clinical operations and reduce treatment variability. Fifty percent say they want to make major changes, while another 42% seek modest changes.

When asked what kinds of value-based capabilities will be important, they pointed to: integrated care pathways, including tracking of deviations (54%); a historic patient timeline for an at-a-glance, longitudinal overview (43%); and real-time alerts on gaps in care/actions to complete for patients (39%). This vision for a value-based EHR goes beyond the scope of what existing legacy solutions provide.

CHARLES SAUNDERS, MD
Dr. Saunders is CEO of Integra Connect, West Palm Beach FL provider of technologies and services for value-based specialty care. Integra Connect partners with large groups in the U.S. focused on oncology and urology, as well as with other key health-care constituents.

Please see VALUE-BASED WORLD, page 31
JONATHAN YARBROUGH
Mr. Yarbrough is a partner with Constantancy, Brooks, Smith & Prophete and is based in the firm’s Asheville, NC office. This article was originally published by Urology Times sister brand Physicians Practice.

While a bully may target some colleagues because of their membership in a protected class, bullying becomes more indiscriminate as the bully tries to control any number of his or her co-workers without regard to personal characteristics—the equal opportunity harasser.

VALUE-BASED WORLD
continued from page 30

described it as “extremely” or “very” important.

* Financial analytics. While many urology practices are satisfied with the analytics that pertain to their fee-for-service revenue cycle, they are rightfully looking for new tools that will better connect clinical decisions with financial implications. These include areas such as utilization of services (32%) and episode of care costs (20%). As the cost component of MIPS increases and urology-specific APMs arise, this will be joined by the need for advanced support for care bundles, risk management, capitation, and more.

• Population analytics. While population health management has evolved more quickly in specialties with major APM programs that involve accountability for episode costs—such as the Oncology Care Model in oncology—urology practices are increasingly incentivized to manage their patient panels more holistically. The increased shift of risk to providers points them toward adopting the population health tools and analytics familiar to payers, including patient risk stratification and condition and case management—all the way through to patient engagement metrics that attest to the success of their interventions.

Conclusions

While the emerging requirements of value-based care will necessitate changes to urology practice infrastructure and tools, it is important to recognize that a larger transformation will also be essential as well. In parallel, practices must expect to embark on a journey to adopt a broader, more holistic patient view; a new array of financial and clinical considerations; and a cultural commitment as they assume risk. Value-based incentives have the ability to determine the future sustainability of most practices, with the inevitable addition of APMs—either from CMS or commercial payers—as a further accelerator.

The combination of practice transformation with suitable enabling technologies will be an important determinant in which fork in the road urologists ultimately follow.
BULLYING

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• excluding employees by, for example, not keeping them informed of departmental changes or social functions

Acts of legitimate authority to control work and supervise employee performance are not considered bullying, nor is, rudeness or other discourteous behaviors among employees.

Isn’t bullying at work also a ‘hostile work environment’?

Under federal, state, and even local laws, the harassment of employees based on membership in a protected category, including race, color, religion, sex (including gender identity and pregnancy), national origin, age, disability or genetic information, is prohibited. Unlawful workplace harassment may consist of offensive conduct based on one or more of the protected categories above that is so severe or pervasive that it creates a hostile or offensive work environment or results in an adverse employment decision (such as being fired or demoted).

While a bully may target some colleagues because of their membership in a protected class, bullying becomes more indiscriminate as the bully tries to control any number of his or her co-workers without regard to personal characteristics—the equal opportunity harasser.

Merely picking on a co-worker, without any consideration for the person’s protected class, is not unlawful harassment (although it may be bullying, despite not being unlawful). As courts have repeatedly noted, equal employment laws do not require employees to be nice to each other. In fact, an employer has no legal obligation to ensure that employees engage in professional conduct when interacting with each other.

Bullying behavior can encompass elements associated with a hostile work environment claim. It commonly includes systematic, annoying, and continued conduct including demands, uninvited/unwelcome conduct, threats, and in certain circumstances can even exceed the egregious conduct often associated with harassment claims.

However, only about 20% of bullying cases contain activity that might be considered “discriminatory” under the law—in other words, while far from desirable, 80% of workplace bullying may not include actual “illegal” conduct. In fact, courts have consistently rejected hostile work environment claims when an employee attempts to establish a case based upon bullying conduct unrelated to the employee’s membership in a protected class.

While bullies may be able to operate outside of the traditional employment harassment laws, it does not mean they can avoid legal liability entirely as evidenced in Raess v. Doescher. Physical threats and conduct can amount to assault and battery, and bullying conduct can open the door to possibly violating other employment laws. In fact, legislators in 30 states have proposed anti-bullying laws but only three states have enacted limited workplace bullying laws which mostly address public employment. In short, there is really no cause of action for workplace bullying.

Is workplace bullying common, particularly in health care?

Unfortunately, according to the Occupational Safety and Health Administration, 21% of nurses reported being physically assaulted at work and more than 50% reported being verbally abused.

A 2017 survey by the WBI found that 19% of American workers were bullied and that 61% were aware of abusive conduct in the workplace. And according to the WBI, bullying is four times more common than sexual or racial harassment. Some studies indicate that as many as 98% of all employees have experienced workplace bullying at some point in their career.

Both males and females can be workplace bullies—although statistically most bullies tend to be male. The WBI’s most recent survey found that 70% of bullies are male, and the remaining 30% are female. When female bullies are involved in the conduct, they target female co-workers 67% of the time. WBI’s 2017 survey also found that 61% of bullies hold a higher rank than the target.

Bullying is not often the characteristic of a deporte employee trying to hold on to his or her job. Studies have found a strong correlation between bullying, social competence, and job performance. Bullies often perform well when meeting their employer’s performance expectations, and they can be charming, presentable, socially skilled, and professionally successful employees.

How to handle the workplace bully

There are common mistakes employers make when handling a bully. Rather than addressing the problem by confronting the employee regarding his/her behavior, employers will try to rationalize the conduct by acknowledging credibility or job performance.

Company culture can enable a bully’s problematic behavior if respect is not a core value and something demanded from employers.

As part of this rationalization, management may try to appease the bully in the short term in hopes that the aggressiveness will stop once the bully gets what he wants; however, bullies frequently engage in aggressive behavior for extended periods of time, rendering this strategy ineffective. Employers may also blame both parties involved for misconduct, or even avoid addressing the issue because most employees think everything is “fine.”

However, health care employers should still take steps to address bullying in the workplace to avoid other possible legal claims and resulting costs such as increased employee turnover.

Company culture can enable a bully’s problematic behavior if respect is not a core value and something demanded from employers.

For years, Mission Hospital, part of the Mission Health System in Asheville, NC, has embraced MERIT principles for employees to require an atmosphere of respect—Mercy, Excellence, Respect, Integrity, Trust/Teamwork. While this may sound simplistic, it largely works.

Employers must also work to eliminate the “bystander effect.” This arises when co-workers observe and fail to assist an individual that may need help. These co-workers assume that someone else will step in and help, so no action is taken.

Proactive employers can prevent these situations by adopting a zero-tolerance approach for workplace bullying. Senior health care executives cannot overlook improper conduct simply because the bully is a profit source or a strong provider or because they would rather avoid a difficult conversation with a nurse or doctor. Bullying needs to be identified and addressed through the proper channels regardless of the employee’s stature.

For instance, physician bullies may be addressed by medical staff by having a conversation over a cup of coffee or through a medical staff peer review process. However, with the increased number of employed physicians, most bullying issues involving employed physicians should be addressed through human resources.

Additionally, all employees must recognize that the employer does not tolerate such conduct and if the employees observe it, they should report it. One way to facilitate this is to have a written policy that not only prohibits bullying but also explains what employees should do when they are either the target of a bully or simply witness a co-worker engaging in bullying behavior.

Having a policy, however, is not enough as health care employers should also train employees to recognize and appropriately address workplace bullying. Training to build teamwork and camaraderie in addition to reinforcing positive behaviors further serves to lessen workplace bullying.
PRIVATE EQUITY

continued from page 1

gence of large urology group practices, which are sustaining and competing with large health care centers and systems, according to urologist Tom Jayram, MD, co-director of the Advanced Therapeutics Center at Urology Associates, an independent group of about 35 providers in Nashville.

“Most big groups have operationalized specialty urology services in a profitable and efficient way [with]: cancer centers that deliver high-cost, high-impact cancer drugs; female and sexual health clinics, which offer high throughput, cash-based services; and so on. Additionally, many large physician groups have equity in their facilities, real estate, and equipment, which is attractive to investors,” Dr. Jayram said.

And there’s plenty of money to invest, according to Hector Torres, JD, partner and principal at ECG Management Consultants, a large, diversified consulting services provider in health care.

“There’s about $1.3 trillion of private equity capital seeking to make investments within the physician group sector in 2019 and beyond,” Torres said. “Really no matter where you stand on the food chain as a provider within the urology space, private equity has become increasingly more available and an increasingly more attractive option.”

What’s the deal?

Private equity deals have a common strategy: recapitalization.

“That means the partners receive an upfront tax-advantaged payment associated with an ongoing salary reduction, while yielding con-
capital,” Dr. Rosevear said. (Also see, “Details, details: How deals are structured,” below.)

Smaller urology groups can use private equity to achieve the cost savings associated with merging back office staff and improve a practice’s ability to meet and report on governmental requirements. Still other examples of how smaller practices might benefit include being better able to track, analyze, and manage quality metrics, according to Dr. Rosevear.

Dr. Jayram of Urology Associates says the next tier in consolidation for many large independent practices is to consider a financial partnership to try and grow or stabilize their practice in today’s diverse marketplace.

“What’s the deal?”

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“That means the partners receive an upfront tax-advantaged payment associated with an ongoing salary reduction, while yielding con-

“Really no matter where you stand on the food chain as a provider within the urology space, private equity has become increasingly more available and an increasingly more attractive option.”

HECTOR TORRES, JD

trol of the business but not the medical aspect of their practice,” according to Colorado Springs, CO urologist Henry Rosevear, MD, who will present “Mergers, acquisitions and private equity: Choosing a practice model that works for you in a constantly changing environment” at the AUA annual meeting in May.

“In general, private equity groups bring with them management experience and access to

“Because of the tax-related issues with how these deals are structured, most physicians will be financially positive if they leave the practice within approximately 10 years of the deal.”

HENRY ROSEVEAR, MD

Details, details: How deals are structured

Private equity deals vary, but in general, private equity groups buy 100% of the practice and then offer a guaranteed percentage of revenue to the physician partners for compensation. Physician partners often can purchase equity in the business and share equally in any downstream event, according to urologist Henry Rosevear, MD.

“There are really two types of investments that private equity firms make in physician groups,” said Hector Torres, JD, of ECG Management Consultants. “The first is what we call the platform investment, and that is typically done with a much larger single-specialty independent group. For example, a private equity firm would go out to the market and find a very large, well-capitalized independent urology group and make that investment as their first investment in the sector.”

The firm, according to Torres, might then use the platform as a vehicle to make ongoing acquisitions of smaller, independent, highly fragmented urology practices—a strategy called bolt-on investment.

The “big buyout” is not the sole driving factor for most contemporary private equity transactions, as younger partners will not benefit from this in the long run. Instead, according to Dr. Jayram, large groups today are looking for resources to grow their footprint, improve infrastructure, better negotiate with payers, and manage an increasing burden of administrative and regulatory requirements.

“It affords independent physician groups a better ability to compete with larger hospital systems, which is ultimately good for all of us. It forces health care costs down and hopefully in turn has a positive impact on quality and value-based care,” Dr. Jayram said.

A big step

Earl Walz, CEO of Urology Group and Urology Center in Cincinnati, said the 39-urologist Urology Group spent nearly a year educating itself on the option of private equity, then contracted with an investment banking firm, which “shopped” the Urology Group and affiliated Urology Center on the market. During this process, private equity firms looked at the Urology Group’s history and performance to decide if they would be interested in a relationship with the practice.

It’s a lengthy process of interviewing multiple private equity firms and of firms interviewing the Urology Group, then performing due diligence on potential suitable partners. Walz and colleagues at the Urology Group continue that process today.

It’s hard not to explore the option for growth nowadays. The urologists in the group want to maintain independence, but to do that practices have to scale up and often need capital, according to Walz.

“You could go to a hospital system, but I think their interest is ownership, not partnership,” he said.

Another option is to bring several groups together and finance growth through debt service. But, according to Walz, that’s probably more complicated and riskier than private equity.

Deciding to partner with a private equity firm is a big step. Decisionmakers at practices need to understand and study the private equity landscape. Everyone, including physician partners and board members, need to be on board with the pursuit of private equity, Walz said.

Choosing a partner means finding a good blend of personalities, culture, trust, and comfort.

“During the interview process, you begin to gain a feeling of a relationship—a partnership—that the two groups can work with each other in a very collaborative way,” Walz said.

Private equity benefits, drawbacks

Private equity offers physician groups three key organizational attributes: economic value

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PRIVATE EQUITY
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in the purchase price, ability to influence the strategy of the organization post-transaction, and incentive and alignment mechanisms for physicians post-deal, according to Torres, who heads ECG’s mergers and acquisitions advisory practice and spent 6 years managing a private equity fund in New York.

But there’s no free lunch, according to Torres. “When an independent urology group partners with a private equity firm, there are a lot of pros, and there are also a lot of considerations. The considerations are, the private equity firm is going to demand a much higher level of performance and therefore a much higher level of organizational discipline in order to attain the growth objectives that are laid out in the proposed partnership,” Torres said. “The private equity firms are used to a very accelerated timeline and hopefully realize a return for its limited partners in that timeline,” Torres said. “That means that typically some decisions can be made with a very short-term perspective.”

Physician groups need to understand a private equity firm’s perspectives on short-term strategies to maximize economic gain. “I think that’s really important to learn what they’re willing to explore and deploy and how a group’s physicians feel in terms of being able to align to that strategy,” Torres said.

Private equity might sound like a timely option for urology practices, but there isn’t much proof that it is. Little research exists on the impact of private equity or venture capital infusion into American medicine, according to Lawrence Downs, JD, advisory committee and board member of the Physicians Foundation Center for the Study of Physician Practice and Leadership at Weill Cornell Medicine in New York and chief executive officer and general counsel to the Medical Society of New Jersey. The Physicians Foundation Center funded the recently published Annals of Internal Medicine paper.

“You could go to a hospital system, but I think their interest is ownership, not partnership.”

EARL WALZ

“Because of the tax-related issues with how these deals are structured, most physicians will be financially positive if they leave the practice within approximately 10 years of the deal,” he said.

Younger physician partners can benefit because private equity groups usually are responsible for risks associated with large capital purchases, while physician partners receive revenue associated with ancillary income without having to purchase shares, according to Dr. Rosevear.

Due diligence is key to making these partnerships successful. “The partner is very important. The medical group has to do its due diligence on what that private equity group’s track record is and how similar investments in their portfolio have matured. The best partner understands when stability and structure can be more profitable and impactful than a short-term flip,” Dr. Jayram said.

It’s important to make sure the practice’s goals align with those of the private equity firm, according to Torres. “One of the aspects with private equity is there is a finite life cycle for the investment. The private equity firm by nature and by structure is designed to invest over a 3- to 5-year timeline and hopefully realize a return for its limited partners in that timeline,” Torres said. “That means that typically some decisions can be made with a very short-term perspective.”

Physician groups need to understand a private equity firm’s perspectives on short-term strategies to maximize economic gain. “I think that’s really important to learn what they’re willing to explore and deploy and how a group’s physicians feel in terms of being able to align to that strategy,” Torres said.

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“How do these practices contrast and compare on cost and quality? That’s one of the reasons we established the Physicians Foundation Center—because there are really not researchers looking at that.”

LAWRENCE DOWNS, JD

“It’s unclear at this point whether those consolidations increase the cost of care or if they produce higher or lower quality. Those are some of the things we’re studying,” Downs said.

“There are some of the questions that physicians should be looking at when they’re entering into arrangements. Is there enough autonomy built in where physicians have an adequate leadership role in that practice to continue to make sure they do the best they can for patients?”

SELLING YOUR PRACTICE? QUESTIONS TO ASK

In the era of mounting costs, expectations to improve outcomes, increasing regulatory demands, and falling reimbursements, “you can go with the flow instead of fighting it,” says Karen Coyne, CFP, of Raymond James Financial Services Inc. in Hagerstown, MD. Selling your practice to a private equity firm or hospital system may be the best approach.

In an article in Medical Economics, Coyne offers a handful of questions to ask yourself if you are considering selling your practice, including:

What are your goals? Do you want to grow? Simplify your life? Know what is most valuable to you, Coyne advises.

Are you looking for economies of scale? Some private equity firms have a deep expertise in a sector and can increase efficiencies in a multitude of ways, from coding to scheduling and marketing. But not all private equity firms are created equally.

Do you understand the risks? Selling your practice to either a non-hospital entity or a hospital entails compliance risks and considerations.

To read the full article, visit bit.ly/sellingyourpractice.
**New data support expanded indication for BPH treatment**

NeoTract announced the publication of 12-month data from the multicenter prospective MedLift Study of the UroLift System treatment for BPH in patients with an obstructive median lobe. The results were published in *Prostate Cancer and Prostatic Diseases* (Dec. 12, 2018 [Epub ahead of print]). The MedLift Study provided clinical evidence to support the safety and efficacy of the UroLift System treatment for BPH involving a median lobe obstruction, according to NeoTract. Results from this study led to the recent FDA clearance of an expanded indication for the UroLift System, making patients who have an obstructive median lobe eligible to receive the UroLift System treatment for BPH symptoms. 

For more information, visit [www.neotract.com](http://www.neotract.com).

**RF platform launched for surgical, non-surgical procedures**

Hologic Inc.’s Cynosure division recently announced the North American launch of the FDA-cleared TempSure Surgical RF technology, a new offering of the TempSure radiofrequency (RF) platform that provides clinicians the ability to perform both surgical and non-surgical aesthetic procedures on a single device. TempSure Surgical RF technology harnesses a 300-watt and 4-MHz radiofrequency platform that enables precise incisions with minimal lateral thermal damage to surrounding tissues. The resulting high-quality coagulation lessens sparking and charring during procedures, which promotes quicker recovery and better healing for patients. The device is designed to improve patient satisfaction and aesthetic outcomes in women’s health procedures, and can be used by clinicians across a variety of specialties.

For more information, visit [www.hologic.com](http://www.hologic.com).

**Agreement allows access to expanded line of catheters, bladder scanners**

Medline has been awarded a group purchasing agreement for General Urology with Premier Inc. Effective March 1, the new agreement allows Premier members, at their discretion, to take advantage of special pricing and terms pre-negotiated by Premier for the ERASE CAUTI Comprehensive Care Solution including all of its product bundles, Foley catheters and insertion trays, bladder scanners, the Men’s Liberty Acute external catheter, intermittent catheters and trays, urine meters, drain bags, leg bags, securement devices, and irrigation syringes and trays.

For more information, visit [www.medline.com](http://www.medline.com).

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**Patient enrollment begins for PCa immunotherapy trial**

Dendreon Pharmaceuticals LLC has begun enrolling patients in the ProVent clinical trial, which is evaluating the effectiveness of sipuleucel-T (PROVENGE) in reducing disease progression in men with prostate cancer on active surveillance (AS). Sipuleucel-T remains the only FDA-approved immunotherapy proven to extend overall survival in metastatic castrate-resistant prostate cancer, and data from two previous studies (NeoACT, STAND) in non-metastatic disease provide strong scientific rationale for evaluating the use of sipuleucel-T in men on AS, according to Dendreon. ProVent is currently enrolling patients at approximately 30 sites across the U.S.

**Complete-response data reported for urothelial cancer agent**

UroGen Pharma Ltd. announced topline results from the ongoing pivotal phase III OLYMPUS clinical trial of mitomycin gel (UGN-101) for instillation, an investigational mitomycin formulation for the non-surgical treatment of low-grade upper tract urothelial cancer (LG UTUC). This analysis showed that on an intent-to-treat basis, 57% of patients achieved a complete response (CR) rate at their primary disease evaluation (the primary endpoint), which was conducted 4 to 6 weeks after completion of UGN-101 treatment. All evaluated patients in CR remain disease free at 6 months. UroGen said it intends to seek regulatory approval of UGN-101 in LG UTUC based on data from all 71 patients and initiated its rolling submission of the New Drug Application to the FDA in December 2018. UroGen previously announced that it has initiated the rolling submission with the FDA of the NDA for UGN-101 for instillation as a treatment for patients with LG UTUC. The company expects to complete its NDA submission by mid-2019, with potential approval in 2019.

**Randomized trial launched for stress incontinence device**

Renovia Inc. recently launched a large, multicenter randomized controlled trial to study the efficacy of a first-line non-surgical digital therapeutic for the treatment of stress-dominant urinary incontinence. Renovia’s next-generation leva Pelvic Digital Therapeutic System allows women to have real-time visual verification as they are performing their pelvic floor muscle exercises (PFME) correctly and consistently by guiding women through pelvic floor muscle treatment. The study seeks to determine whether home use of the device leads to more significant improvements in pelvic floor muscle performance than a PFME program without leva and improves adherence to a long-term maintenance program of home PFME.

**Trial of NMIBC agent yields positive 12-month results**

Sesen Bio, Inc. reported positive preliminary efficacy data for the primary endpoint of its ongoing phase III VISTA registration trial of VB4-845 (Vicinium) for the treatment of patients with high-grade nonmuscle-invasive bladder cancer (NMIBC) who have been previously treated with bacillus Calmette-Guérin (BCG) and deemed BCG unresponsive. The data show clinically meaningful complete response rates in evaluable carcinoma in situ patients at 3, 6, 9, and 12 months of follow-up in the trial consistent with the data in the completed phase I and phase II clinical trials. The agent continues to be generally well tolerated, Senes Bio reported.

**Early results for urothelial Ca test show 100% sensitivity**

Nucleix Ltd. announced preliminary results from an ongoing prospective, single-center study, indicating the effectiveness of its Bladder EpiCheck urine test in detecting upper tract urothelial carcinoma (UTUC). The data were published in the *World Journal of Urology* (Jan. 2, 2019 [Epub ahead of print]). Bladder EpiCheck is already CE approved for monitoring bladder cancer, and the new study will evaluate its potential role in the diagnosis and surveillance of UTUC. The trial is a prospective, single-center study that will include 80 patients with suspected primary or recurrent UTUC. Urine samples from the bladder and the upper urinary tract will be collected by ureteroscopy and will be analyzed by both EpiCheck and urinary cytology. Primary endpoints include assessment of sensitivity, specificity, and positive and negative predictive values, in high- and low-grade tumors, as well as comparison with cytology. Preliminary results from urine samples of six patients demonstrated 100% sensitivity in high-grade UTUC patients and specificity of 100%, correctly identifying the healthy patient.

**Enrollment completed for phase III trial of overactive bladder drug**

Urovant Sciences has completed enrollment in its international phase III clinical trial, EMPOWER-UR, evaluating the safety and efficacy of vibegron as a treatment for adults with symptoms of overactive bladder. Vibegron is an investigational oral beta-3 adrenergic agonist. EMPOWERUR is a randomized, double-blind placebo- and active comparator-controlled clinical trial in men and women with symptoms of OAB, including frequent urination, sudden urge to urinate, and urge incontinence or leakage. Co-primary endpoints are change from baseline in the average number of micturitions per 24 hours in all patients and change from baseline in the average number of urge urinary incontinence (UUI) episodes per 24 hours in patients who have one or more UUI episodes per day prior to treatment.
What are your thoughts on the use of medical marijuana?

There are better ways to manage people’s medical problems with drugs, especially in routine urologic care. I just don’t agree with marijuana. It’s possibly useful in other areas, and I could perhaps use it for palliative care, but not for routine care.

I don’t manage chronic pain patients. With the opioid crisis and state mandates, I send them to pain management. I only manage pain in the immediate postoperative period.

I actually had this question recently. Somebody asked if I would prescribe it, and I said it’s outside my scope. I would never prescribe it.

If a pain management specialist recommended medical marijuana to one of my ongoing patients, I would probably say, “You’ve got to do what you think is best”—but I’m still unswayed.

A lot of people with chronic pain have other unmet needs, whether they’re psychological or not. Chronic pain issues are often treated with antidepressants. With increasing anxiety in our population, it probably helps, but maybe they should have better therapy.

We have a shortage of psychiatric doctors, and that’s bad considering the growing need for mental health care. A lot of chronic pain is psychosomatic. I’m not saying it all is—some people have chronic pain from metastatic cancer. That’s totally different, but some have chronic pain with no identifiable cause. Medical marijuana may help because people relax and experience less anxiety.

There’s no data really supporting any of this yet. I would like to see proof marijuana’s actually helpful. I don’t like just medicating people without getting to the actual problem.

I think it definitely has a place. Some patients with neurologic issues, chronic pain, cancer patients have seen exceptional benefit from it. I haven’t used it, but some of my patients have obtained it from outside sources. They’ve reported they’ve felt improvements. It helps create more positive outlooks on life for people who’ve had depression from chronic disease or neurologic disease or cancer or chronic pain. These patients have had psychological counseling, they’ve had antidepressants, but medical marijuana has given them more relief. It definitely does more than a placebo. People on antidepressants or anxiolytics report at least augmented improvement on medical marijuana compared to prescribed medicines.

The literature also shows benefits medically since it can relieve pain—some of it neurological and some from chronic disease.

If it were legalized in Georgia, I would certainly investigate any potential urologic implications.

Patients with advanced cancer, perhaps in hospice, might benefit from it—if they have chronic pain syndrome, pelvic pain particularly—I would have to investigate that. I have not prescribed it. I just have anecdotal reports from my patients telling me they’ve had improvement.

There are exceptional alternative medical treatments, but a lot of narcotics have side effects: chronic constipation, increasing tolerance, and blunting of mentation.

I don’t take care of depression and anxiety, but a lot of urologic conditions, like in all fields of medicine, have some relationship with depression and anxiety.

George Jabren, MD / Stockbridge, GA

There’s definitely a role for marijuana in certain conditions. Some studies show it helps with some side effects of treatment. If it’s done properly and not abused, it probably has benefits.

My concern is that sometimes people use the label ‘medical marijuana’ for things other than what may actually be legitimate. I’ve seen people say they have a condition requiring medical marijuana when they actually don’t, but they’re able to get what they want because it is available. A lot of patients may benefit from medical marijuana, and we should offer it in a way that allows those patients to benefit.

I have patients who use it. I don’t routinely prescribe it. I did many years ago but not now. I had a patient I thought could benefit from it; I stopped because I feel it’s something that requires monitoring and follow-up. I wasn’t able to do that on a regular basis. Now, I turn those patients over to pain specialists or primary care physicians.

Patients are pretty positive about its benefit. Physicians who use it think it relieves nausea from chemotherapy, and it helps certain pain conditions.

Medical marijuana was available here before recreational became legal, so it’s been out for a while. As I said, I don’t have a huge experience with it, but I’m open to it if patients feel like there’s benefit. My only concern is making sure that people are monitored and it’s used appropriately.

James Porter, MD / Seattle

Companies featured in this issue

To obtain additional information about products advertised in this issue, use the contact information below. This index is provided as an additional service. The publisher does not assume any liability for errors or omissions.
The Department of Surgery at the University of Vermont College of Medicine is seeking a Clinical Practice Physician in the Division of Urology to join the Champlain Valley Physicians Hospital (CVPH) in Plattsburgh, New York. CVPH is a progressive medical center with nine state-of-the-art OR’s and Ambulatory Surgery Center. This position offers the unique opportunity to work in a community setting while having an active affiliation with Vermont’s only Academic Medical Center; the only ACS verified Level 1 trauma center in the state providing tertiary care to patients from Vermont and Northern NY. S

Applicants must be board certified or board eligible and eligible for medical licensure in the state of New York. This is a full-time, 12 month, salaried position.

Plattsburgh is located on the shores of Lake Champlain, near the Adirondack Mountains, Olympic-Lake Placid region, Montreal and Burlington, VT.

The University is especially interested in candidates who can contribute to the diversity and excellence of the academic community through their research, teaching, and/or service. Applicants are requested to include in their cover letter information about how they will further this goal.

The University of Vermont is an Equal Opportunity/Affirmative Action Employer. All qualified applicants will receive consideration for employment without regard to race, color, religion, sex, sexual orientation, gender identity, national origin, disability, protected veteran status, or any other category legally protected by federal or state law. The University encourages applications from all individuals who will contribute to the diversity and excellence of the institution.

Interested individuals should apply online at https://www.uvmjobs.com/postings/31529 (position number 00024781). Inquiries may be directed to Mark Plante, MD, FRCS(C), FACS, Division Chief, via Kathryn Raymond Kathryn.Raymond@uvmhealth.org.
The Tallwood Institute is comprised of a world-class Urology and Kidney care team of local and national leaders in their fields. Many of our physicians have advanced sub-specialty training and are backed by a full team of interdisciplinary medical and surgical specialists. The institute is structured around six interdisciplinary disease management teams including urologic oncology, pelvic health and urinary incontinence, stones, men’s health, chronic kidney disease and general urology. The teams meet regularly with the mission of establishing care pathways based on evidence-based medicine, providing education and improving process and quality. As a member of the Tallwood Urology and Kidney Institute, you will be able to participate in any of these teams.

Hartford HealthCare is Connecticut’s most comprehensive healthcare network. Our fully integrated health system includes a tertiary-care teaching hospital, five community hospitals, the most extensive behavioral health services network in Connecticut, a large primary care physician practice group, a regional home care system, an array of senior care services, and a large physical therapy rehabilitation network.

Our hospitals are located in a variety of settings giving you the chance to live in a vibrant town near a city, on the Connecticut shore or in a rural community with easy access to hiking, biking and skiing.

These opportunities for physicians, created by our growth, blend the best aspects of being part of a community-based team while being connected to a system of support.

**Physician opportunities include:**

- **Generalist with a focus on female urology** to provide office-based care in suburban Central Connecticut and surgical care at The Hospital of Central Connecticut, in New Britain, CT and share call with Charlotte Hungerford Hospital in Torrington, CT.

- **Generalist or endo-urologist** to provide office-based care in the suburbs of Hartford and surgical care at Hartford Hospital.

- **Generalist or andrology trained urologist** to provide office-based care at the Connecticut shore and surgical care at William W. Backus Hospital in Norwich, CT.

All positions have a desirable call schedule.

Interested candidates please call Ben Eberly at 860-539-1818 or email Ben.Eberly@hhchealth.org.
The Department of Surgery at the University of Vermont College of Medicine and its affiliated medical centers, the University of Vermont Medical Center and Vermont Children’s Hospital, is seeking a Pediatric Urologic Surgeon. The University of Vermont Medical Center and Vermont Children’s Hospital, along with the university, offers a full spectrum of pediatric medical and surgical specialties. The institution has a Level III NICU, a fully staffed PICU, and serves as the regional adult and pediatric regional trauma center. The Division of Urology holds a long-standing reputation as a premier urologic surgery practice for the surrounding communities’ pediatric and adult patients with urologic care needs and enjoys an excellent relationship with the Department of Pediatrics. With a highly respected residency training program with a robust compliment of dynamic faculty across the network hospitals, the Division seeks applications from individuals seeking an academic career in a collegial and collaborative setting.

Applicants must be BE/BC in Urology and Pediatric Urology, eligible for licensure in the State of Vermont, and eligible to work in the United States. They must have experience in the teaching of medical students and surgical residents, and the clinical and research activities of an academic division of Pediatric Surgery.

This is a full-time, 12-month salaried faculty appointment in the Clinical Scholar Pathway at the rank of Assistant or Associate Professor and carries with it attending staff privileges at University of Vermont Medical Center, a level 1 trauma center that serves as a tertiary care facility serving Vermont and northern New York State. Salary is competitive and commensurate with ability and experience.

Burlington, is located on the eastern shore of Lake Champlain between the Adirondack and Green Mountains, is consistently ranked one of the top places to live and work. Numerous recreational and cultural opportunities across four seasons are available, with Vermont considered to be an outstanding environment to practice medicine.

The University is especially interested in candidates who can contribute to the diversity and excellence of the academic community through their research, teaching, and/or service. Applicants are requested to include in their cover letter information about how they will further this goal.

The University of Vermont is an Equal Opportunity/Affirmative Action Employer. Applications from women, veterans, individuals with disabilities and people from diverse racial, ethnic, and cultural backgrounds are encouraged.

Interested individuals should apply online at https://www.uvmjobs.com/postings/30302 (position number 00024730). Inquiries may be directed to Mark Plante, MD, FRCS(C), FACS, Division Chief, via Kathryn Raymond Kathryn.Raymond@uvmhealth.org.

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Court reverses 340B reimbursement cut
CMS exceeded authority with reduction, court says

Reversing a decision by the Department of Health and Human Services (DHS) to impose a nearly 30% reduction in 340B reimbursement rates, the U.S. District Court for the District of Columbia has disappointed providers who believed that action was finally being taken to help control the cost of expensive physician-administered drugs.

The District Court's decision came Dec. 27, 2018, when it issued a permanent injunction on the Centers for Medicare & Medicaid Services' (CMS) payment reductions in the 2018 Hospital Outpatient Prospective Payment System final rule for drugs acquired through the 340B program. CMS had reduced payment rates for those drugs from Average Sales Price (ASP) plus 6% to ASP minus 22.5%, but the court ruled the agency exceeded its authority in making the adjustment.

CMS expected to appeal ruling
However, the court did not vacate the 2018 final rule and award payment to the members of the American Hospital Association and its co-plaintiffs equal to the payments they would have received in 2018 had the cut not been in effect. The court ordered further briefings on the matter to determine an appropriate remedy. CMS is expected to appeal the ruling to the U.S. Court of Appeals for the DC Circuit.

Richard Harris, MD, the new president of LUGPA, pointed out that the cost savings under CMS's rule for 2018 was $1.6 billion. Such savings, if continued, would help reduce patient costs, he said, noting that while the drugs are covered by Medicare, patients still are subject to a 20% co-pay.

“The 340B program, as noble as its intentions were at its inception, has taken on a new meaning because hospitals have benefited by utilizing these resources.”

RICHARD HARRIS, MD
LUGPA PRESIDENT

Widespread support for site-neutral payments
The poll also revealed more than two-thirds of American adults want a solution to the trend of hospital purchases of independent practices, with the most desired solution being a requirement that insurers compensate all medical practices equally, a concept known as “site-neutral payments.”

Additional responses show that 36% of Americans think Congress should either incentivize independent physicians and level the playing field with hospitals, or regulate hospital purchases of independent practices to prevent them from gaining excessive market share.

LUGPA pointed out that in addition to its poll, multiple studies have shown that consolidation under hospitals increases prices and reduces options for purchasers of health services, which includes individual patients, self-insured businesses, insurers and government programs. Even worse, LUGPA said, less competition has been shown to affect care quality.

“For not only are independent physicians across the country negatively affected by growing consolidation under hospitals, the public is aware of the consequences at an individual level,” Dr. Harris said. “Given the rapidly increasing rate of hospital mergers and acquisitions, patients will continue to feel the pain in their wallets and in their quality of care. Congress has begun to take notice of the public health impact, and we encourage them to continue building on site-of-service reforms, so that patients pay the same amount for a service regardless of where it is performed or if that practice was acquired by a hospital.”

Other key findings in the LUGPA poll include:
• 65% of respondents trust an independent physician to give them the best recommendation over a hospital-employed physician.
• 69% think the government should take some kind of action to prevent the continued trend of hospital mergers and acquisitions.
• Americans are most likely to associate independent, doctor-owned medical practices with personalized, patient-focused care. They also associate independent medical practices with trustworthiness and high quality.
Undetected kidney tumor leads to lawsuit
Plaintiff contends diagnosis should have occurred sooner

The plaintiff claimed the decedent’s cancer should have been diagnosed by the original urologist at least 3 years before the actual diagnosis, and claimed that timely diagnosis and treatment would have prevented the spread of the cancer.

Ms. Perko is an attorney in the Columbus, OH office of Reminger Co., LPA, where she specializes in medical malpractice defense litigation and transactional matters. She welcomes your feedback at APerko@reminger.com.

LEGAL PERSPECTIVE: While this outcome is starkly different from the $4.5 million settlement that we last discussed, this urologist was confident in his defense that the patient’s infections were controlled with antibiotics, that a urinalysis was performed during each of his 75 examinations of the patient, and that the tumor could not be palpated on physical exam.

Further, this urologist had a patient leave his care 3 months before the tumor was even diagnosed. As the defendant urologist maintained at trial, he would have performed imaging after antibiotic treatment. At the end of a 10-day jury trial, this six-member jury agreed that the urologist did not breach any standard of care.

Our last kidney cancer case resulted in a sizable settlement, whereas this also-tragic outcome resulted in a defense verdict. What then, can we conclude in comparing the two cases? Quite simply, each case presents its own storyline. Depending on the players, some should be tried and others settled.
**Indications for Use:**

Sacral Neuromodulation delivered by the InterStim™ system for Urinary Control is indicated for the treatment of urinary retention and the symptoms of overactive bladder, including urinary urge incontinence and significant symptoms of urgency, frequency alone or in combination, in patients who have failed or could not tolerate more conservative treatments.

The following Warning applies only to Sacral Neuromodulation for Urinary Control.

**Warning:** This therapy is not intended for patients with mechanical obstruction such as benign prostatic hypertrophy, cancer; or urethral stricture.

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**Contraindications for Urinary Control and for Bowel Control:**

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**Warnings/Precautions/Adverse Events:**

For Urinary Control: Safety and effectiveness have not been established for bilateral stimulation, pregnancy, unborn fetus, and delivery; pediatric use under the age of 16; or for patients with neurological disease origins.

For Bowel Control: Safety and effectiveness have not been established for bilateral stimulation, pregnancy, unborn fetus, and delivery; pediatric use under the age of 16; or for patients with progressive, systemic neurological diseases.

For Urinary Control and for Bowel Control: The system may be affected by or adversely affect, output devices, electrocautery, defibrillators, ultrasonic equipment, radiation therapy, MRI, theft detectors/ screening devices. Adverse events include site of the implant sites, new pain, lead migration, infection, technical or device problems, adverse change in bowel or voiding function, and undesirable stimulation or sensations including jolting or shock sensations. Patients should be assessed preoperatively for the risk of increased bleeding. For full prescribing information, please call Medtronic at 1-800-328-0818 and/or consult Medtronic’s website at www.medtronic.com. Product technical manual must be reviewed prior to use for detailed disclosure.

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Reconstruction Cases: Antegrade and Retrograde URS
Oliver Wiseman, MD

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