

Prostate Biopsy Features: A Comparison Between the Pre– and Post–2012 United States Preventive Services Task Force Prostate Cancer Screening Guidelines With Emphasis on African American and Septuagenarian Men

Navin Shah, MD,¹ Vladimir Ioffe, MD,² Shannon Cherone, MM³

¹Mid-Atlantic Urology Associates, Greenbelt, MD; ²21st Century Oncology, Greenbelt, MD; ³Integrated Cellular and Molecular Diagnostics, Greenbelt, MD

We compare prostate biopsy (Pbx) characteristics from 3 years prior to the 2012 United States Preventive Services Task Force (USPSTF) prostate cancer (PCa) screening guidelines with those of 2018, with a focus on African American (AA) men and healthy men aged 70 to 80 years. We completed a retrospective comparative analysis of 1703 sequential patients that had had a Pbx from 2010 to 2012 (3 years) with 383 patients biopsied in 2018. Data was collected on patient age, race, prostate-specific antigen (PSA), digital rectal examination (DRE), total number of biopsies performed, and Gleason sum score (GSS). The data was analyzed to determine whether the 2012 USPSTF screening recommendations affected PCa characteristics. Two study groups were defined as group A and B, Pbx prior to the 2012 USPSTF screening guidelines and that of 2018, respectively. The study population consisted of 71% high-risk AA patients. In Group A (pre-2012 USPSTF guidelines), 567 patients/year underwent a Pbx versus Group B, 383 patients/year, a 32% reduction post-USPSTF. The annual positive Pbx rate for Group A is 134/year versus Group B with 175/year, a 31% increase post-USPSTF. In Group B, there was a 94% relative increase in total positive biopsies. Group A had high-grade PCa (GSS 7-10) in 51.5% versus 60.5% in Group B, a 9% increase post-USPSTF. The proportion of patients with a PSA 10 ng/mL or higher was 25.4% in group A versus 29.3% in group B. The age group of 70 to 80 years demonstrated an increasing trend for patients with PSA 10 ng/mL and higher, 31% in Group A versus 38% in Group B; high-grade tumors (GSS 7-10) occurred in 61% in Group A versus 65% in Group B. After the 2012 USPSTF guidelines against

PCa screening, our study shows decreased prostate cancer screening with decreased Pbx, increased PCa diagnosis, and increased high-grade (GSS 7-10) PCa. These trends were especially notable in the 70- to 80-year age group, which showed a larger proportion of total patients (compared with pre-2012 USPSTF guidelines), increased PCa grades, increased PSA levels, and a higher percentage of patients with greater than 50% positive cores. As our patient population consists of 71% AA patients, our results support aggressive PCa screening for high-risk patients, which includes AA men, men with a family history of PCa, and healthy men aged 70 to 80 years.

[Rev Urol. 2019;21(1):1–7]

© 2019 MedReviews®, LLC

KEY WORDS

Prostate cancer • Prostate-specific antigen (PSA) • Screening • United States Preventive Services Task Force • African American men • Elderly men

In 2018, the American Cancer Society reported 164,690 new cases of prostate cancer (PCa) and 29,430 deaths due to PCa in the United States; in 2017 the report cited 161,360 new cases and 26,730 deaths. PCa is the third leading cause of cancer-related deaths in American men. The incidence of PCa among all races is 123.2 (per 100,000 population); it is the highest, at 198.4, in African American (AA) men and 114.8 in white men. The incidence of PCa is the highest in men aged 65 years and older (66%).¹ In the 20 years prior to 2012, prostate-specific antigen (PSA)– and digital rectal examination (DRE)–based PCa screening has reduced PCa mortality by 50%.² There are three million PCa survivors in the United States.³

In 2012, the United States Preventive Services Task Force (USPSTF) recommended against PCa screening for all age groups (grade D).^{4,5} Survey data indicate that subsequent to 2013, 50% of primary care doctors did not offer PCa screening to their patients.⁶ In 2013, national PCa screening decreased by 18%.⁷ Unfortunately, a 72% rise in metastatic PCa compared with 2004 rates has been reported.^{8–10} In 2015, 1400 additional cases of PCa-specific mortality have been documented.¹¹ It is estimated that if PCa screening is discontinued, 6000 additional deaths due to PCa will occur annually in the United States.¹²

In 2018, the USPSTF upgraded its recommendation for PCa screening to Grade C in men aged 55 to 69 years and continued to recommend against

screening in men 70 years and older.¹³ As the life expectancy for US men is approximately 84 years, an increasing number of healthy elderly men will be at risk for high-grade PCa.¹⁴ A 10-year study of 230,081 US veterans found that 10.5% died from PCa and 77.4% of the PCa deaths occurred in men between the age of 70 and 89 years.¹⁵ There are approximately 24 million US men age 70 years and older.

In this study, we reviewed our 2018 prostate biopsy data and compared it with our 2010-2012 data to determine whether PCa diagnoses and PCa characteristics have changed in our community clinical practice after the publication of the 2012 USPSTF recommendations.

Methods and Materials

In 2014, we published a retrospective analysis of 402 PCa patients diagnosed by Pbx.¹⁶ The study examined the Pbx characteristics of PCa patients from 2010-2012 (3 years). In 2018, we published a comparison of prostate biopsy characteristics prior to (2010-2012) and after (2015-2017) the 2012 USPSTF recommendations against PCa screening.¹⁷ The current study analyzed an additional 383 patients who had had a Pbx in 2018. Data was collected on patient age, race, PSA, DRE, number of biopsies, and Gleason sum score (GSS). In this study, we compared the Pbx characteristics of our patient cohort prior to the 2012 USPSTF PCa screening guidelines with the 2018 Pbx data.

All cases are collected from our community clinical practice of a group of 10 board-certified urologists located in Prince George's County, Maryland, in the Washington DC metro area. Pbx were performed on men with a PSA of over 2.5 ng/mL, an abnormal DRE, or both. Most of the patients had a transrectal ultrasound-guided 12-core Pbx under intravenous sedation on an outpatient basis (a few patients were biopsied under local anesthesia). All patients were cleared for the procedure by their primary care physician.

Patient age was stratified as 55 years or younger, 56 to 69 years, and 70 to 80 years. The charts of consecutive patients from our practice were reviewed and the information was entered in a database. The data was analyzed to determine whether the 2012 USPSTF screening recommendations affected PCa characteristics. Two study groups were defined, group A [patients diagnosed prior to the USPSTF screening recommendations (2010-2012)] and group B (patients diagnosed in 2018, after the USPSTF screening recommendations). We separated the Gleason sum score (GSS) into two groups, GSS 6 and GSS 7-10. We defined the GSS 7-10 group as aggressive because it harbors a Gleason score 4 or higher component.

Chi-square or Fisher's exact tests were used to compare frequencies. All analyses were conducted using the SAS/STAT (SAS Institute Inc, Cary, NC) software program.

The study was approved by the Western Institutional Review Board (study number 1087891).

Results

Prostate Biopsy

In the pre-USPSTF period (Group A), 1703 total Pbx were performed over 3 years. The PBx rate was

567 biopsies/year, and there were 402 positive Pbx (23.6%). The annual positive biopsy rate was 134 positive biopsies/year. In the post-USPSTF period (Group B), there were 383 total Pbx, an annual rate of 383 biopsies/year. The number of Pbx decreased in Group B by 32%. There were 175 positive Pbx (45.7%), an annual rate of 175 positive Pbx/year. In Group B, there was a 94% increase of the total number of positive Pbx (23.6% in Group A vs 45.7% in Group B) (Table 1).

Age

The age was stratified as 55 years and younger, 55 to 69 years, and 70 to 80 years. A comparison was made with group A of 402 PCa patients and group B of 175 PCa patients. In group A, 9% were 55 years or younger, 56% were age 55 to 69 years, and 35% were age 70 to 80 years. In group B, 9% were 55 years or younger, 57% were age 55 to 69 years, and 34% were age 70 to 80 years. The age groups were well matched in both groups (Table 2).

Prostate-specific Antigen

The PSA in group A was under 4 ng/mL in 11%, 4 to 9.9 ng/mL in 63%, and 10 ng/mL or higher in 25%. In group B, the PSA was under 4 ng/mL in 7%, 4 to 9.9 ng/mL in 63%, and 10 ng/mL or higher

in 29%. In group B, there were more patients with a PSA 10 ng/mL or higher in all age groups compared with group A. This was especially notable in the age group 70-80 years, 31% versus 38% in groups A versus B, respectively (Table 2).

Race

The study was conducted in Prince George's County (PGC), Maryland (Washington DC metro area), a county with a three-fold higher prevalence of AA men compared with the national average. According to the 2015 American Community Survey, PGC is made up of 62% African Americans, 14% whites, and 25% other races. Our study had an African American representation of 71%, 16% whites, and 14% other races, consistent with the census demographic data. We were not able to extract the race from the data set for group A because the study consisted of patients in the same county and in the same urology practice, we assume that the demographics are consistent between study groups A and B (Table 3).

Gleason Sum Score

A GSS of 6 was found in 195 patients (49%) in group A and in 70 patients (40%) in group B. In group A, GSS

TABLE 1

Comparison of Biopsy Statistics in Group A vs Group B

Prostate Biopsy	Group A (2010-2012)	Group B (2018)	Note
Total biopsies	1703	383	
Annual biopsy rate	567	383	32% reduction
Total positive biopsies	402 (23.6%)	175 (45.7%)	94% relative increase
Annual positive biopsy rate	134/year	175/year	31% increase

TABLE 2**Comparison of Prostate-Specific Antigen (PSA) Levels by Age in Patients With a Positive Prostate Biopsy, Group A vs Group B**

Age (years)	n	PSA <4 ng/mL	PSA 4-9.9 ng/mL	PSA 10 ng/mL and Higher
Group A				
<55	36	5 (13.9%)	25 (69.4%)	6 (16.6%)
56-69	226	23 (10.2%)	150 (66.4%)	53 (23.5%)
70-80	140	17 (12.1%)	80 (57.1%)	43 (30.7%)
Total	402	45 (11.2%)	255 (63.4%)	102 (25.4%)
Group B				
<55	15	1 (6.7%)	11 (73.3%)	3 (20%)
56-69	100	8 (8%)	67 (67%)	25 (25%)
70-80	60	4 (7%)	33 (55%)	23 (38%)
Total	175	13 (7.4%)	111 (63.4%)	51 (29.2%)

PSA, Prostate-specific antigen.

TABLE 3**Race by Age in Group B Stratified by Positive vs Negative Prostate Cancer Biopsy**

Age (years)	n	African American	White	Other
Group B				
PCa Positive				
<55	15	12 (80%)	1 (7%)	2 (13%)
56-69	100	79 (79%)	9 (9%)	12 (12%)
70-80	60	40 (66.7%)	14 (23%)	6 (10%)
Total	175	131 (75%)	24 (13.8%)	20 (11.2%)
PCa Negative				
<55	21	16 (76.19%)	1 (4.76%)	4 (19.05%)
56-69	118	77 (65.25%)	20 (16.95%)	21 (17.80%)
70-80	69	47 (68.12%)	15 (21.74%)	7 (10.14%)
Total	208	140 (67.31%)	36 (17.31%)	32 (15.38%)

PCa, prostate cancer.

TABLE 4**Comparison of Gleason Sum Score in Group A vs Group B by Age**

Age	n	GSS 6	GSS 7-10
Group A			
<55	36	18 (50.0%)	18 (50.0%)
56-69	226	122 (54%)	104 (46.0%)
70-80	140	55 (39.3%)	85 (60.7%)
Total	402	195 (48.5%)	207 (51.5%)
Group B			
<55	15	10 (66.7%)	5 (33.3%)
56-69	100	39 (39%)	61 (61%)
70-80	60	21 (35%)	39 (65%)
Total	175	70 (39.55%)	105 (60.0%)

GSS, Gleason sum score.

of 7-10 was found in 207 patients (52%) and in group B, 105 patients (60%). GSS 7-10 was higher in group B by 8.5% as compared with Group A. In patients age 70 to 80 years, high-grade (GSS 7-10) disease was 4% higher in Group B versus Group A (65% vs 61%, respectively) (Table 4).

Digital Rectal Examination Results in Patients With Prostate Cancer

In group A, a normal DRE result was found in 151 patients and an abnormal DRE result was found in 251 patients. In group B, a normal DRE result was found in 135 patients and abnormal DRE result was found in 40 patients.

Normal Digital Rectal Examination and Gleason Sum Score

In group A, 78 patients with normal DRE results (52%) had a GSS of 6 and 73 (48%) had a GSS of 7-10. In group B, 55 patients with normal DRE results (41%) had GSS of 6 and 80 (59%) had a GSS of 7-10. In patients with a normal DRE, there was an 11% increase in GSS 7-10

in group B versus group A (59% vs 48%, respectively).

Abnormal Digital Rectal Examination and Gleason Sum Score

In group A, 113 patients (45%) had a GSS of 6 and 138 patients (55%) had a GSS of 7-10. In group B, 14 patients (35%) had a GSS of 6 and 26 patients (65%) had a GSS of 7-10. Patients with abnormal DRE results had a 10% increase in GSS 7-10 in group B versus group A (65% vs 55%, respectively).

In patients age 70 to 80 years, the overall frequency of high-grade disease was high for both normal and abnormal DRE result groups. Specifically, in group B, high-grade disease (GSS 7-10) was found in 73% of patients age 70 to 80 years with an abnormal DRE and 62% in patients age 70 to 80 years with a normal DRE.

Discussion

This study reviewed our community-based urologic practice and found that the Pbx rate decreased

by 32% in the post-2012 USPSTF period. Additionally, the PCa detection rate was 31% higher post-USPSTF. We also found a 9% higher rate of high-grade PCa (GSS 7-10) in the post-USPSTF period. Despite a 32% reduction in the number of biopsies post-USPSTF guidelines, there was a 94% relative increase in the total number of positive biopsies.

The Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO), on which the USPSTF based their 2012 recommendation against PCa screening, was found to be 90% contaminated and hence should not form the basis of national guidelines.^{18,19} Unfortunately, following the 2012 USPSTF guidelines against PCa screening, there was a 64% decrease in DRE and a 39% decrease in PSA testing.²⁰ Other large studies have replicated our results and have shown that after the 2012 USPSTF guidelines, Pbx have decreased and positive Pbx have increased and are associated with increased rates of high-grade Gleason scores and more advanced disease presentations.²¹⁻²⁷

The benefit of PCa screening was recently confirmed by Alpert, in which a review of 400,887 patients under age 80 years showed that annual PSA-based screening reduced PCa deaths by 64% and all-cause mortality by 24%.²⁸

Our study is unique because 71% of the study population was African American, a documented high-risk group. The 2012 USPSTF guidelines were based on studies in which high-risk populations were under-represented (only 4% were African American in the PLCO study).²⁹⁻³¹ In some of the non-US-based studies that were considered by the USPSTF, there is also minimal representation of African Americans and men age 70 to 80 years. A recent study showed that GSS 6 is more aggressive in

African American men compared with non-African Americans and is associated with a 100% increase in PCa death.³² High-risk populations, especially AA and healthy men age 70 to 80 years are disproportionately adversely affected by the current USPSTF guidelines.

Our data showed 61% of men age 70 to 80 years had high-grade disease (GSS 7-10). In our prior study of 5100 US men age 70 to 80 years with average-risk PCa (84% with PSA lower than 10 ng/mL), 61% had high-grade GSS of 7-10.³³ As surgical series have found that 50% of GSS 6 patients on biopsy are upgraded to GSS 7-10 at the time of prostatectomy, it is likely that 80% of our patients age 70 to 80 years had GSS 7-10.^{34,35} Furthermore, the proportion of Pbx patients age 70 to 80 years has increased to 40% in 2018 versus 35% in 2010-2012. To determine whether patients age 70 to 80 years had an increased rate of 50% or higher number of positive biopsy cores, we reviewed our 552 positive biopsies (total of 1194 Pbx from 2015-2017) and 175 positive biopsies (total of 383 Pbx from 2018). In 2015-2017, 28% had 50% or higher positive biopsy

cores whereas in 2018 it was 35%. The published US literature shows that men 70 years and older have more prevalence of PCa, more locally advanced PCa, more metastatic PCa, and more deaths due to PCa.³⁶⁻³⁸ Our study shows that limiting screening for high-risk men over age 70 years is harmful.

Since 2013, more locally advanced PCa, metastatic PCa, and PCa-specific deaths have been documented. The 5-year survival rate in metastatic PCa is 28% and the cost of treating metastatic PCa is well over \$200,000.³⁹ More importantly, patients with metastatic PCa have more pain, a much lower quality of life, and almost certain death. The annual cost of the screening PSA test is \$25.

The 2018 USPSTF guidelines upgraded PCa screening in men age 55 to 69 years from a D grade to a C grade but still excludes men age 70 years and older. We believe the reports strongly indicate that PCa screening should also be made available to detect early PCa in healthy men age 70 to 80 years.⁴⁰ Based on our data and others, the USPSTF should urgently endorse PCa screening for men, especially

for high-risk populations including African American men, men with a family history of PCa, and healthy men age 70 to 80 years.⁴¹

Over the past several years, new tools to facilitate PCa detection and risk stratification have entered clinical practice. These include imaging technology such as the multi-parametric prostate MRI,⁴² novel genetic and molecular tests,⁴³ and chemical assays.⁴⁴ These new diagnostic and risk stratification tools give clinicians the ability to counsel patients regarding which prostate cancers are indolent and appropriate for active surveillance and which are aggressive and need treatment. These technological innovations have significantly reduced PCa overdiagnosis and overtreatment in clinical practice.

Conclusions

This study shows that the annual Pbx rate decreased by 32% after the 2012 USPSTF PCa screening guidelines but the annual PCa detection rate increased by 31%. High-grade GSS (7-10) PCa increased by 9% after the 2012 USPSTF guidelines.

MAIN POINTS

- This study shows that, in the authors' patient population, the annual prostate biopsy (Pbx) rate decreased by 32% after the 2012 US Preventive Services Task Force (USPSTF) prostate-cancer (PCa) screening guidelines but the annual PCa detection rate increased by 31%.
- High-grade Gleason sum score (GSS; 7-10) PCa increased by 9% after the 2012 USPSTF guidelines.
- Despite a 32% reduction in the total number of biopsies there was a 94% increase in the total number of positive biopsies in 2018.
- As the patient population included 71% African American (AA) men, these findings suggest that the USPSTF should immediately endorse PCa screening in high-risk populations to decrease the rising trend of PCa morbidity, mortality, and the high cost to treat advanced PCa.
- The authors strongly recommend that prostate-specific antigen- and digital rectal examination-based PCa screening should be made available, especially to AA men, men with a family history of PCa, and healthy men age 70 to 80 years.

Despite a 32% reduction in the total number of biopsies there was a 94% increase in the total number of positive biopsies in 2018. As our patient population included 71% AA men, these findings suggest that the USPSTF should immediately endorse PCa screening in high-risk populations to decrease the rising trend of PCa morbidity, mortality, and the high cost to treat advanced PCa. We strongly recommend that PSA- and DRE-based PCa screening should be made available, especially to AA men, men with a family history of PCa, and healthy men age 70 to 80 years. ■

The authors thank Sharon Salenius for her thoughtful review of our manuscript and data analysis.

References

- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin*. 2018;68:7-30.
- Etzioni R, Gulati R. Recent trends in PSA testing and prostate cancer incidence: a look at context. *JAMA Oncol*. 2016;2:955-956.
- American Cancer Society. *Cancer Treatment and Survivorship Facts & Figures 2014-2015*. Atlanta: American Cancer Society; 2014.
- US Preventive Services Task Force. Screening for prostate cancer: US Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2008;149:185-191.
- Moyer VA, US Preventive Services Task Force. Screening for prostate cancer: US Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2012;157:120-134.
- Rosevear H. PSA screening decline is troubling trend. *Urol Times*. 2015;43:4.
- Jemal A, Fedewa SA, Ma J, et al. Prostate cancer incidence and PSA testing patterns in relation to USPSTF screening recommendations. *JAMA*. 2015;314:2054-2061.
- Weiner AB, Matulewicz RS, Eggener SE, Schaeffer EM. Increasing incidence of metastatic prostate cancer in the United States (2004-2013). *Prostate Cancer Prostatic Dis*. 2016;19:395-397.
- Hu JC, Nguyen P, Mao J, et al. Increase in prostate cancer distant metastases at diagnosis in the United States. *JAMA Oncol*. 2017;3:705-707.
- Kelly SP, Anderson WF, Rosenberg PS, Cook MB. Past, current, and future incidence rates and burden of metastatic prostate cancer in the United States. *Eur Urol Focus*. 2018;4:121-127.
- Hall M, Schultheiss T, Fariño G, Wong J. Increase in higher risk prostate cancer cases following new screening recommendation by the US Preventive Services Task Force (USPSTF). *J Clin Oncol*. 2015;33(7 suppl):143.
- Gulati R, Tsodikov A, Etzioni R, et al. Expected population impacts of discontinued prostate-specific antigen screening. *Cancer*. 2014;120:3519-3526.
- Grossman DC, Curry SJ, Owens DK, et al. Screening for prostate cancer: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2018;319:1901-1913.
- Actuarial Life Table. US Social Security Administration website. <https://www.ssa.gov/oact/STATS/table4c6.html>. Accessed March 26, 2019.
- MacKintosh FR, Sprenkle PC, Walter LC, et al. Age and prostate-specific antigen level prior to diagnosis predict risk of death from prostate cancer. *Front Oncol*. 2016;6:157.
- Shah N, Ioffe V, Kapur A. A comparative analysis of prostate cancer pre-treatment characteristics stratified by age. *Can J Urol*. 2014;21:7213-7216.
- Shah N, Huebner T, Ioffe V, Hum R. Prostate biopsy characteristics: a comparison between pre- and post-United States Preventive Service Task Force Prostate Cancer Screening Guidelines of 2012. *Rev Urol*. 2017;19:25-31.
- Shoag JE, Mittal S, Hu JC. Reevaluating PSA testing rates in the PLCO trial. *N Engl J Med*. 2016;374:1795-1796.
- Pinsky PF, Prorok PC, Kramer BS. Prostate cancer screening—a perspective on the current state of the evidence. *N Engl J Med*. 2017;376:1285-1289.
- Shoag J, Halpern JA, Lee DJ, et al. Decline in prostate cancer screening by primary care physicians: an analysis of trends in the use of digital rectal examination and prostate specific antigen testing. *J Urol*. 2016;196:1047-1052.
- McGinley KE, McMahon GC, Brown GA. Impact of the US Preventive Services Task Force grade d recommendation: assessment of evaluations for elevated prostate-specific antigen and prostate biopsies in a large urology group practice following statement revision. *Rev Urol*. 2015;17:171-177.
- Olsson CA, Lavery HJ, Yadav KK, et al. Histologic changes in prostate cancer detected subsequent to the 2012 United States Preventive Services Task Force (USPSTF) prostate cancer screening recommendation. *Rev Urol*. 2018;20:125-130.
- Gejerman G, Ciccone P, Goldstein M, et al. US Preventive Services Task Force prostate-specific antigen screening guidelines result in higher Gleason score diagnoses. *Investig Clin Urol*. 2017;58:423.
- Blair BM, Robyak H, Clark JY, et al. Impact of United States Preventive Services Task Force recommendations on prostate biopsy characteristics and disease presentation at a tertiary-care medical center. *Prostate Int*. 2018;6:110-114.
- Zakaria AS, Dragomir A, Brimo F, et al. Changes in the outcome of prostate biopsies after preventive task force recommendation against prostate-specific antigen screening. *BMC Urol*. 2018;18:69.
- Li J, Siegel DA, King JB. Stage-specific incidence rates and trends of prostate cancer by age, race, and ethnicity, United States, 2004-2014. *Ann Epidemiol*. 2018;28:328-330.
- Ahlering T, Huynh LM, Kaler KS, et al. Unintended consequences of decreased PSA-based prostate cancer screening. *World J Urol*. 2019;37:489-496.
- Alpert PF. New evidence for the benefit of prostate-specific antigen screening: data from 400,887 Kaiser Permanente patients. *Urology*. 2018;118:119-126.
- Andriole GL, Crawford ED, Grubb RL 3rd, et al. Mortality results from a randomized prostate-cancer screening trial. *N Engl J Med*. 2009;360:1310-1319.
- Schröder FH, Hugosson J, Roobol MJ, et al. Screening and prostate-cancer mortality in a randomized European study. *N Engl J Med*. 2009;360:1320-1328.
- Schröder FH, Hugosson J, Roobol MJ, et al. Screening and prostate cancer mortality: results of the European Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow-up. *Lancet Lond Engl*. 2014;384:2027-2035.
- Mahal BA, Berman RA, Taplin M-E, Huang FW. Prostate cancer-specific mortality across gleason scores in black vs nonblack men. *JAMA*. 2018;320:2479-2481.
- Shah N, Ioffe V. Frequency of Gleason score 7 to 10 in 5100 elderly prostate cancer patients. *Rev Urol*. 2016;18:181-187.
- Vellekoop A, Loeb S, Folkvaljon Y, Stattin P. Population based study of predictors of adverse pathology among candidates for active surveillance with gleason 6 prostate cancer. *J Urol*. 2014;191:350-357.
- Dinh KT, Mahal BA, Ziehr DR, et al. Incidence and predictors of upgrading and up staging among 10,000 contemporary patients with low risk prostate cancer. *J Urol*. 2015;194:343-349.
- Richstone L, Bianco FJ, Shah HH, et al. Radical prostatectomy in men aged > 70 years: effect of age on upgrading, upstaging, and the accuracy of a preoperative nomogram. *BJU Int*. 2008;101:541-546.
- Sun L, Caire AA, Robertson CN, et al. Men older than 70 years have higher risk prostate cancer and poorer survival in the early and late prostate specific antigen eras. *J Urol*. 2009;182:2242-2248.
- Loeb S, Hernandez DJ, Mangold LA, et al. Progression after radical prostatectomy for men in their thirties compared to older men. *BJU Int*. 2008;101:1503-1506.
- Survival Rates for Prostate Cancer. American cancer Society website. <http://www.cancer.org/cancer/prostatecancer/detailedguide/prostate-cancer-survival-rates>. Revised February 7, 2019. Accessed March 26, 2019.
- Final Recommendation Statement: Prostate Cancer: Screening. U.S. Preventive Services Task Force. October 2018. <https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/prostate-cancer-screening1>. Accessed March 26, 2019.
- Shenoy D, Packianathan S, Chen AM, Vijayakumar S. Do African-American men need separate prostate cancer screening guidelines? *BMC Urol*. 2016;16:19.
- Thompson JE, Moses D, Shnier R, et al. Multiparametric magnetic resonance imaging guided diagnostic biopsy detects significant prostate cancer and could reduce unnecessary biopsies and over detection: a prospective study. *J Urol*. 2014;192:67-74.
- Van Den Eeden SK, Lu R, Zhang N, et al. A Biopsy-based 17-gene genomic prostate score as a predictor of metastases and prostate cancer death in surgically treated men with clinically localized disease. *Eur Urol*. 2018;73:129-138.
- Loeb S, Sanda MG, Broyles DL, et al. The prostate health index selectively identifies clinically significant prostate cancer. *J Urol*. 2015;193:1163-1169.