Urology birmingham CENTERS OF ALABAMA

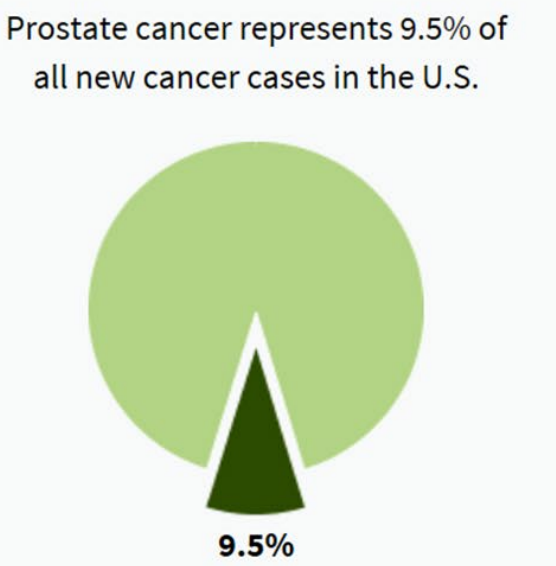
Bring Clarity to Controversy: PSA and Prostate Cancer Screening Guidelines

Jared Cox, MD

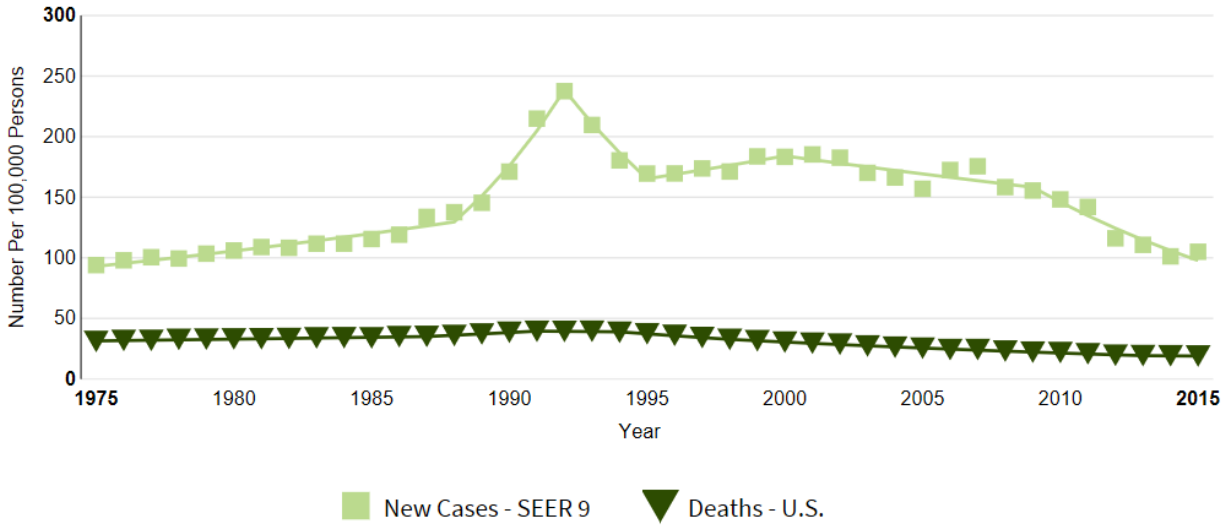
How Common is this Cancer?

- Compared to other cancers, prostate cancer is fairly common

	Common Types of Cancer	Estimated New Cases 2018	Estimated Deaths 2018
1.	Breast Cancer (Female)	266,120	40,920
2.	Lung and Bronchus Cancer	234,030	154,050
3.	**Prostate Cancer**	**164,690**	**29,430**
4.	Colorectal Cancer	140,250	50,630
5.	Melanoma of the Skin	91,270	9,320
6.	Bladder Cancer	81,190	17,240
7.	Non-Hodgkin Lymphoma	74,680	19,910
8.	Kidney and Renal Pelvis Cancer	65,340	14,970
9.	Uterine Cancer	63,230	11,350
10.	Leukemia	60,300	24,370



New Cases, Deaths and 5-Year Relative Survival



National:

164,690 New Cases in 2018

29,430 Deaths in 2018

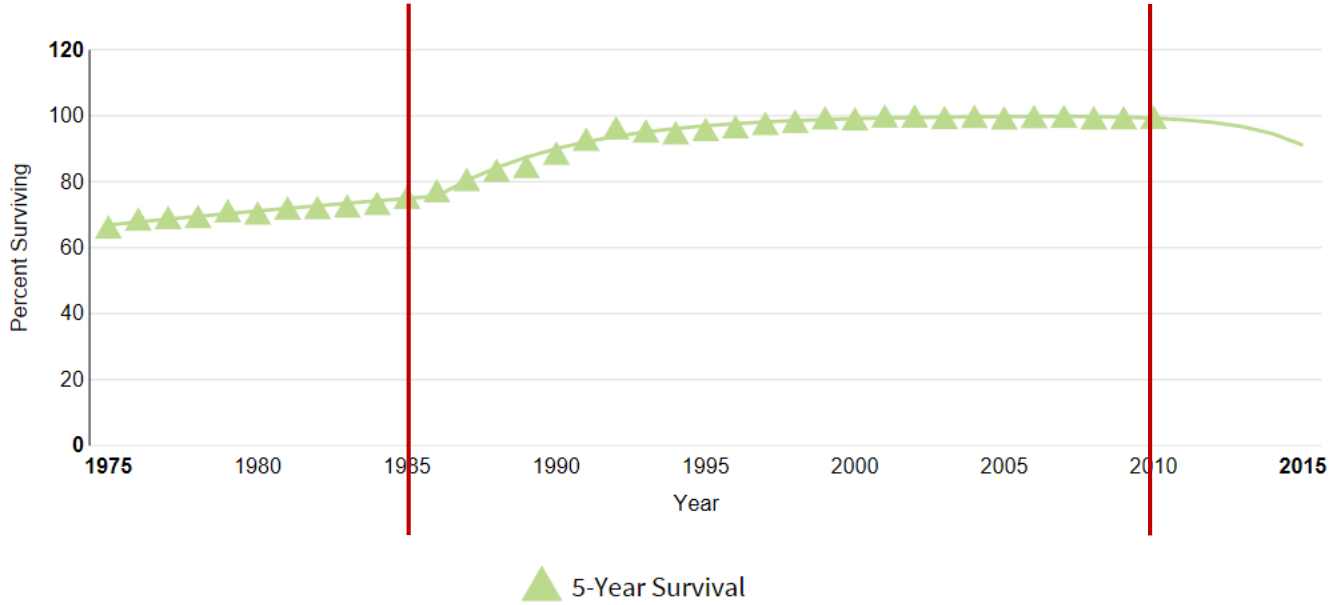
Alabama:

2,460 New Cases

490 Deaths

1985			
	Data	Observed Rate	Modeled Rate
	5-Year Survival	75.3	74.9

2010			
	Data	Observed Rate	Modeled Rate
	5-Year Survival	99.6	99.3



Prostate Cancer:
To Screen or Not to Screen

Cancer Trends

- Pre-PSA era
  - 75% with extraprostatic disease
  - 35% with metastatic disease

- Post-PSA era
  - 15% with extraprostatic disease
  - 4% with metastatic disease

Why?

- USPSTF – 2012

Archived: Prostate Cancer: Screening

Original Release Date: May 2012

This version of this topic is currently archived and inactive. It should be used for historical purposes only.

Archived: Recommendation Summary

Population	Recommendation	Grade (What's This?)
Men	The U.S. Preventive Services Task Force (USPSTF) recommends against prostate-specific antigen (PSA) –based screening for prostate cancer.	D

- "Moderate or high certainty that the service has no benefit or that the harms outweigh the benefits"

Screening Studies

- PLCO (Prostate, Lung, Colon, Ovarian Cancer) Study – March 2009
- European Randomized Study of Screening for Prostate Cancer (ERSPC) – March 2009
- Goteborg Randomized Population-based Prostate Cancer Screening Trial – July 2010

Screening Studies

- Limitations of all studies:
  - Patients at highest risk were not addressed
  - Only sextant biopsies done
  - More advanced age in all studies
  - Low intensity of screening intervals
  - Possibly suboptimal treatment when these trials began

Cancer

Original Article | Open Access

Annual Report to the Nation on the Status of Cancer, part II: Recent changes in prostate cancer trends and disease characteristics

Serban Negoita MD, DrPH, Eric J. Feuer PhD, Angela Mariotto PhD, Kathleen A. Cronin PhD, Valentina I. Petkov MD, MPH, Sarah K. Hussey MS, Vicki Benard PhD, ... See all authors

First published: 22 May 2018 | https://doi.org/10.1002/cncr.31549

RESULTS

For all age groups, overall prostate cancer incidence rates declined approximately 6.5% per year from 2007. However, the incidence of distant-stage disease increased from 2010 to 2014. The incidence of disease according to higher PSA levels or Gleason scores at diagnosis did not increase. After years of significant decline (from 1993 to 2013), the overall prostate cancer mortality trend stabilized from 2013 to 2015.

CONCLUSIONS

After a decline in PSA test usage, there has been an increased burden of late-stage disease, and the decline in prostate cancer mortality has leveled off. ***Cancer* 2018.** © 2018 The Authors. *Cancer* published by Wiley Periodicals, Inc. on behalf of American Cancer Society.

Is President Obama's Prostate Gland More Important Than Yours?

Capital Flows Contributor
Guest commentary curated by Forbes Opinion. Avik Roy, Opinion Editor.

By Paul Hsieh, M.D.

When President Obama turned 50 last year, he made an "informed patient request" for a PSA (Prostate Specific Antigen) test. This is the blood test routinely used to screen men over 50 for possible prostate cancer.

USPSTF – Update May 2018

U.S. Preventive Services TASK FORCE

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Final Recommendation Statement

Prostate Cancer: Screening

Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

For more information on the final recommendation on screening for prostate cancer, go to www.screeningforprostatecancer.org.

Recommendation Summary

Population	Recommendation	Grade (What's This?)
Men aged 55 to 69 years	For men aged 55 to 69 years, the decision to undergo periodic prostate-specific antigen (PSA)–based screening for prostate cancer should be an individual one. Before deciding whether to be screened, men should have an opportunity to discuss the potential benefits and harms of screening with their clinician and to incorporate their values and preferences in the decision. Screening offers a small potential benefit of reducing the chance of death from prostate cancer in some men. However, many men will experience potential harms of screening, including false-positive results that require additional testing and possible prostate biopsy; overdiagnosis and overtreatment; and treatment complications, such as incontinence and erectile dysfunction. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of family history, race/ethnicity, comorbid medical conditions, patient values about the benefits and harms of screening and treatment-specific outcomes, and other health needs. Clinicians should not screen men who do not express a preference for screening.	C
Men 70 years and older	The USPSTF recommends against PSA-based screening for prostate cancer in men 70 years and older.	D

Grade Definitions After July 2012

What the Grades Mean and Suggestions for Practice

The USPSTF updated its definition of and suggestions for practice for the grade C recommendation. This new definition applies to USPSTF recommendations voted on after July 2012. Describing the strength of a recommendation is an important part of communicating its importance to clinicians and other users. Although most of the grade definitions have evolved since the USPSTF first began, none has changed more noticeably than the definition of a C recommendation, which has undergone three major revisions since 1998. Despite these revisions, the essence of the C recommendation has remained consistent: at the population level, the balance of benefits and harms is very close, and the magnitude of net benefit is small. Given this small net benefit, the USPSTF has either not made a recommendation "for or against routinely" providing the service (1998), recommended "against routinely" providing the service (2007), or recommended "selectively" providing the service (2012). Grade C recommendations are particularly sensitive to patient values and circumstances. Determining whether or not the service should be offered or provided to an individual patient will typically require an informed conversation between the clinician and patient.

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Things to Remember

- Shared decision
- PSA is not the enemy
- Men still die from prostate cancer
- Alabama is not comparable to other parts of the country/world

UCA Biopsy Results

1/17-12/17		
Month	**Total Cases**	**Positive per Month**
January	123	76
Febuary	124	66
March	151	74
April	115	54
May	151	70
June	120	74
July	138	66
August	150	82
September	116	67
October	165	77
November	130	59
December	125	58
TOTAL:	**1608**	**823**

- 51% positive biopsy results
  - Compared to 25-30% national average

UCA Biopsy Results

Gleason 3+3	
Surgery:	22
Radiation:	38
Active Surveillance:	100
HIFU:	5
Undecided/Unknown:	11
TURP:	12
Of these 1 is now deceased	

188

Gleason 3+4	
Surgery:	150
Radiation:	126
Active Surveillance:	33
HIFU:	15
Undecided/Unknown:	16
ADT:	4
Research:	1
Cryo:	2
of these 2 are now deceased	

347

275

Gleason 4+3	
Surgery:	73
Radiation:	66
Active Surveillance:	3
HIFU:	4
Undecided/Unknown:	12
ADT:	4
Orchiectomy:	2
Proton Therapy:	1
Mets at diagnosis:	2
of these 1 is now deceased	

167

Gleason 4+4	
Surgery:	10
Radiation:	28
Active Surveillance:	3
Undecided/Unknown:	3
Research:	1
ADT:	3
Mets at diagnosis:	4

52

Gleason 4+5	
Surgery:	15
Radiation Therapy:	19
Active Surveillance:	1
HIFU:	1
ADT:	4
Undecided/Unknown:	2
Mets at diagnosis:	7

49

Gleason 5+3	
Radiation:	1

1

Gleason 5+4	
Surgery:	2
Radiation:	1
unknown/undecided:	1

4

Gleason 5+5	
mets at diagnosis:	2

2

The American Urological Association's Prostate Cancer Screening Guideline: Which Cancers Will Be Missed in Average-risk Men Aged 40 to 54 Years?

Thomas E. Moody, MD, Curtis L. Spraitzar, Elizabeth Eisenhart, Scott Tully, Jr.
Urology Centers of Alabama, Homewood, AL

To determine the impact of the American Urological Association's (AUA) guideline for early detection of prostate cancer that recommends against routine screening in men aged 40 to 54 years at average risk (eg, white men without a family history of prostate cancer), we undertook a study of 973 men who previously underwent a prostate biopsy at Urology Centers of Alabama (UCA) over the 5-year period from 2010 to 2014. We retrospectively reviewed the results of the prostate biopsies performed by urologists at UCA—and, where applicable, the final surgical pathology results and compared the results by race and family history. In white men with a family history of prostate cancer, 47% had cancer and 30% had Gleason score (GS) ≥ 7 disease. In white men without a family history of prostate cancer, 32% had cancer and 23% had GS ≥ 7 disease. By comparison, in African American men with a family history of prostate cancer, 56% had cancer and 42% had GS ≥ 7 disease. In African American men without a family history, 42% had cancer and 29% had GS ≥ 7 disease. In our study, 144 of 456 (32%) of the group of average-risk men had cancer and 105 of 456 (23%) had GS ≥ 7 cancer. Had the AUA guidelines been followed, these cancers would have been missed or the diagnoses delayed.

[Rev Urol. *2017;19(2):106–112 doi: 10.3909/riu0748]*

Screening Difficulty

Everyone has <u>different recommendations</u> for screening guidelines

- AUA
- NCCN
- ASCO
- ACS
- USPSTF
- EAU/ESTRO

Screening Guidelines

All Agree on ONE THING:

- PSA-based prostate cancer screening requires an informed, shared decision-making process, and the decision should reflect the patient's understanding of the possible risks and benefits and should reflect the patient's preferences and values

All Differ in:

- Whether or not routine screening is recommended
- What age groups and life expectancies
- What intervals

American Cancer Society (ACS)

- Last updated 2010
- No routine screening in any age group, offered for asymptomatic men with at least 10 year life expectancy
- For those unable to decide, provider can make decision
- PSA recommended, DRE may be done

American Cancer Society (ACS)

Ages

- 50 for those at average risk
- 45 for those at high risk
  - African Americans
  - 1st degree relative with prostate cancer prior to age 65
- 40 for those at higher risk
  - More than one 1st degree relative with prostate cancer at any age

If cancer not suspected or detected:

- PSA <2.5 ng/ml – Retest every 2 years
- PSA >2.5 ng/ml – Retest annually

American Urological Association (AUA)

No routine screening in:

- Any man with life expectancy <10 years
- Men under 40
- Men between ages 40 to 54 years at average risk
- Men over 70

For men ages 55 to 69:

- Shared decision making, proceed based on patient preference
- Routine screening interval of 2 years or more determined by baseline PSA

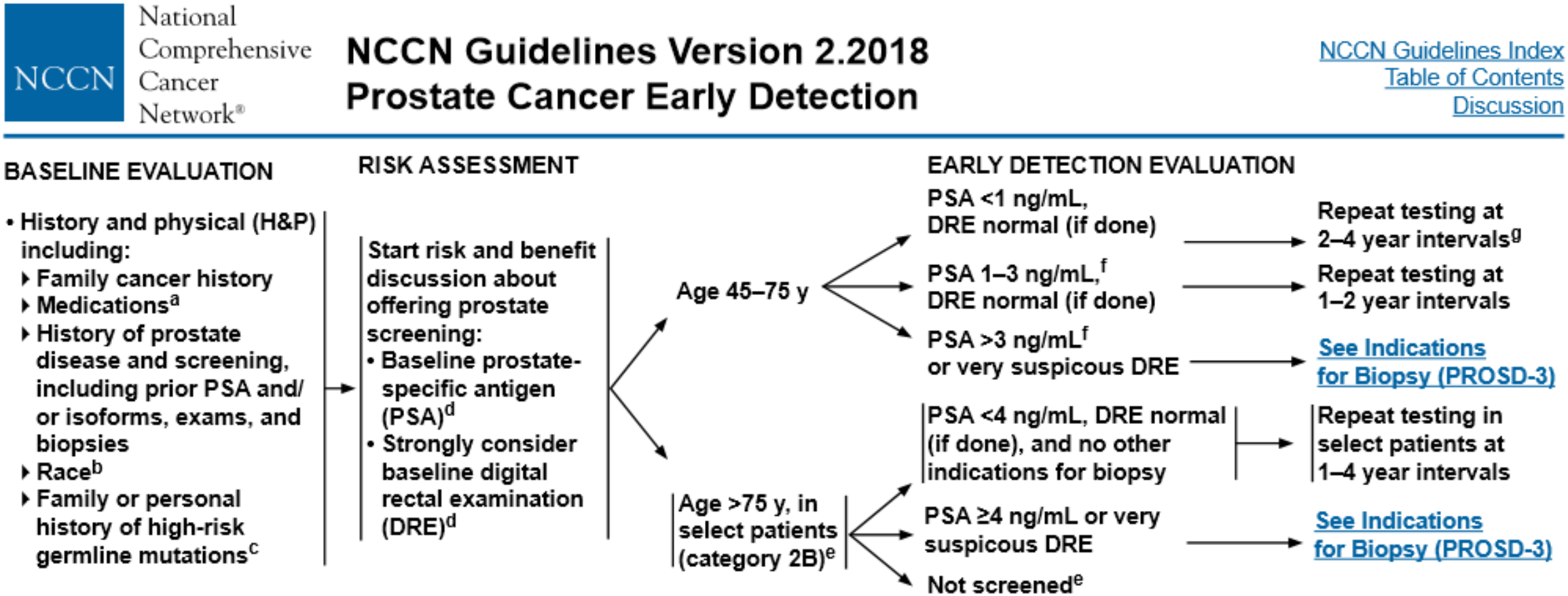
United Stated Preventative Task Force (USPSTF)

Individualized decision in men 55 to 69 years old

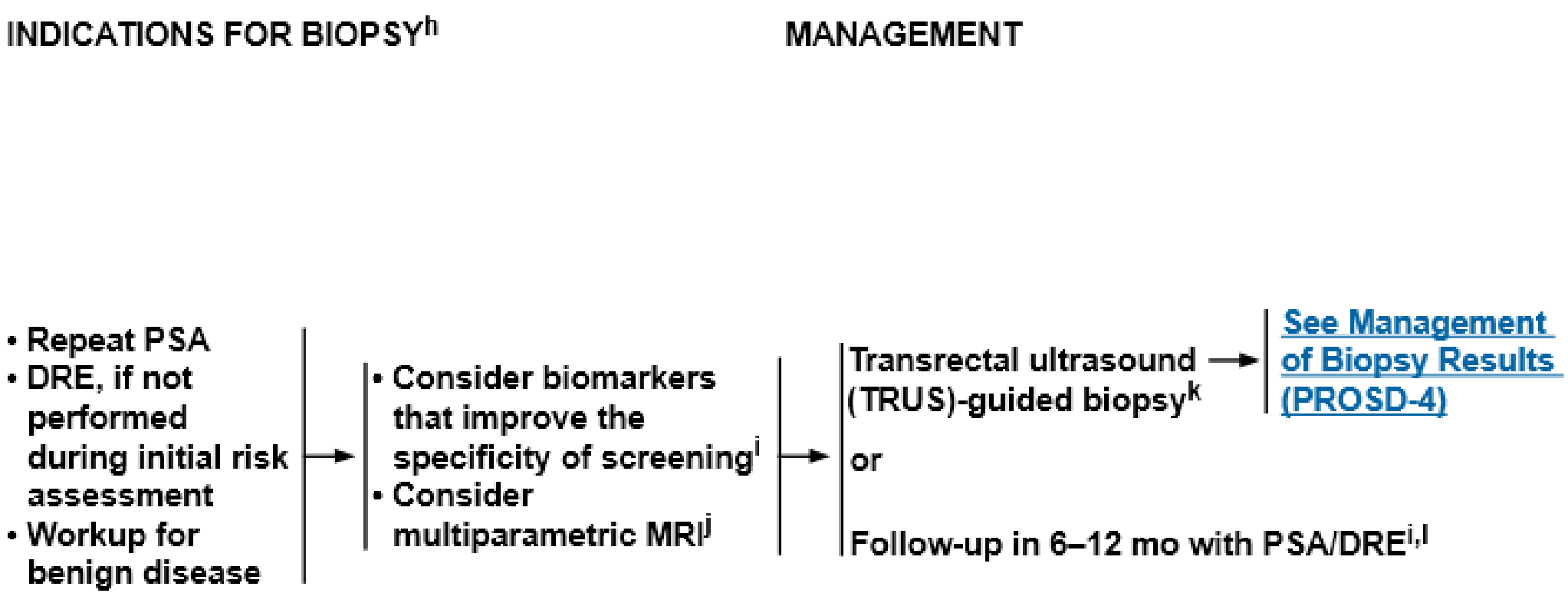
For men ages 55 to 69:

- Shared decision making, proceed based on patient preference
- Routine screening interval of 2 years or more determined by baseline PSA

NCCN Guidelines



NCCN Guidelines



NCCN Guidelines

likelihood of prostate cancer.

- Biomarkers that improve the specificity of detection are not, as yet, mandated as first-line screening tests in conjunction with serum PSA. However, there may be some patients who meet PSA standards for consideration of prostate biopsy, but for whom the patient and/or the physician wish to further define the probability of high-grade cancer. A percent-free PSA <10%, PHI >35, EPI score greater than 15.6, or 4Kscore (which provides an estimate of the probability of high-grade prostate cancer) are potentially informative in patients who have never undergone biopsy or after a negative biopsy; a PCA3 score >35 is potentially informative after a negative biopsy. The predictive value of the serum biomarkers discussed above has not been correlated with that of MRI. Therefore, it is not known how such tests could be applied in optimal combination.

NCCN Guidelines

[j] Emerging data suggest that, in men undergoing initial biopsy, targeting using MRI/ultrasound fusion may significantly increase the detection of clinically significant, higher-risk (Grade Group ≥3) disease while lowering the detection of lower-risk (Gleason Group 1 or lower-volume Grade Group 2) disease. Siddiqui M, Rais-Bahrami S, Turkbey B, et al. Comparison of MRI/ultrasound fusion–guided biopsy with ultrasound-guided biopsy for the diagnosis of prostate cancer. JAMA 2015;313:390-7. Ahmed H, El-Shater Bosaily A, Brown L, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet 2017;389:815-822. Kasivisvanathan V, Rannikko A, Borghi M, et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med 2018;378;1767-1777.

[k] For patients with abnormal DRE, biopsy or additional testing should be considered based on concern for cancer.

[l] Patients with a persistent and significant increase in PSA should be encouraged to undergo biopsy.

[m] A negative MRI does not exclude the possibility of cancer. Consider biomarkers and/or PSA density when deciding whether to avoid a biopsy in a man with a negative mpMRI result.

[n] MRI targeting can be considered in those centers with MRI availability and with experience and expertise in MRI interpretation and targeting.

Practical Considerations

Age to Initiate Screening

- Baseline PSA in 40s and early 50s can give risk stratification
- Higher baseline levels in this age group can predict death from prostate cancer
- Interval of testing can be determined by PSA level at early age

Age to Discontinue

- Continue beyond 75 years old in healthy individuals

Practical Considerations

Genetic Mutations

- HOX genes, BRCA1/BRCA2

Imaging

- Limited by Insurance and availability

PSA derivatives

- Age-specific Ranges – does this work?
- PSAV (Velocity)
- %free PSA
- PSAD (Density) – need an US, ? more use with increased MRI use

Practical Considerations

Factors affecting PSA levels

- Infection
- Recent instrumentation
- Ejaculation
- Trauma
- 5 ari use (finasteride, dutasteride)

<u>Empiric antibiotics DO NOT have a clinical benefit in elevated PSA workup of an asymptomatic man</u>

Risk of biopsy

- UTI, epididymitis, orchitis, prostatitis, sepsis
- Rectal bleeding, pain, hematuria, vasovagal episode, fever, hematospermia, dysuria

Practical Considerations

Biomarkers

- PCA3
  - Post DRE urine specimen,
  - Useful in determining need for repeat bx
- PHI (Prostate Health Index)
  - Combination of tPSA, fPSA, proPSA
  - Help determine need for initial biopsy or rebiopsy
- 4k Score
  - Combines tPSA, fPSA, human kallikrein 2 (hk2) and clinical data (age, DRE, prior bx)
  - Reports % likelihood of finding higher grade cancers (≥ Gleason 7)
- Confirm MDx
  - Risk stratify men for repeat prostate biopsy
  - Looks for hypermethylation of certain genes
- EPI (ExoDx Prostate IntelliScore)
  - Urine based, non DRE related
  - Discriminate high from low risk disease

QUESTIONS?

THANK YOU

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Urology birmingham CENTERS OF ALABAMA

UCA | WOMEN'S CENTER