Impact of the USPSTF Recommendations on PSA Screening

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Disclosures

- Clinical Investigator:
  - Medivation, Progenics, Blue Earth Diagnostics, Traxxsson
- Consultant/Advisor:
  - Augmenix, Tolmar Pharm., Janssen, Aytu
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  - National Cancer Institute
  - NIH-NIDDK
  - Prostate Cancer Foundation
  - Peter Michael Foundation
  - St. Louis Men's Group Against Cancer
  - Barnes-Jewish Hospital Foundation

CLINICAL GUIDELINE | Annals of Internal Medicine

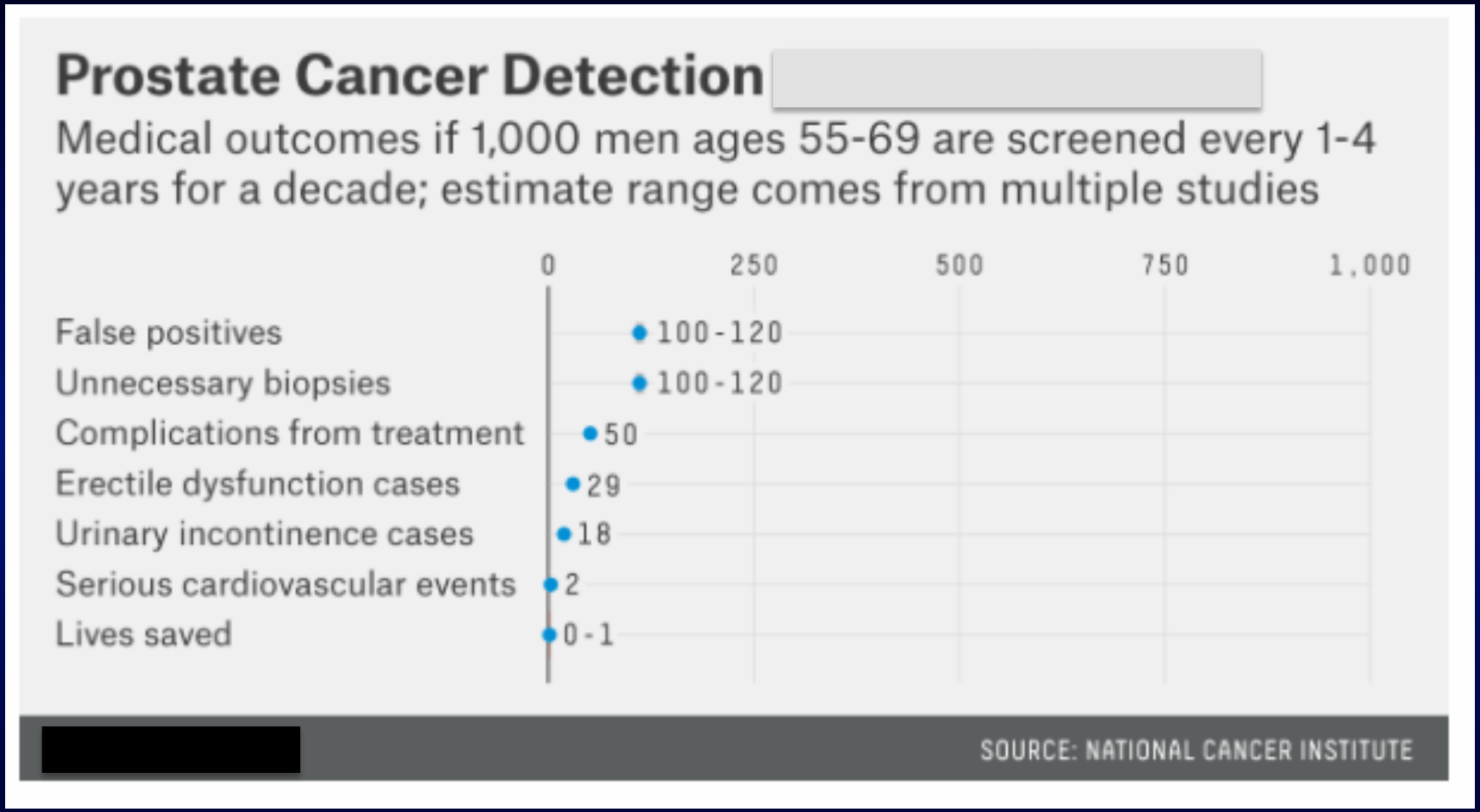
Screening for Prostate Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, PhD, on behalf of the U.S. Preventive Services Task Force*

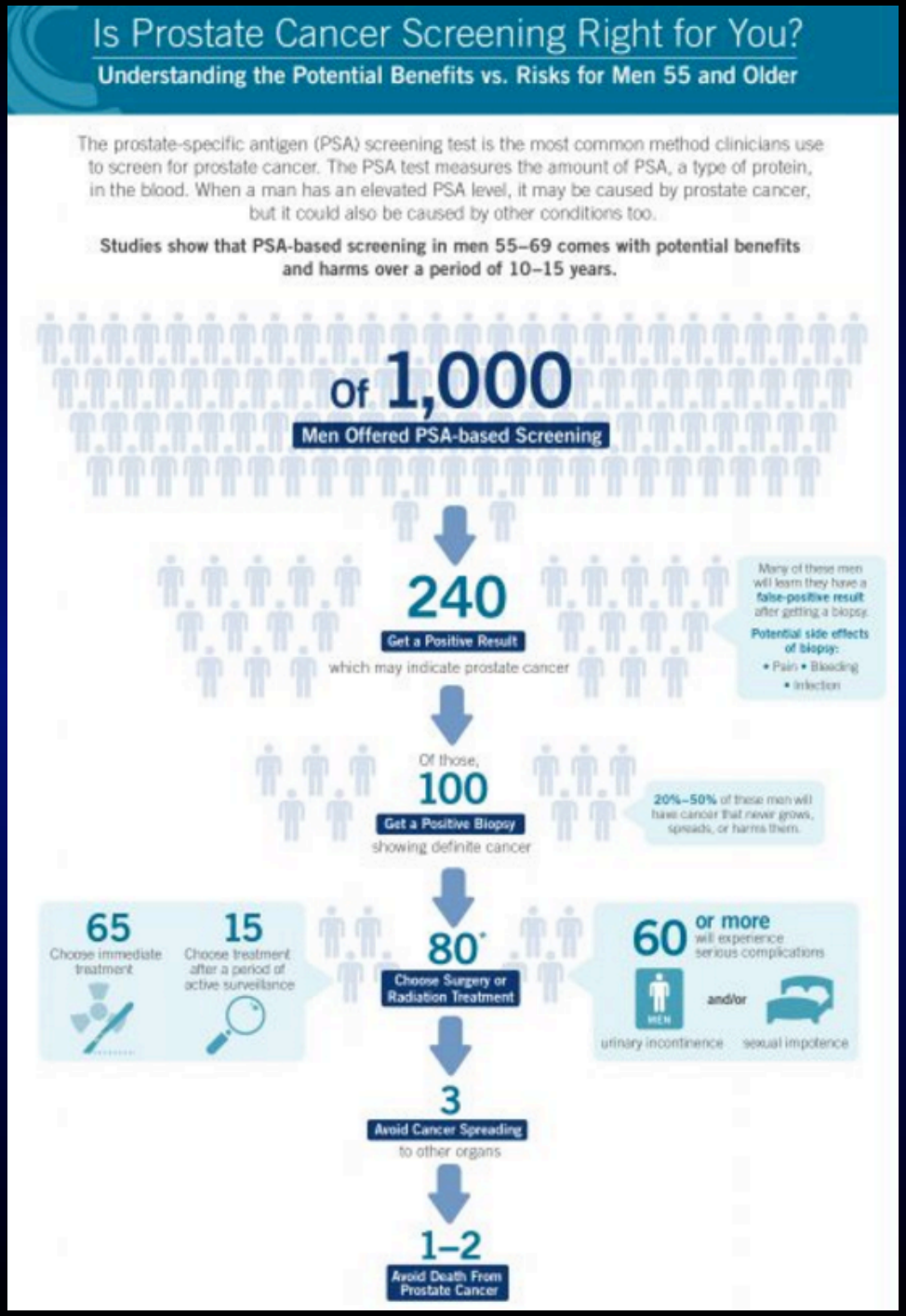
Population	Adult Males
Recommendation	Do not use prostate-specific antigen (PSA)–based screening for prostate cancer.
	Grade: D
Screening Tests	Contemporary recommendations for prostate cancer screening all incorporate the measurement of serum PSA levels; other methods of detection, such as digital rectal examination or ultrasonography, may be included. There is convincing evidence that PSA-based screening programs result in the detection of many cases of asymptomatic prostate cancer, and that a substantial percentage of men who have asymptomatic cancer detected by PSA screening have a tumor that either will not progress or will progress so slowly that it would have remained asymptomatic for the man's lifetime (i.e., PSA-based screening results in considerable overdiagnosis).

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.

2012 USPSTF Data Summary



2017 Draft USPSTF Data Summary



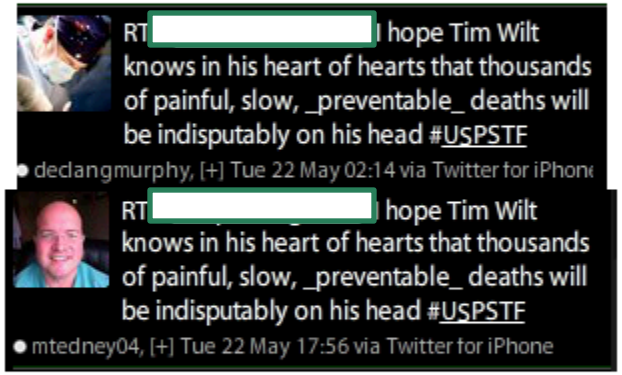
How Did the Medical Community React to the 2012 USPSTF Recommendation?

- Acute Reaction
- Medical Community at Large over the last few years

Reactive rhetoric by some was raging – none more so than this tweet from [redacted] urologist [redacted]

> "I hope (Task Force member) Tim Wilt knows in his heart of hearts that thousands of painful, slow, preventable deaths will be indisputably on his head."

(Addendum on May 23: [redacted] has now apparently removed that message from Twitter. The link – which worked when I first posted this yesterday – now is greeted by a "Sorry, that page doesn't exist" message. But what I entered in quotes above was a direct cut-and-paste of what appeared there earlier. In fact, below are screen shots of other Twitter users retweeting [redacted] original message.)



That's similar to the vitriol employed in the past by executives of Zero – The Project to End Prostate Cancer against Dr. Otis Brawley of the American Cancer Society. One Zero exec wrote:

> "Otis Brawley has killed more men by giving them an excuse to not be tested."

Yesterday Brawley's editorial supporting the USPSTF decision was published in the Annals of Internal Medicine. Excerpt:

> "…some will continue to forcefully advocate PSA-based screening because of a blind faith in early detection. We need to practice medicine on the basis of evidence and not on the basis of faith."

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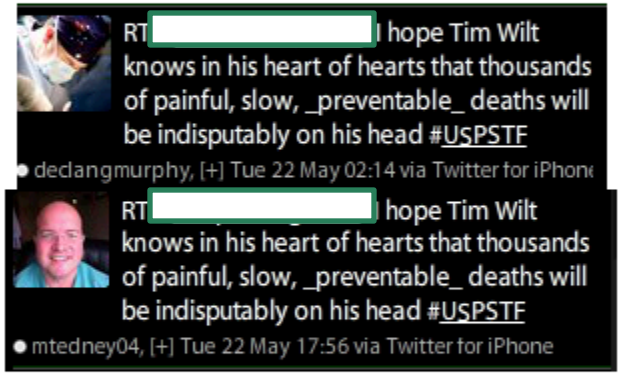

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> "...some will continue to forcefully advocate PSA-based screening because of a blind faith in early detection. We need to practice medicine on the basis of evidence and not on the basis of faith."

The comments left in response to a CBS News article on the issue are depressing, reflecting more of the same rhetorical reactions seen in response to the USPSTF mammography recommendations in November, 2009. But some are even uglier:

- "One can hope that all of those on this panel who made this decision, and Dr. Otis Brawley, all get cancer and find out too late."
- "Could someone please tell me how it is that Dr. Virginia Moyer – a woman and a pediatrician – is chair or a committee considering the issue of prostate cancer?"
- "This is a Democratic war on men. They obviously want us all to die from prostate cancer. And the Task Force Chair is a WOMAN and a professor of pediatrics. What do they think; we men are bunch of babies (well OK; maybe a little childish at times). But still shows the demoncrats (sic) want all men to die."
- "This is a prelude to the world of death panels, where ignorant bureaucrats make your health decisions for you. "

Susan Fitzgerald posted on May 23, 2012 at 6:42 pm

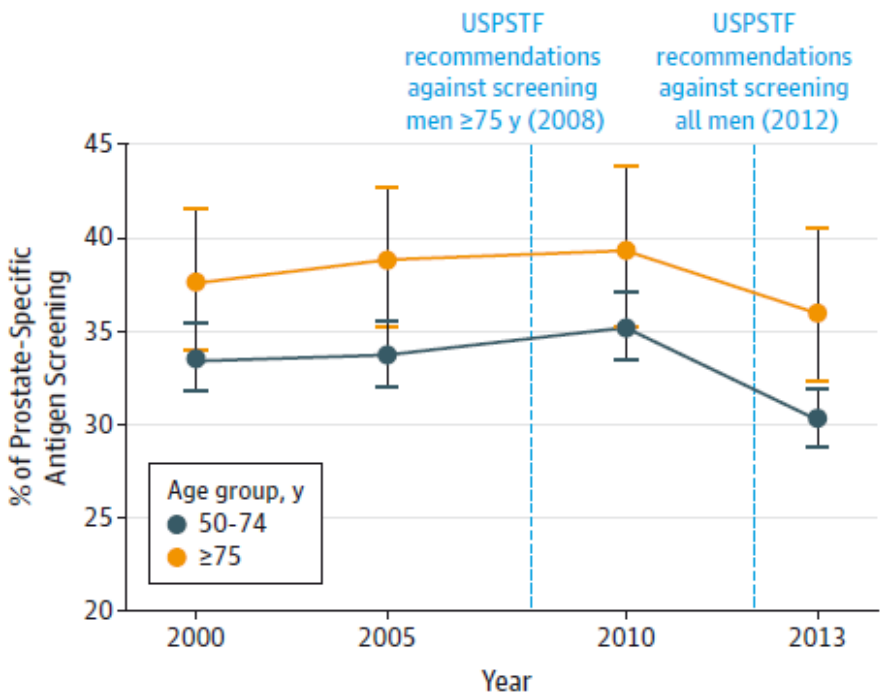
I, too, hope the backlash doesn't end up toasting the task force. This is important work.

A scientist (especially one who disagrees with you) is the FIRST one to tell you that the plural of "anecdotes" is NOT "evidence." But that seems to be the urologists' only come-back to the evidence examined by the task force.

I understand the gut reaction of a woman pediatrician heading this up, but this certainly falls into line with having disinterested parties examine the evidence. Though we all have men in our lives that we love – that's not the issue at hand.

Prostate-Specific Antigen Screening After 2012 US Preventive Services Task Force Recommendations

Figure. Prevalence of Prostate-Specific Antigen Screening From National Health Interview Survey (2000, 2005, 2010, and 2013)



No. surveyed				
With age ≥75 y	761	834	707	984
With age 50-74 y	3937	4277	3891	5366

Error bars indicate 95% confidence intervals.

Original Investigation

Prostate Cancer Incidence and PSA Testing Patterns in Relation to USPSTF Screening Recommendations

Ahmedin Jemal, DVM, PhD; Stacey A. Fedewa, MPH; Jiemin Ma, PhD; Rebecca Siegel, MPH; Chun Chieh Lin, PhD; Otis Brawley, MD; Elizabeth M. Ward, PhD

Table. Adjusted Screening Rate and Rate Ratios of PSA Testing in the Past Year for Screening Reasons Among Men 50 Years and Older[a]

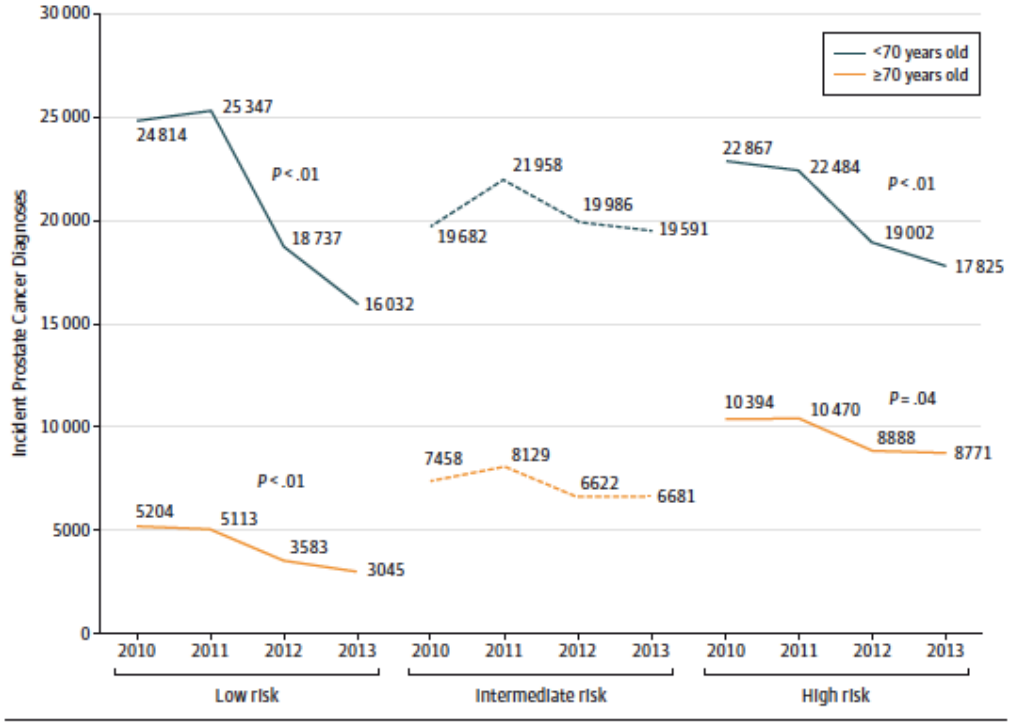
	National Health Interview Survey Year			
	2005	2008	2010	2013
No. of men				
≥50 y	4580	3476	4157	6172
50-74 y	3854	2900	3540	5221
≥75 y	726	576	617	951
No. of men with PSA test in past year				
≥50 y	1633	1345	1457	1771
50-74 y	1332	1079	1220	1464
≥75 y	301	266	237	307
Adjusted screening rate (99% CI)[b]				
≥50 y	36.9 (34.5-39.1)	40.6 (37.9-43.3)	37.8 (35.3-40.2)	30.8 (29.0-32.7)
50-74 y	35.8 (33.4-38.3)	39.1 (36.2-42.0)	36.8 (34.3-39.4)	29.9 (28.0-32.0)
≥75 y	42.6 (37.6-47.9)	50.1 (43.7-56.4)	43.1 (37.1-49.2)	36.3 (31.1-41.9)
Adjusted SRR (99% CI)[c]				
≥50 y		1.10 (1.01-1.21)	0.93 (0.84-1.02)	0.82 (0.75-0.89)
50-74 y		1.09 (0.99-1.21)	0.94 (0.85-1.05)	0.81 (0.74-0.89)
≥75 y		1.18 (0.99-1.40)	0.86 (0.71-1.04)	0.84 (0.68-1.05)

JAMA. 2015;314(19):2054-2061. doi:10.1001/jama.2015.14905

RESEARCH LETTER

Current Status of Prostate Cancer Diagnosis and Management in the United States

Figure 1. Incidence of Clinically Localized Prostate Cancer at US National Cancer Data Base (NCDB) Facilities,[a] 2010-2013, Stratified by Age and Risk Group



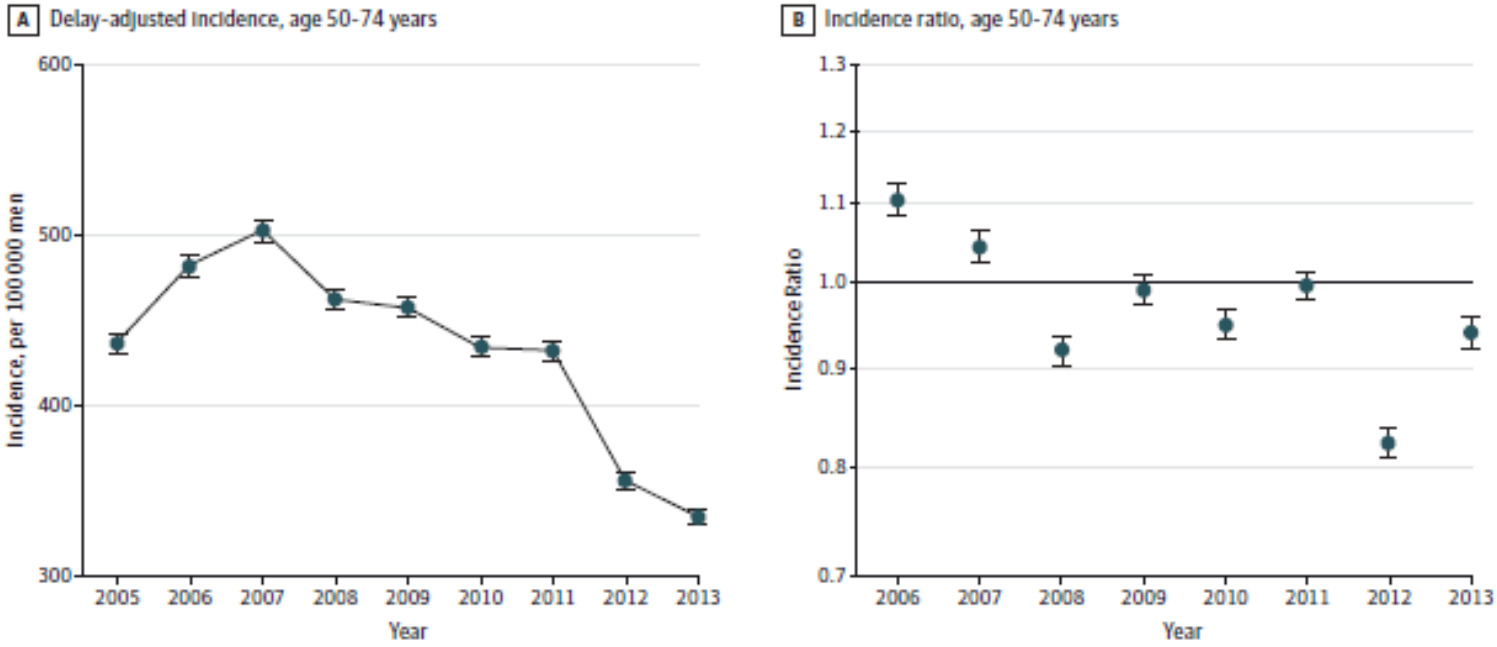
JAMA Oncology Published online June 23, 2016

Published Online: June 23, 2016. doi:10.1001/jamaoncol.2016.1785.

RESEARCH LETTER

Prostate Cancer Incidence Rates 2 Years After the US Preventive Services Task Force Recommendations Against Screening

Figure 1. Delay-Adjusted Incidence (per 100 000 Men) and Incidence Ratio for Localized/Regional Prostate Cancer by Age Group, Surveillance, Epidemiology, and End Results 18, 2005-2013



JAMA Oncology Published online August 18, 2016

JAMA Surgery | Original Investigation

National Trends in Prostate Biopsy and Radical Prostatectomy Volumes Following the United States Preventative Services Task Force Guidelines Against Prostate-Specific Antigen Screening

Joshua A. Halpern, MD, MS; Jonathan E. Shoag, MD; Amanda S. Artis, MS, MPH; Karla V. Ballman, PhD; Art Sedrakyan, MD, PhD; Dawn L. Hershman, MD, MS; Jason D. Wright, MD; Ya Chen Tina Shih, PHD; Jim C. Hu, MD, MPH

Table 1. Median Biopsy Volume of Certifying Urologists

Variable	Median (IQR) Total	2009-2012	2013-2016	*P* Value
Biopsies per urologist, No.	25 (14-40)	29 (16-44)	21 (12-34)	<.001
Biopsies by sex, No.				
Male	26 (16-41)	30 (18-45)	22 (13-36)	.001
Female	11 (5-21)	11 (5-23)	10 (4-19)	
Biopsies by specialty, No.				
General	27 (16-41)	31 (19-46)	22 (13-35)	
Oncology	21 (11-39)	24 (11-40)	20 (11-39)	<.001
Urolithiasis	21 (13-39)	29 (15-42)	17 (11-31)	
Other/unknown	17 (7-29)	17 (9-31)	16 (7-26)	

JAMA Surg. doi:10.1001/jamasurg.2016.3987
Published online November 2, 2016.

JAMA Surgery | Original Investigation

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Following the USPSTF recommendation, the total number of annual biopsies decreased by 12.7%. The greatest decrease in biopsy volume was seen in those biopsies performed for an indication of abnormal PSA (26.7%), whereas biopsy volume for an indication of cancer surveillance increased by 28.8% during the study period (597 vs 769; $P<.001$).

JAMA Surg. doi:10.1001/jamasurg.2016.3987
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. Male urologist sex was associated with higher biopsy volume (PE [SE], 1.00 [0.07]; $P < .001$), whereas oncologic subspecialty was associated with lower biopsy volume (PE [SE], −0.15 [0.07];

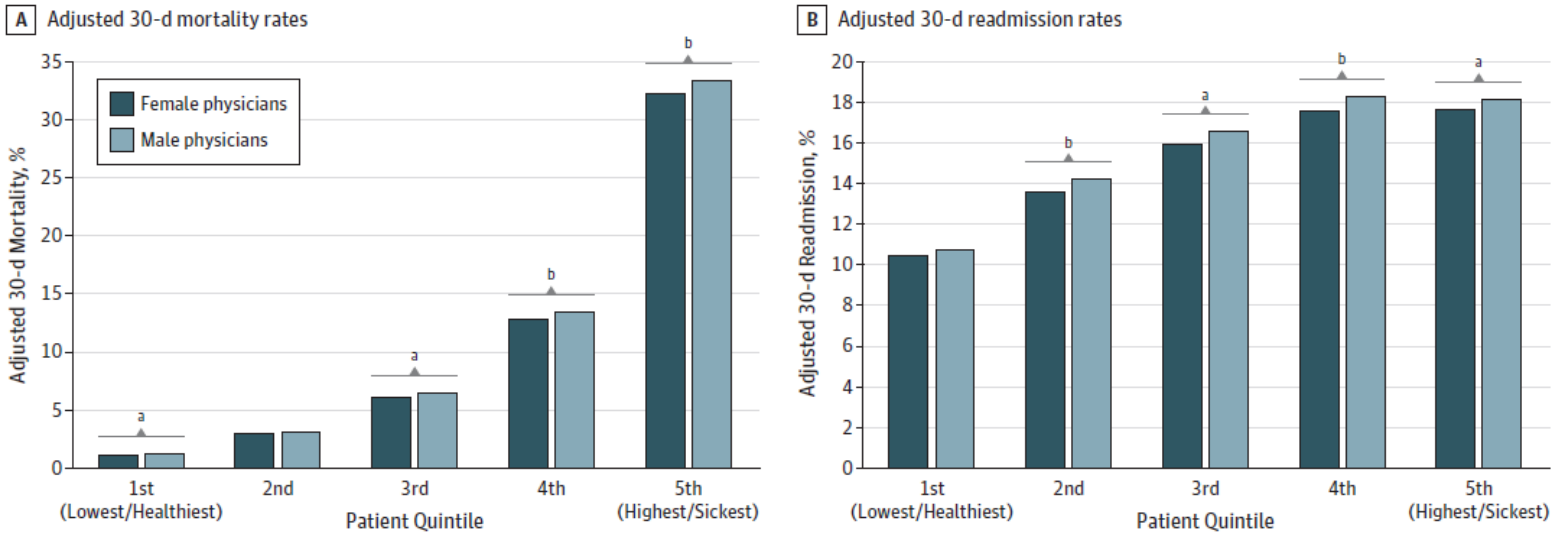
JAMA Surg. doi:10.1001/jamasurg.2016.3987
Published online November 2, 2016.

JAMA Internal Medicine | Original Investigation

Comparison of Hospital Mortality and Readmission Rates for Medicare Patients Treated by Male vs Female Physicians

Yusuke Tsugawa, MD, MPH, PhD; Anupam B. Jena, MD, PhD; Jose F. Figueroa, MD, MPH; E. John Orav, PhD; Daniel M. Blumenthal, MD, MBA; Ashish K. Jha, MD, MPH

Figure. Association Between Physician Sex and Patient Outcomes by Expected Mortality Rates



A, Adjusted 30-day mortality rates. B, Adjusted 30-day readmission rates. Risk-adjusted mortality rates were calculated with additional adjustment for physician characteristics and with hospital fixed effects (model 3). Standard errors were clustered at the physician level.

[a]$P < .05$.

[b]$P < .001$.

JAMA Intern Med. doi:10.1001/jamainternmed.2016.7875
Published online December 19, 2016.

JAMA Surgery | Original Investigation

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Table 3. Median RP Volume of Certifying Urologists

Variable	Median (IQR) Total	2009-2012	2013-2016	*P* Value
RP per urologist, No.	6 (3-13)	7 (3-15)	6 (2-12)	<.001
RP by sex, No.				
Male	6.5 (3-14)	7 (3-15)	6 (3-12)	<.001
Female	3 (1-7)	3 (1-8)	4 (2-7)	
RP by specialty, No.				
General	6 (2-12)	6 (3-14)	5 (2-10)	
Oncology	12 (6-23)	14 (7-30)	11 (6-22)	<.001
Urolithiasis	7 (2-10)	8 (3-16)	5 (2-10)	
Other/unknown	5 (2-14)	5 (2-15)	6 (2-13)	

JAMA Surg. doi:10.1001/jamasurg.2016.3987
Published online November 2, 2016.

RESEARCH LETTER

Recent Patterns of Prostate-Specific Antigen Testing for Prostate Cancer Screening in the United States

Model 2[b]: Age and Year Interaction	
2013 vs 2010 among men	
50-64 y	0.80 (0.71-0.90)
65-74 y	0.89 (0.71-1.02)
>75 y	0.82 (0.68-0.99)
2015 vs 2013 among men	
50-64 y	1.06 (0.94-1.19)
65-74 y	0.92 (0.81-1.04)
>75 y	0.95 (0.79-1.15)

Stacey A. Fedewa, PhD
Elizabeth M. Ward, PhD
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JAMA Internal Medicine Published online April 24, 2017

RESEARCH LETTER

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JAMA Internal Medicine Published online April 24, 2017

Original Investigation

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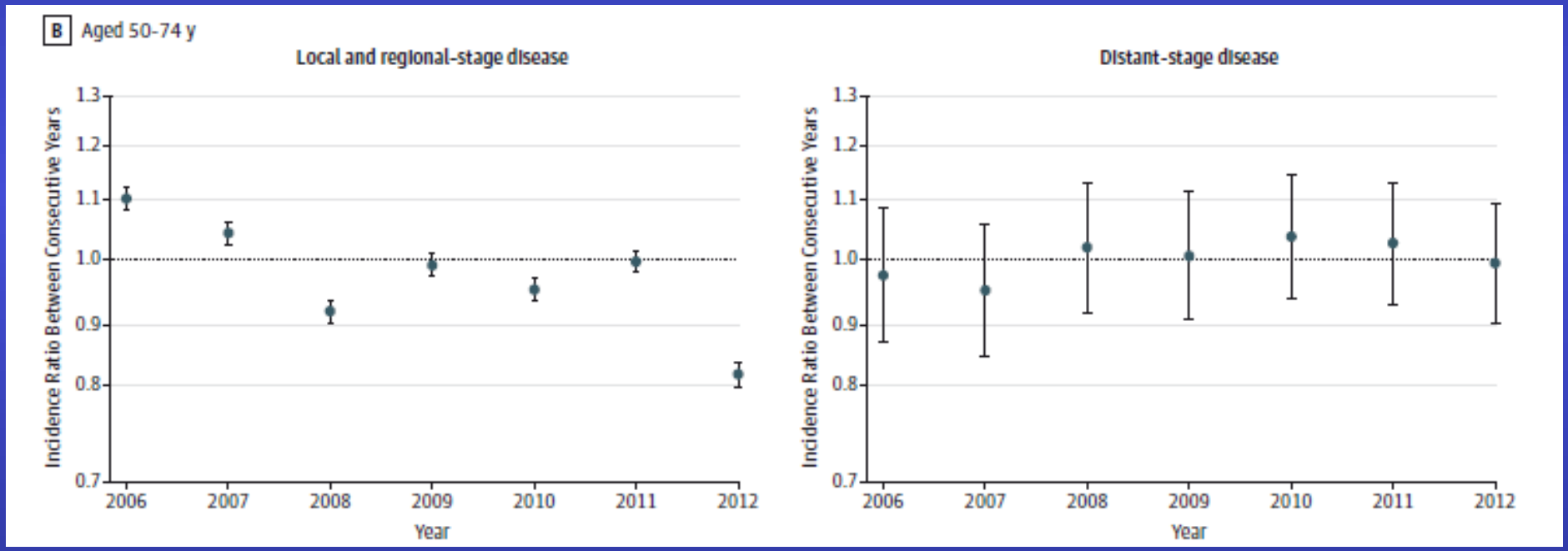

JAMA. 2015;314(19):2054-2061. doi:10.1001/jama.2015.14905

RESEARCH LETTER

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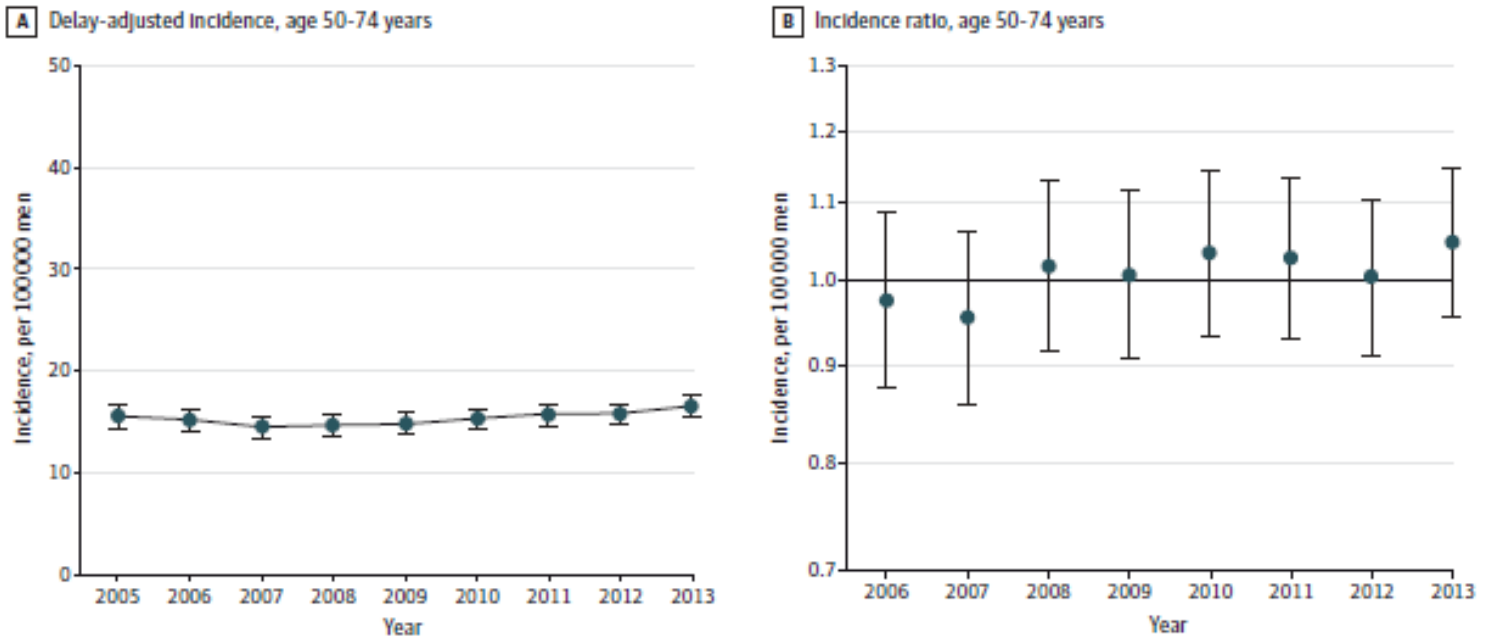
Figure 2. Delay-Adjusted Incidence (per 100 000 Men) and Incidence Ratio for Distant Prostate Cancer by Age Group, Surveillance, Epidemiology, and End Results 18, 2005-2013

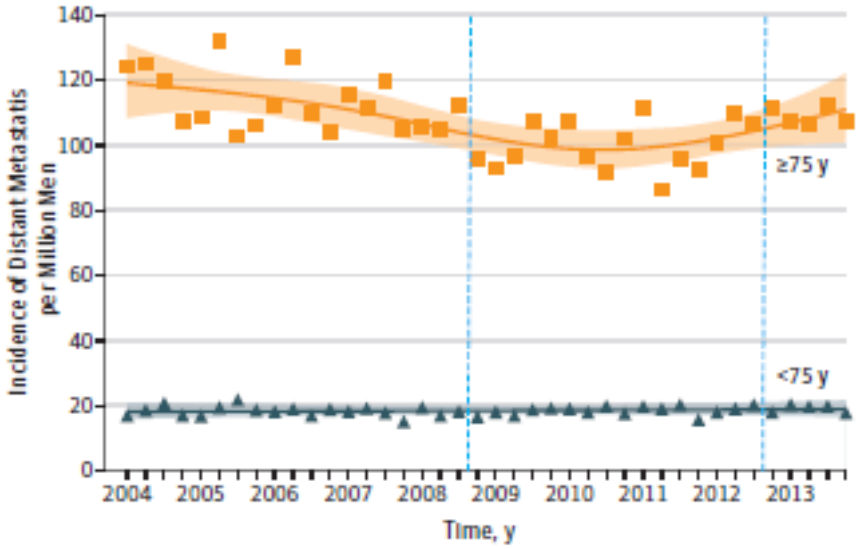


JAMA Oncology Published online August 18, 2016

RESEARCH LETTER

Increase in Prostate Cancer Distant Metastases at Diagnosis in the United States

Figure. Standardized Incidence of Prostate Cancer Distant Metastasis at Diagnosis by Quarter Between 2004 and 2013 Among Men Aged 75 Years and Older and Younger Than 75 Years



Dashed vertical blue lines demonstrate the release of the 2008 and 2012 screening recommendations.

JAMA Oncology Published online December 29, 2016

Editor's Note

Determining Penetration of Prostate-Specific Antigen Screening Recommendations

to 2013. It is possible that these seemingly contradictory results are simply a statistical random variation of incidence that can change over time depending on the frequency of measurement as well as the variation in staging definition. In the case of these 2 articles, while both analyze SEER data, Summary Staging (from the *SEER Summary Staging Manual - 2000: Codes and Coding Instructions*) was used by Jemal et al, while the current article by Hu et al used Collaborative Staging (from the SEER Training Modules; https://training.seer.cancer.gov

Charles R. Thomas Jr, MD
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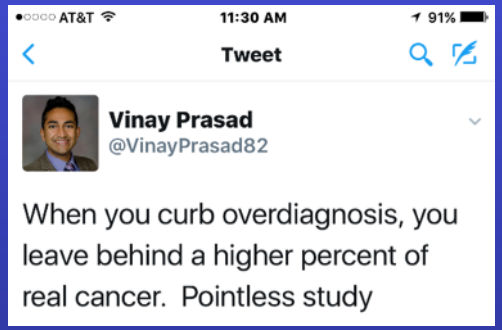
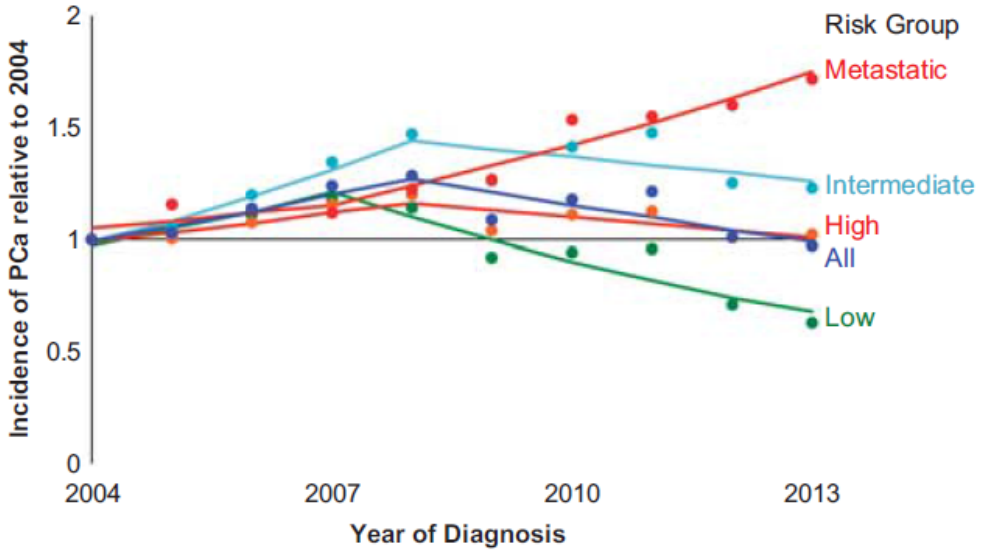


Charles R. Thomas Jr, MD
Yu Shyr, PhD

ORIGINAL ARTICLE

Increasing incidence of metastatic prostate cancer in the United States (2004–2013)

AB Weiner[1], RS Matulewicz[1], SE Eggener[2] and EM Schaeffer[1]



Risk Group	Trend 1			Trend 2		
	Interval	APC	p	Interval	APC	p
Low	2004-2007	7.5	0.3	2007-2013	-9.3	<0.05
Intermediate	2004-2008	10	<0.05	2008-2013	-2.7	0.3
High	2004-2008	4.1	0.1	2008-2013	-2.7	0.1
Metastatic	2004-2007	3.3	0.4	2007-2013	7.1	<0.05
All	2004-2008	6.3	0.1	2007-2013	-4.8	0.1

Prostate Cancer and Prostatic Diseases (2016) **19,** 395–397;

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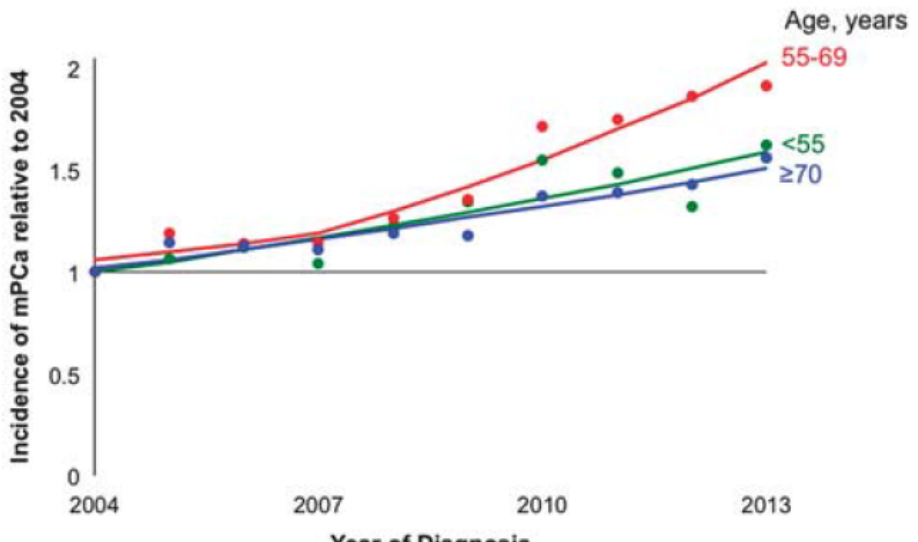


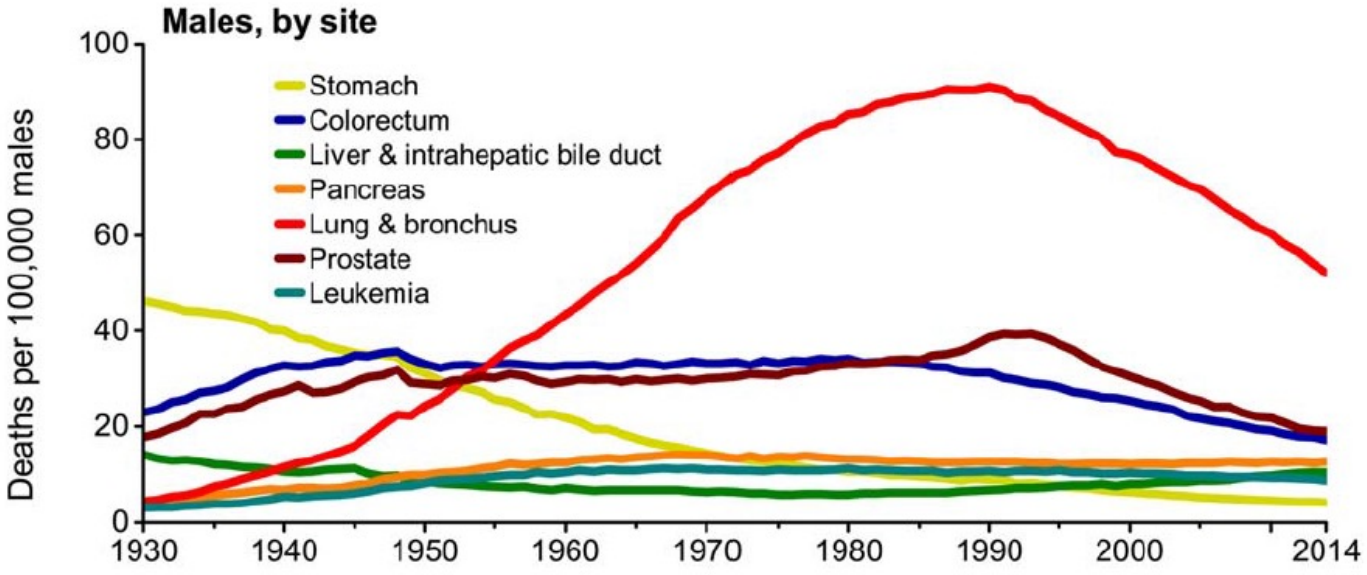
Age, years	Trend 1			Trend 2		
	Interval	APC	p	Interval	APC	p
<55	2004-2013	5.3	<0.05			
55-69	2004-2007	4	0.5	2007-2013	9.3	<0.05
≥70	2004-2013	4.5	<0.05			

Figure 2. Annual incidence of metastatic prostate cancer based on age relative to 2004 in the United States. Joinpoint regressions were

Prostate Cancer and Prostatic Diseases (2016) **19,** 395–397;

Cancer Statistics, 2017

Rebecca L. Siegel, MPH[1]; Kimberly D. Miller, MPH[2]; Ahmedin Jemal, DVM, PhD[3]



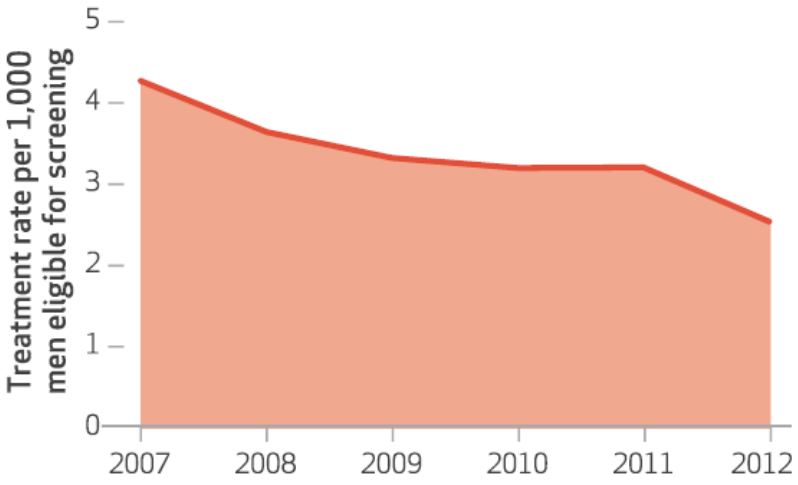
doi: 10.3322/caac.21387.

By Tudor Borza, Samuel R. Kaufman, Vahakn B. Shahinian, Phyllis Yan, David C. Miller, Ted A. Skolarus, and Brent K. Hollenbeck

Sharp Decline In Prostate Cancer Treatment Among Men In The General Population, But Not Among Di[illegible]

EXHIBIT 2

Trend in the rate of curative prostate cancer treatment for all men eligible for screening



SOURCE Authors' analysis of Medicare data for 2007–12. **NOTE** The decline of 42 percent in the rate of treatment was significant ($p < 0.001$).

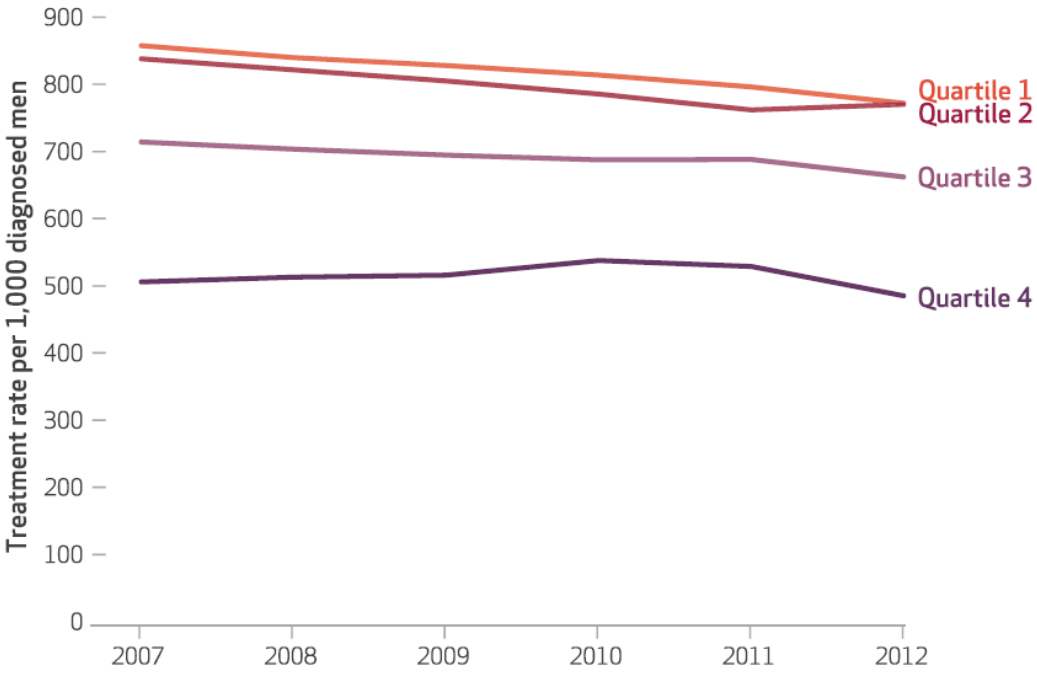
DOI: 10.1377/hlthaff.2016.0739
HEALTH AFFAIRS 36,
NO. 1 (2017): 108–115

By Tudor Borza, Samuel R. Kaufman, Vahakn B. Shahinian, Phyllis Yan, David C. Miller, Ted A. Skolarus, and Brent K. Hollenbeck

Sharp Decline In Prostate Cancer Treatment Among Men In The General Population, But Not Among Diagnosed Men

EXHIBIT 4

Trends in the rate of curative prostate cancer treatment for men diagnosed with prostate cancer, stratified by quartiles of 10-year risk of noncancer mortality



DOI: 10.1377/hlthaff.2016.0739
HEALTH AFFAIRS 36,
NO. 1 (2017): 108–115

Changes since USPSTF

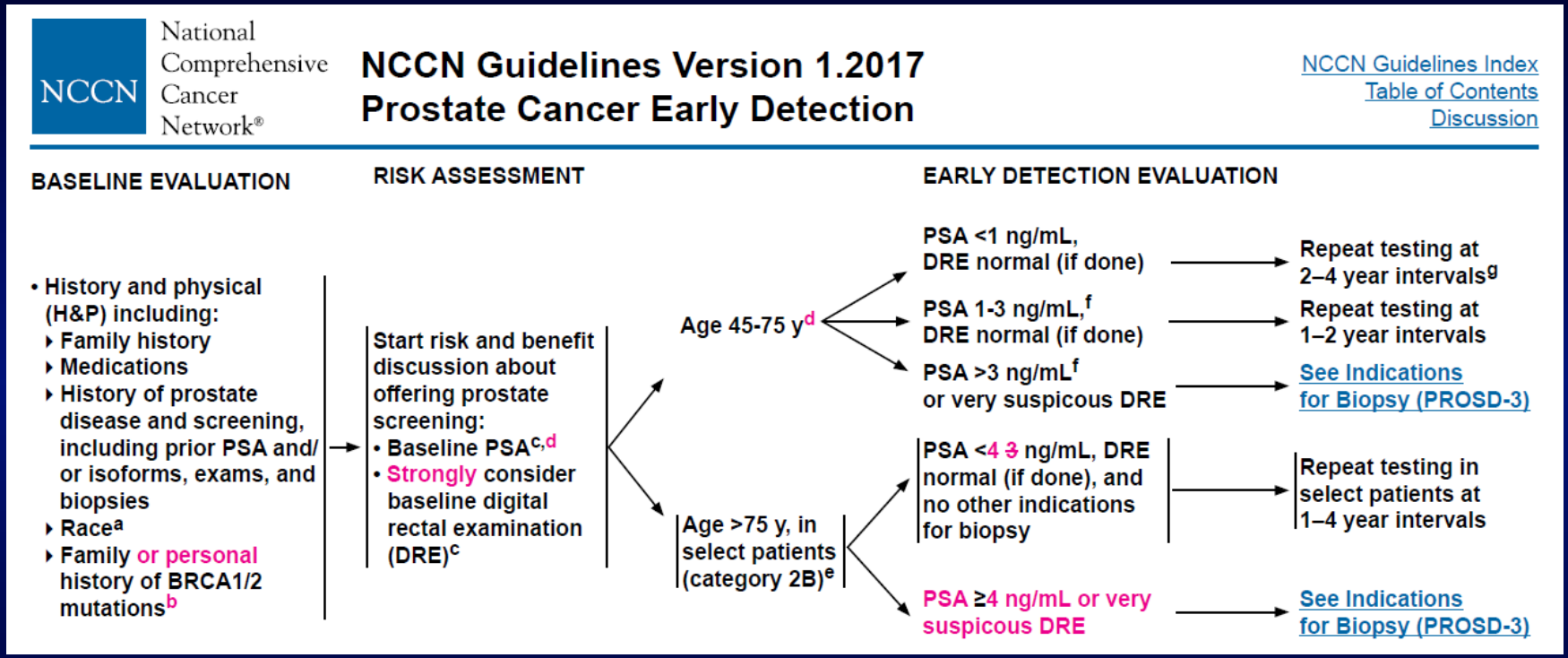
- Reduced PSA testing that may have stabilized
- Likely lower rates of biopsy, cancer and Rad Px.
- Possible increase in distant disease

My Hope: “Make PSA Great Again”

My Hope: "Make PSA Great Again"

- Test the men who need to be tested
- Consider reflex tests if PSA abnormal
- Do a "quality" biopsy
- Avoid overtreatment

Test the Men Who need to Be Tested



Role of Genetic Testing for Inherited Prostate Cancer Risk: Philadelphia Prostate Cancer Consensus Conference 2017

Giri VN[a], Knudsen KE[a], Kelly WK[a], Abida W[b], Andriole GL[c], Bangma C[d], Benson M[e], Blanco A[f], Burnett A[g], Catalona W[h], Cooney KA[i], Cooperberg M[f], Crawford D[j], Den R[a], Dicker A[a], Eggener S[k], Fleshner N[l], Freedman ML[m], Hamdy F[n], Hoffman-Censits J[a], Hurwitz MD[a], Hyatt C[a], Isaacs W[g], Kane C[o], Kantoff P[b], Karnes RJ[p], Karsh L[q], Klein E[r], Lin D[s], Loughlin KR[m], Lu-Yao G[a], Malkowicz SB[t], Mann M[a], Mark JR[a], McCue P[a], Miner M[u], Morgan T[v], Moul JW[w], Myers R[a], Nielsen S[k], Obeid E[x], Pavlovich C[g], Peiper S[a], Penson D[y], Petrylak D[z], Pettaway C[aa], Pilarski R[bb], Pinto P[cc], Poage W[dd], Raj G[ee], Rebbeck TR[m], Robson M[b] Rosenberg M[ff], Sandler H[gg], Sartor O[hh], Schaeffer E[h], Schwartz G[ii], Shahin M[jj], Shore N[kk], Shuch B[z], Soule H[ll], Tomlins S[v], Trabulsi EJ[a], Uzzo R[x], Vander Griend DJ[k], Walsh PC[g], Weil C[cc], Wender R[mm], and Gomella LG[a].

Table 1: Current Genes on Prostate Cancer Multigene Panels, Associated Cancer Risks, and Guidelines Available

Gene	Syndrome	Associated Cancer Risks*								Availability of Cancer Screening and/or risk reduction guidelines**	
		PR	BR	OV	CO	EN	ME	PA	GA	OC	PR	Non-PR Cancers
BRCA1	HBOC	A	A	A				B			X[#]	X
BRCA2	HBOC	A	A	A			C	A			X[#]	X
DNA Mismatch repair genes	LS	B		A	A	A		A	A	A		X
HOXB13	HPC	A										
TP53	LFS		A		C		C	C		A		X
ATM		B	A					C				X
CHEK2		C	A		A					C		X
PALB2			A					A				X
NBN		C	B									X
RAD51D				A								X

Note: Table adapted from Giri et al. *JCO Precision Oncology* 2017 (in press) to include consensus panel review.

Abbreviations: **HBOC**-Hereditary Breast and Ovarian Cancer; **LS**-Lynch syndrome; **LFS**-Li-Fraumeni syndrome; **PR**-prostate cancer; **BR**-breast cancer; **OV**-ovarian cancer; **CO**-colon cancer; **EN**-endometrial cancer; **ME**-melanoma; **PA**-pancreatic cancer; **GA**-gastric cancer; **OC**-other cancer

Consider "Reflex" Tests if PSA is Abnormal

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2017
Prostate Cancer Early Detection

NCCN Guidelines Index
Table of Contents
Discussion

INDICATIONS FOR BIOPSY[h]

MANAGEMENT

- Repeat PSA
- DRE
- Workup for benign disease

→

- Consider percent free PSA, 4Kscore, or PHI[i]
- Consider multiparametric MRI

→

TRUS-guided biopsy[j,k] → See Management of Biopsy Results (PROSD-4)

or

Follow up in 6–12 mo with PSA/DRE[i,l]

TRUS-GUIDED BIOPSY
Initial and Repeat
Extended-pattern biopsy (12 cores)

- Number of cores:
  - Sextant (6),
  - Lateral peripheral zone (6), and
  - Lesion-directed at palpable nodule or suspicious image
- Anteriorly directed biopsy is not supported in routine biopsy. However, the addition of a transition zone biopsy to an extended biopsy protocol may be considered in a repeat biopsy if PSA is persistently elevated.
- Multiparametric MRI (MP MRI) followed by lesion targeting may maximize the detection of higher risk disease and limit the detection of lower risk disease.[i]
- Local anesthesia can decrease pain/discomfort associated with prostate biopsy and should be offered to all patients.

[h]The level of PSA correlates with the risk of prostate cancer. The Prostate Cancer Prevention Trial (PCPT) demonstrated that 15% of men with a PSA level of ≤4.0 ng/

Predicting High-Grade Cancer at Ten-Core Prostate Biopsy Using Four Kallikrein Markers Measured in Blood in the ProtecT Study

Richard J. Bryant*, Daniel D. Sjoberg*, Andrew J. Vickers, Mary C. Robinson, Rajeev Kumar, Luke Marsden, Michael Davis, Peter T. Scardino, Jenny Donovan, David E. Neal, Hans Lilja, Freddie C. Hamdy

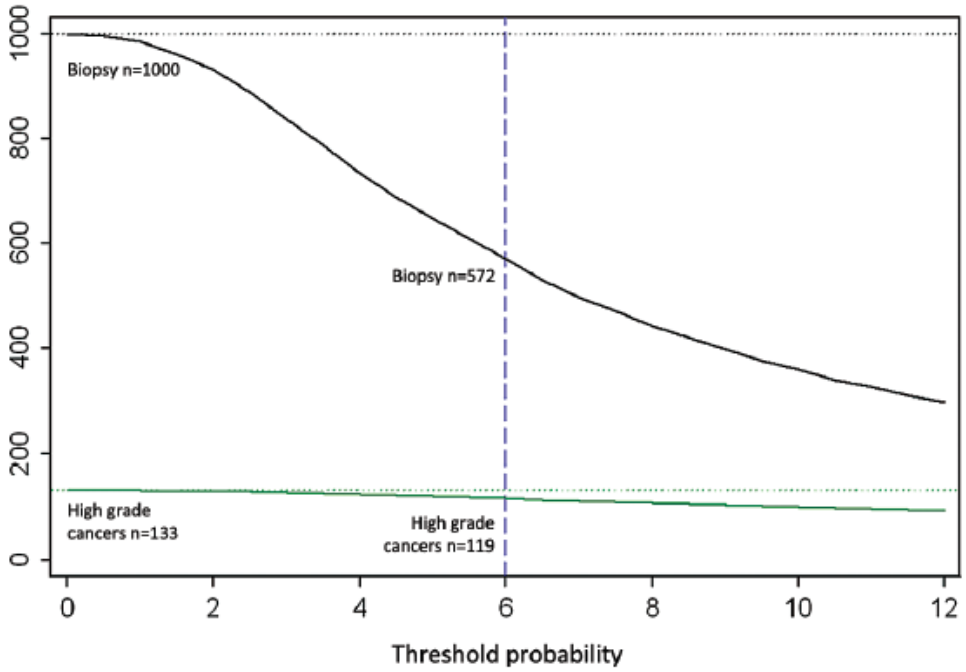
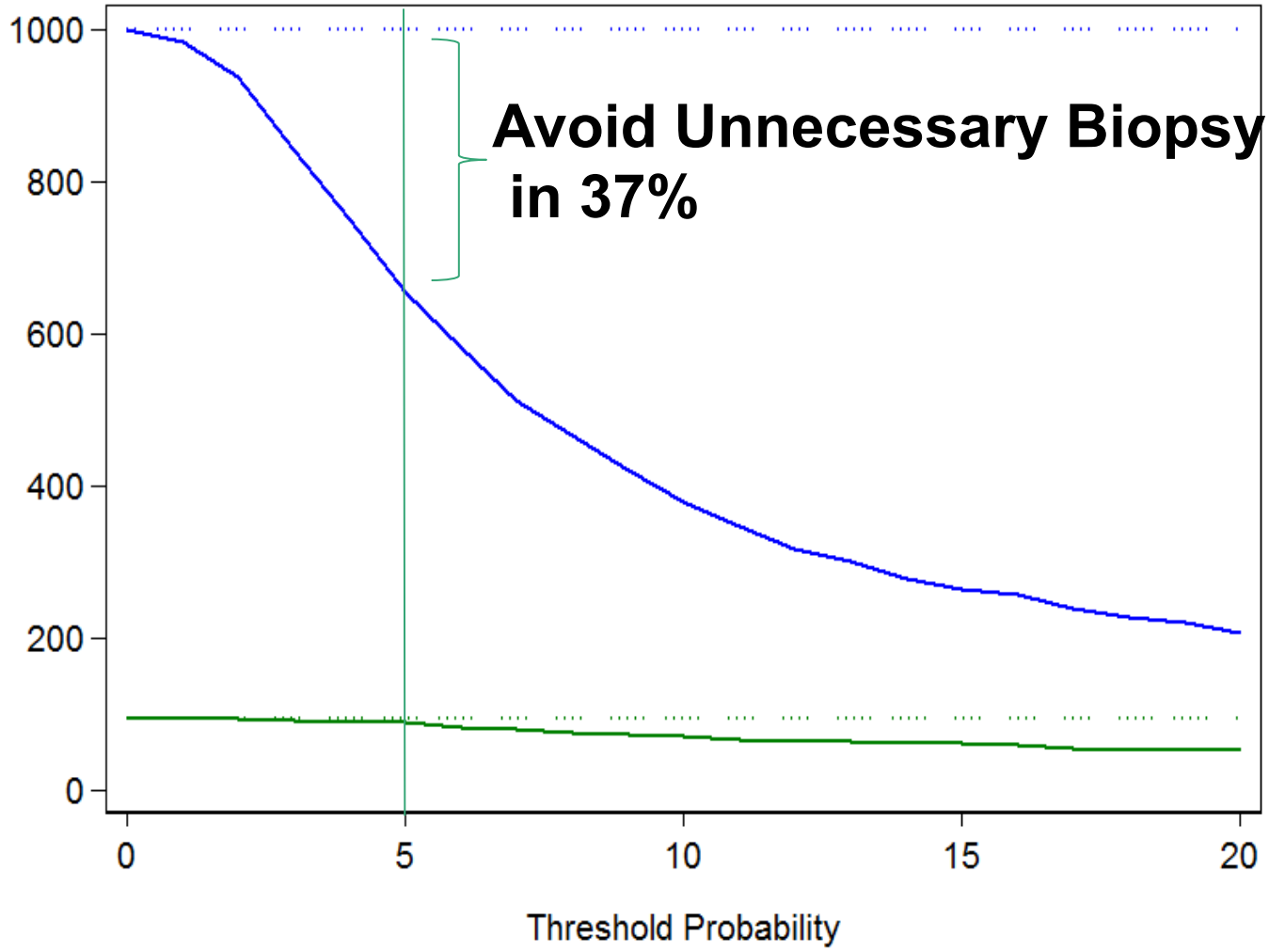


Figure 1. Clinical implications of various biopsy strategies using a model developed to predict the risk of Gleason score 7 or higher (high-grade) prostate cancer based on four kallikrein markers measured in anticoagulated plasma collected from 4765 biopsied ProtecT participants. The graph illustrates the results of differing biopsy strategies per 1000 biopsied ProtecT-participants, with the x-axis denoting the risk of high-grade cancer and the y-axis indicating the number of men biopsied (**black line**) or detected with evidence of high-grade cancer (**green line**) using different biopsy strategies. The **dotted vertical blue line** illustrates a tentative cutpoint (6% risk of high-grade cancer) at which only 572 of 1000 of the men would be biopsied, which would result in the detection of 119 of 133 high-grade cancers.

JNCI J Natl Cancer Inst (2015) 107(7): djv095

doi:10.1093/jnci/djv095

Biopsies Avoided using 4K in PLCO



Kim, Andriole, Crawford et al: J Urol 197:1041, 2017

Do a “Quality” Biopsy

Random Office Biopsy Likely not the Best Biopsy

Comparison of MR/Ultrasound Fusion–Guided Biopsy With Ultrasound-Guided Biopsy for the Diagnosis of Prostate Cancer

JAMA. 2015;313(4):390-397. doi:10.1001/jama.2014.17942

Figure 3. Comparison of Pathology From Standard Extended-Sextant Biopsy and Targeted MR/Ultrasound Fusion Biopsy for Prostate Cancer

Targeted MR/Ultrasound Fusion Biopsy Results		No Cancer	Standard Extended-Sextant Biopsy Results				Totals
			Low-Risk Cancer		Intermediate-Risk Cancer	High-Risk Cancer	
			Gleason 6	Gleason 3+4 Low Volume[a]	Gleason 3+4 High Volume[b]	Gleason ≥4+3	
	No cancer	439	74	12	12	5	542
Low-Risk Cancer	Gleason 6	38	84	12	10	3	147
	Gleason 3+4 Low volume[c]	17	14	9	19	7	66
Intermediate-Risk Cancer	Gleason 3+4 High volume[d]	14	21	7	29	4	75
High-Risk Cancer	Gleason ≥4+3	26	13	12	19	103	173
	Totals	534	206	52	89	122	1003

Presence of Magnetic Resonance Imaging Suspicious Lesion Predicts Gleason 7 or Greater Prostate Cancer in Biopsy-Naive Patients

John K. Weaver, Eric H. Kim, Joel M. Vetter, Kathryn J. Fowler, Cary L. Siegel, and Gerald L. Andriole

Table 3. Multivariate logistic regression analysis for predictors of Gleason 7 + biopsy result in biopsy-naive patients

Variable	OR	*P* Value
Age (continuous variable)	1.12	.18
Family history of PCa	1.35	.78
Prior 5-ARI use	0.22	.27
Abnormal DRE	15.1	.12
PSA > 10 ng/mL	7.25	.41
PSA density > 0.15 ng/mL^2	1.88	.60
Presence of MSR	40.2	.01

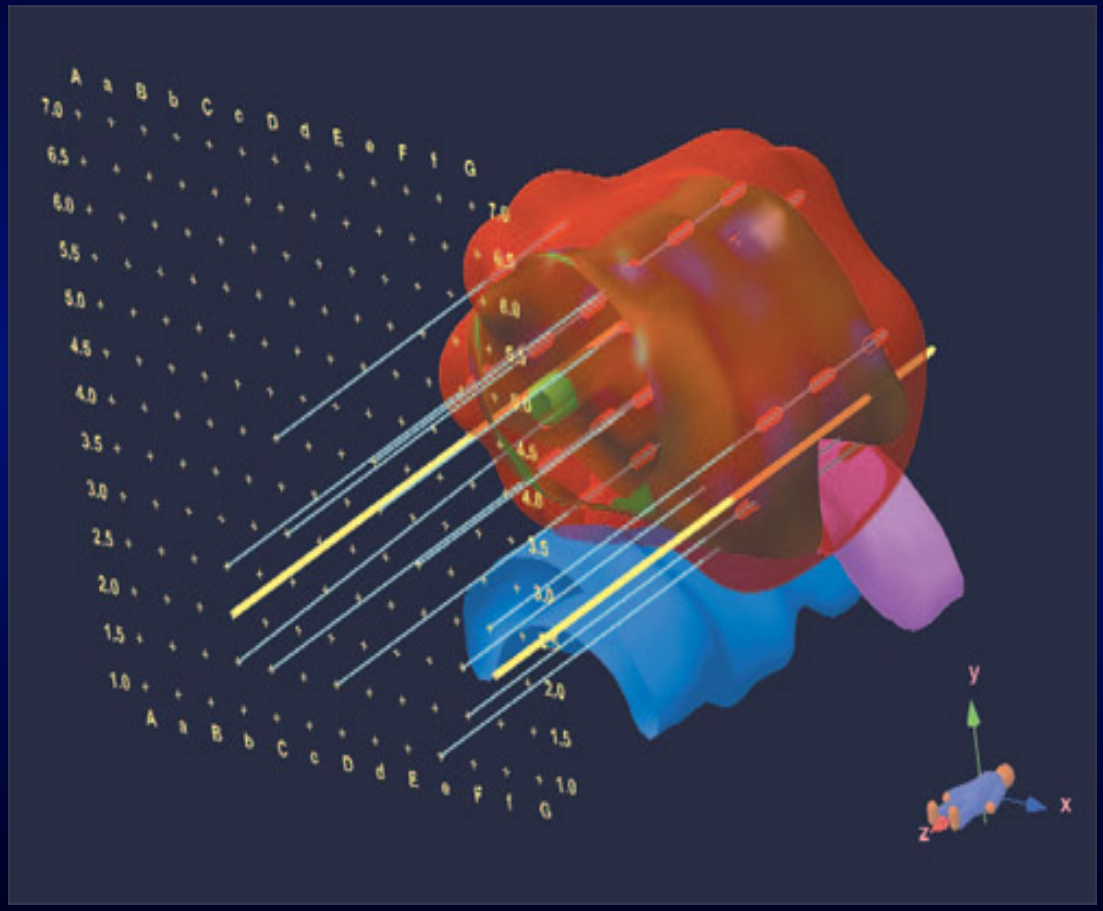
UROLOGY 88: 119–124, 2016.

PROMIS Trial: Randomized Men with Elevated PSA and no prior Bx

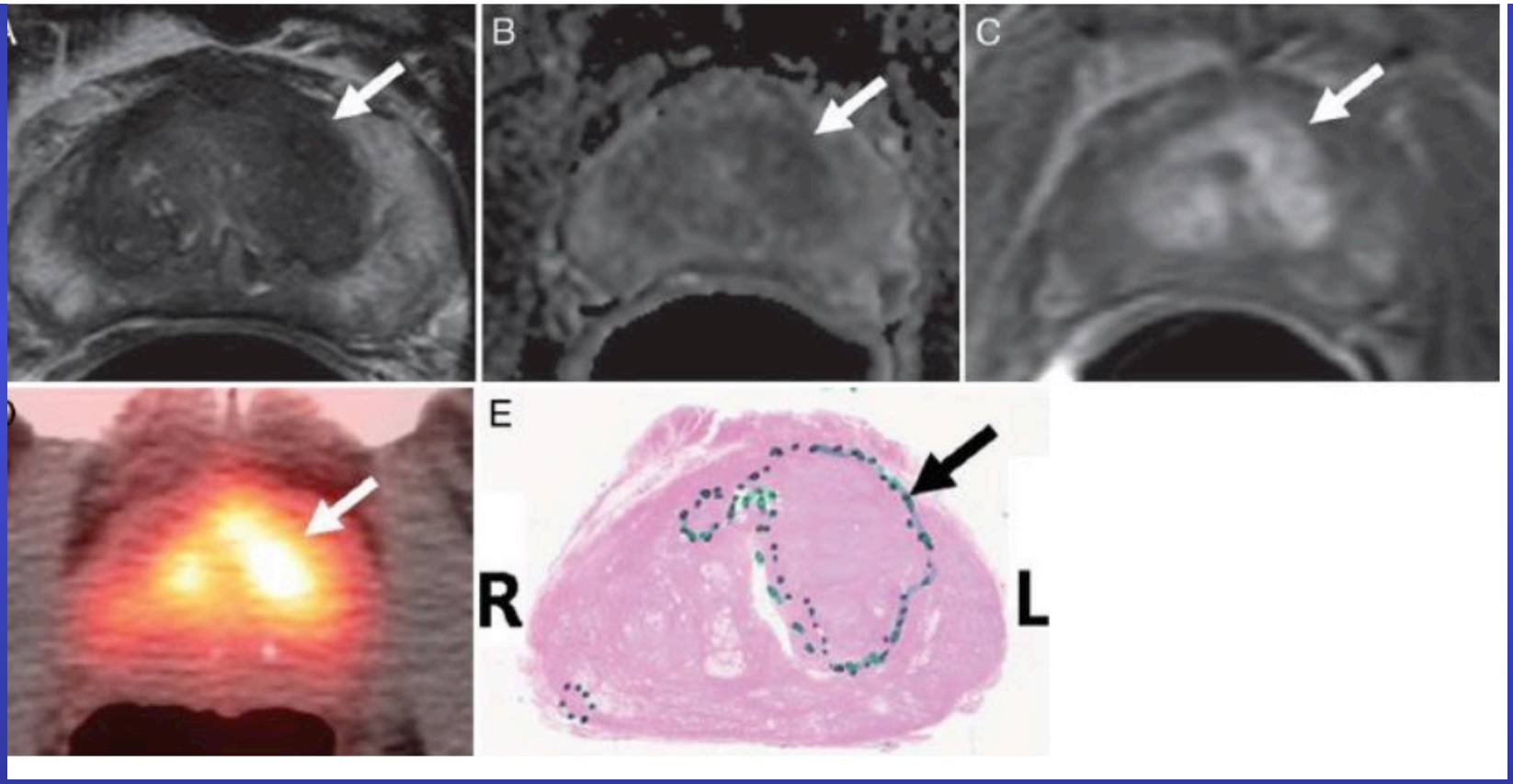
	Standard 12-core TRUS Bx	MRI-targeted Only
No. Pts.	576	576
No. pts. having a Bx.	576	418 (73%)
"Over" Dx. CaP	90 (16%)	62 (11%)
Significant CaP	111 (19%)	213 (37%)

Emberton et al

Transperineal Mapping Prostate Biopsy



Localized Prostate Cancer Detection with ^{18}F FACBC PET

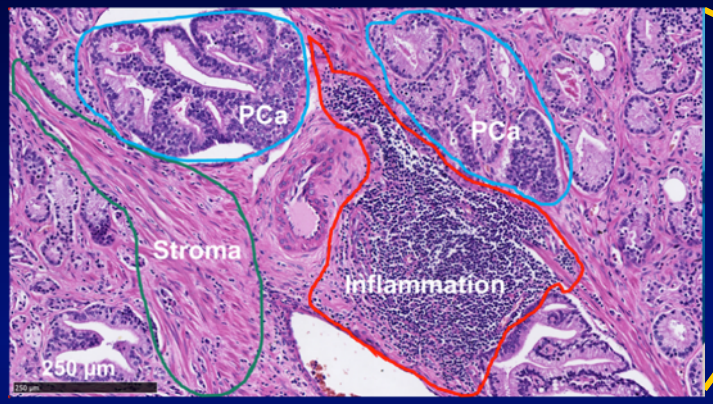


Radiology: Volume 270: Number 3—March 2014 ▪

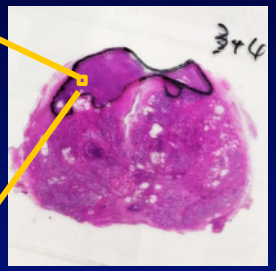
Imaging to Detect Prostate Cancer at Wash U

1. Clinical PET/MR using ^{64}Cu radiopharmaceuticals
   - Joe Ippolito M.D.,Ph.D. and Farrokh Dehdashti M.D.
2. High resolution virtual pinhole PET (vp-PET) imaging – a new clinical imaging tool for prostate cancer?
   - Yuan-Chuan Tai, Ph.D.
3. Diffusion Basis Spectral Imaging (D-Histo) of prostate cancer
   - Sheng-Kwei (Victor) Song Ph.D.
4. Multimodality clinical molecular imaging of aggressive prostate cancer variants with PET/MR/D-Histo/MALDI imaging
   - Joe Ippolito, Victor Song, and Rick Drake (MUSC)

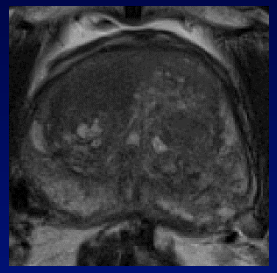
D-Histo: Resolving False Positive PCa by mpMRI



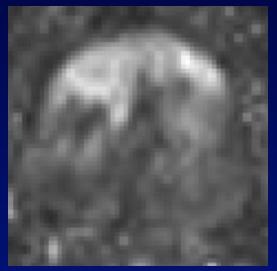
Histology



mpMRI

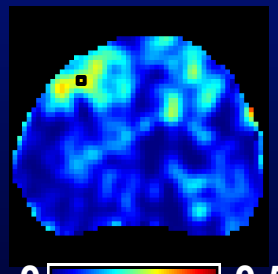


T2W



DWI

D-Histo



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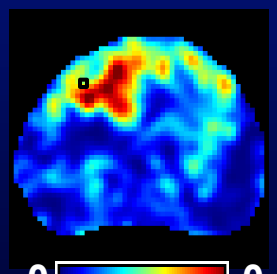
Inflammation



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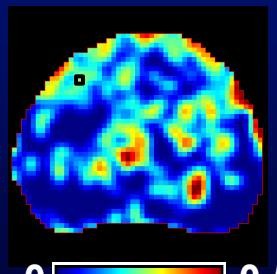
PCa



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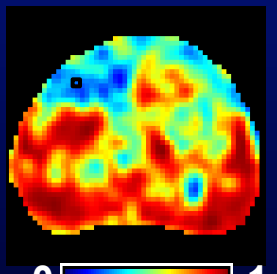
Stromal BPH



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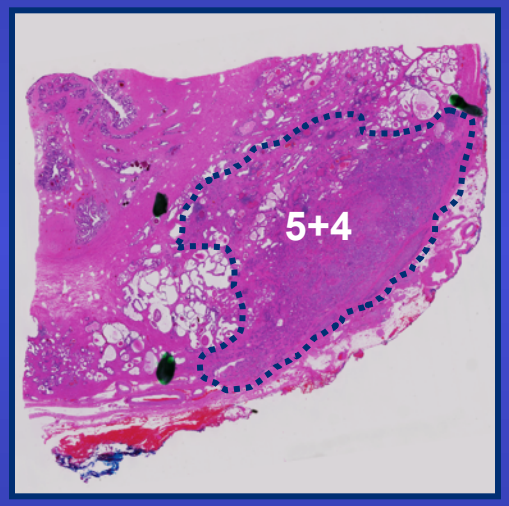
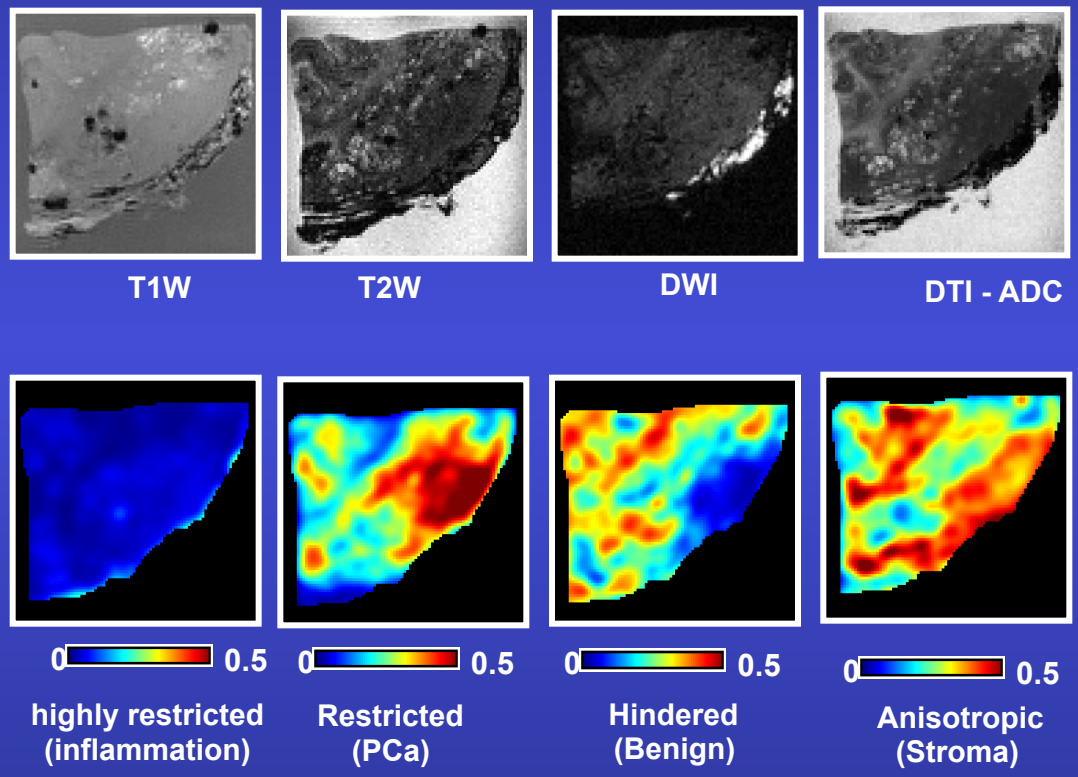
Normal Prostate

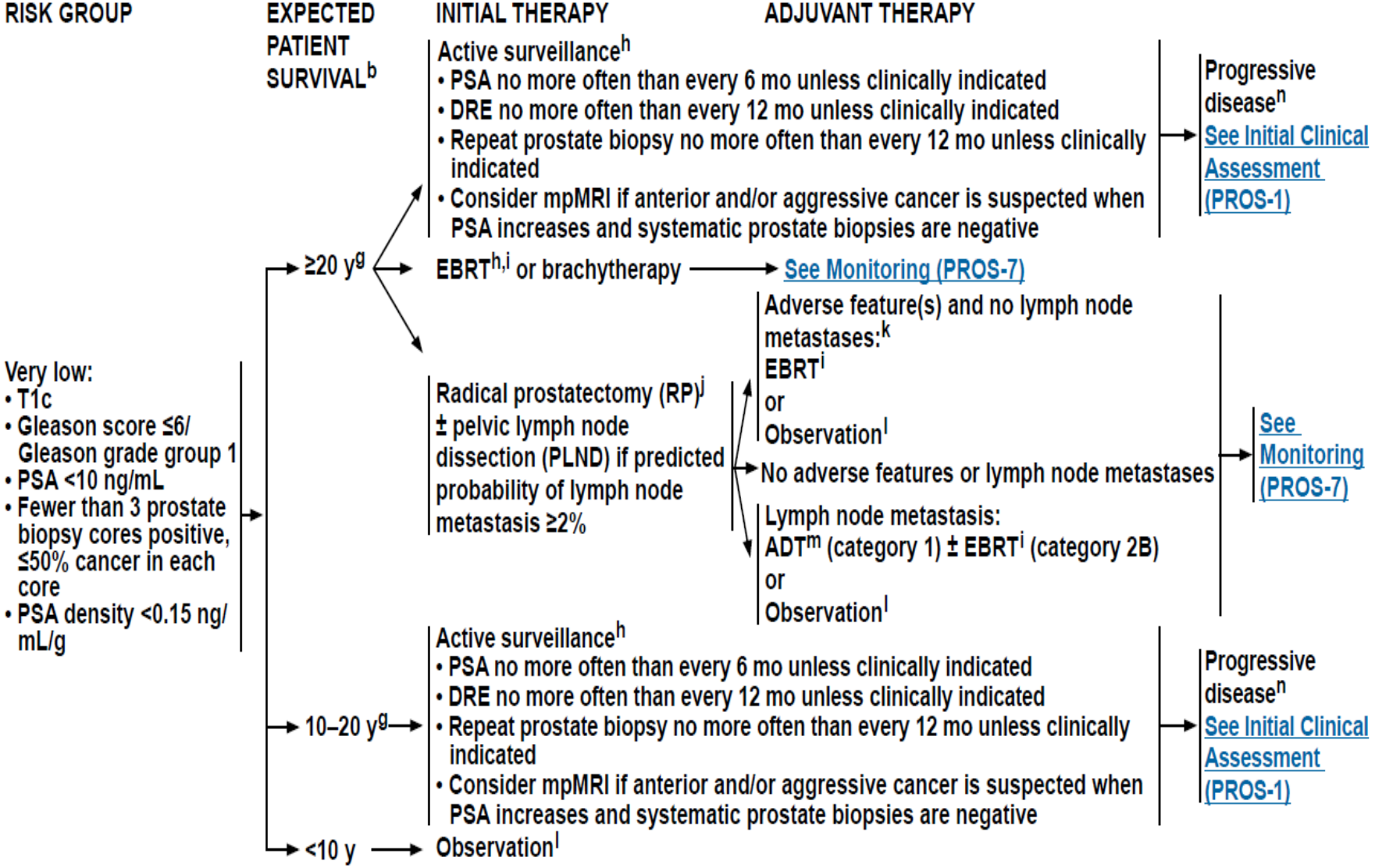
D-Histo resolves co-existing PCa, inflammation, and BPH into component images allowing a direct inspection.

Patient #1 C9


5+4


T1W
T2W
DWI
DTI - ADC
0
0.5
highly restricted (inflammation)
Restricted (PCa)
Hindered (Benign)
Anisotropic (Stroma)

Avoid Overtreatment


RISK GROUP
EXPECTED PATIENT SURVIVAL[b]
INITIAL THERAPY
ADJUVANT THERAPY
Very low:
• T1c
• Gleason score ≤6/ Gleason grade group 1
• PSA <10 ng/mL
• Fewer than 3 prostate biopsy cores positive, ≤50% cancer in each core
• PSA density <0.15 ng/mL/g
≥20 y[g]
Active surveillance[h]
• PSA no more often than every 6 mo unless clinically indicated
• DRE no more often than every 12 mo unless clinically indicated
• Repeat prostate biopsy no more often than every 12 mo unless clinically indicated
• Consider mpMRI if anterior and/or aggressive cancer is suspected when PSA increases and systematic prostate biopsies are negative
Progressive disease[n]
See Initial Clinical Assessment (PROS-1)
EBRT[h,i] or brachytherapy
See Monitoring (PROS-7)
Radical prostatectomy (RP)[j] ± pelvic lymph node dissection (PLND) if predicted probability of lymph node metastasis ≥2%
Adverse feature(s) and no lymph node metastases:[k]
EBRT[i]
or
Observation[l]
No adverse features or lymph node metastases
Lymph node metastasis:
ADT[m] (category 1) ± EBRT[i] (category 2B)
or
Observation[l]
See Monitoring (PROS-7)
10–20 y[g]
Active surveillance[h]
• PSA no more often than every 6 mo unless clinically indicated
• DRE no more often than every 12 mo unless clinically indicated
• Repeat prostate biopsy no more often than every 12 mo unless clinically indicated
• Consider mpMRI if anterior and/or aggressive cancer is suspected when PSA increases and systematic prostate biopsies are negative
Progressive disease[n]
See Initial Clinical Assessment (PROS-1)
<10 y
Observation[l]

RISK GROUP | **EXPECTED PATIENT SURVIVAL**[b] | **INITIAL THERAPY** | **ADJUVANT THERAPY**

Low:
- T1-T2a
- Gleason score ≤6/ Gleason grade group 1
- PSA <10 ng/mL

→ **≥10 y**[g]

→ Active surveillance[h]
- PSA no more often than every 6 mo unless clinically indicated
- DRE no more often than every 12 mo unless clinically indicated
- Repeat prostate biopsy no more often than every 12 mo unless clinically indicated
- Consider mpMRI if anterior and/or aggressive cancer is suspected when PSA increases and systematic prostate biopsies are negative

→ Progressive disease[n] → See Initial Clinical Assessment (PROS-1)

→ EBRT[i] or brachytherapy → See Monitoring (PROS-7)

→ RP[j] ± PLND if predicted probability of lymph node metastasis ≥2%
- → Adverse feature(s) and no lymph node metastases:[k] EBRT[i] or Observation[l]
- → No adverse features or lymph node metastases
- → Lymph node metastasis: ADT[m] (category 1) ± EBRT[i] (category 2B) or Observation[l]

→ See Monitoring (PROS-7)

→ **<10 y** → Observation[l]

Table 1. Available Tissue-Based Tests for Prostate Cancer Prognosis

Test	Platform	Populations studied	Outcome Reported (Test independently predicts)	References	Molecular Diagnostic Services Program (MolDX) Recommendations
Decipher	Whole-transcriptome 1.4M RNA expression (44,000 genes) oligonucleotide microarray optimized for FFPE tissue	Post radical prostatectomy (RP), adverse pathology/high-risk features	Metastasis Prostate cancer-specific mortality	142,507-518	Cover post-RP for 1) pT2 with positive margins; 2) any pT3 disease; 3) rising PSA (above nadir)
		Post RP, biochemical recurrence	Metastasis Biochemical failure		
		Post RP, adjuvant or salvage radiotherapy	Metastasis		
Ki-67	IHC	Biopsy, intermediate- to high-risk treated with EBRT	Metastasis	519-522	Not recommended
		Biopsy, conservatively managed (active surveillance)	Prostate cancer-specific mortality		
Oncotype DX Prostate	Quantitative RT-PCR for 12 prostate cancer-related genes and 5 housekeeping controls	Biopsy, low- to intermediate-risk treated with RP	Non-organ-confined pT3 or Gleason grade 4 disease on RP	63,523	Cover post-biopsy for NCCN very-low- and low-risk prostate cancer in patients with at least 10 years life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy
Prolaris	Quantitative RT-PCR for 31 cell cycle-related genes and 15 housekeeping controls	Transurethral resection of the prostate (TURP), conservatively managed (active surveillance)	Prostate cancer-specific mortality	59-62,524,525	Cover post-biopsy for NCCN very-low- and low-risk prostate cancer in patients with at least 10 years life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy
		Biopsy, conservatively managed (active surveillance)	Prostate cancer-specific mortality		
		Biopsy, localized prostate cancer	Biochemical recurrence Metastasis		
		Biopsy, intermediate-risk treated with EBRT	Biochemical failure		
		RP, node-negative localized prostate cancer	Biochemical recurrence		
ProMark	Multiplex immunofluorescent staining of 8 proteins	Biopsy, Gleason grade 3+3 or 3+4	Non-organ-confined pT3 or Gleason pattern 4 disease on RP	526	Cover post-biopsy for NCCN very-low- and low-risk prostate cancer in patients with at least 10 years life expectancy who have not received treatment for prostate cancer and are candidates for active surveillance or definitive therapy.
PTEN	Fluorescent in situ hybridization or IHC	Transurethral resection of the prostate (TURP), conservatively managed (active surveillance)	Prostate cancer-specific mortality	527-531	Not recommended
		Biopsy, Gleason grade 3+3	Upgrading to Gleason pattern 4 on RP		
		RP, high-risk localized disease	Biochemical recurrence		

Best use of Genomic Tests (E. Klein)

Clinical Scenario	Use of Genomic Test	Best Endpoint
Very Low Risk	No (except for youngest pts)	Adverse Pathology
Low risk: low volume GI 3 + 3	Selectively based on life expectancy and risk tolerance	
Low risk: high volume GI 3 + 3	Yes	
Intermediate Risk: low volume GI 3+ 4	Yes	Adverse Pathology, Metastasis Risk, or Mortality
Intermediate Risk: high volume 3+4 or any 4+ 3	No	
High Risk	No	