UCSF
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Personalizing prostate cancer care:

A clinical perspective on imaging and other biomarkers in 2017

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October 26, 2017

Disclosures

Research funding: GenomeDx, Genomic Health

Consulting: Myriad Genetics, MDx Health, Dendreon, Astellas

I order many mpMRI and PSMA PET/CT scans in my clinical practice!

Prostate cancer 2017

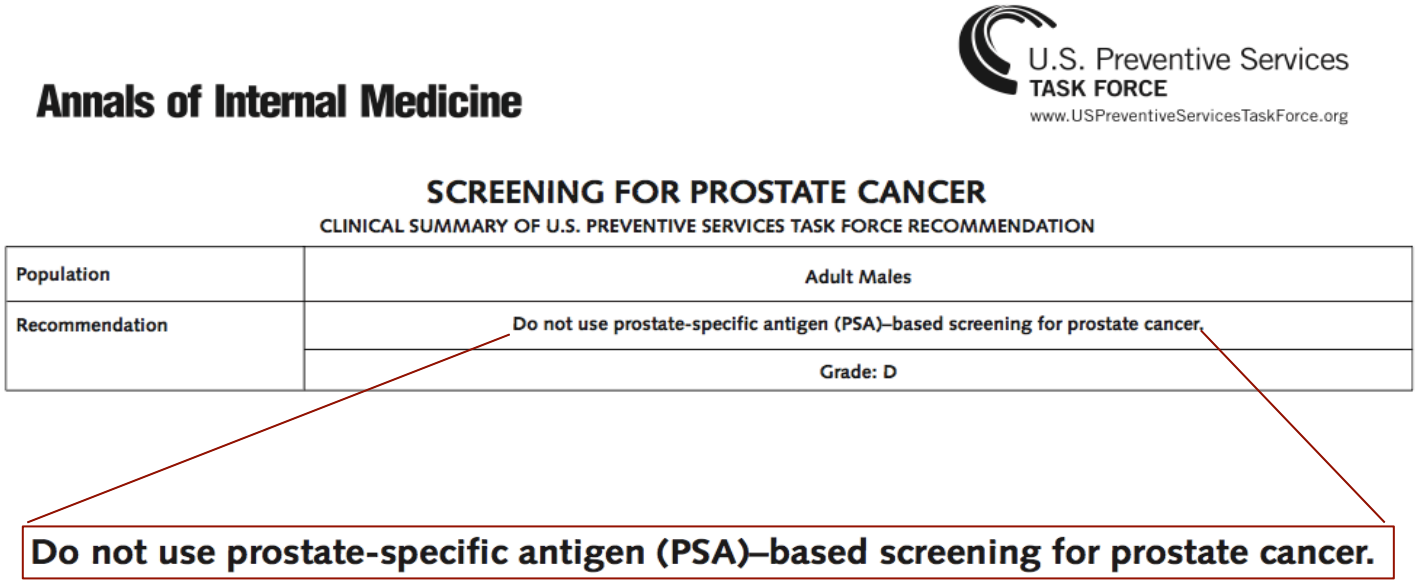
Incidence

Prostate	161,360	19%
Lung & bronchus	116,990	14%
Colon & rectum	71,420	9%
Urinary bladder	60,490	7%
Melanoma of the skin	52,170	6%
Kidney & renal pelvis	40,610	5%
Non-Hodgkin lymphoma	40,080	5%
Leukemia	36,290	4%
Oral cavity & pharynx	35,720	4%
Liver & intrahepatic bile duct	29,200	3%
All Sites	**836,150**	**100%**

Mortality

Lung & bronchus	84,590	27%
Colon & rectum	27,150	9%
Prostate	26,730	8%
Pancreas	22,300	7%
Liver & intrahepatic bile duct	19,610	6%
Leukemia	14,300	4%
Esophagus	12,720	4%
Urinary bladder	12,240	4%
Non-Hodgkin lymphoma	11,450	4%
Brain & other nervous system	9,620	3%
All Sites	**318,420**	**100%**

So how did we wind up here?



Annals of Internal Medicine

U.S. Preventive Services TASK FORCE
www.USPreventiveServicesTaskForce.org

SCREENING FOR PROSTATE CANCER

CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

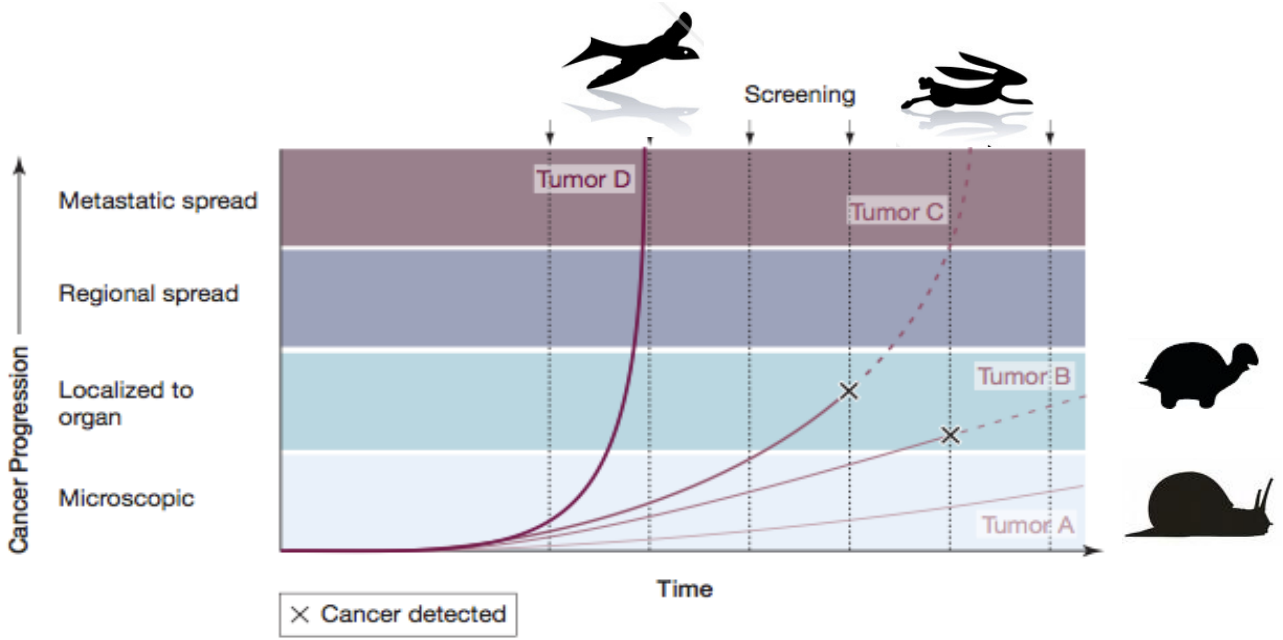
Population	Adult Males
Recommendation	Do not use prostate-specific antigen (PSA)–based screening for prostate cancer.
	Grade: D

Do not use prostate-specific antigen (PSA)–based screening for prostate cancer.

Moyer et al. Ann Intern Med 157:120, 2012.

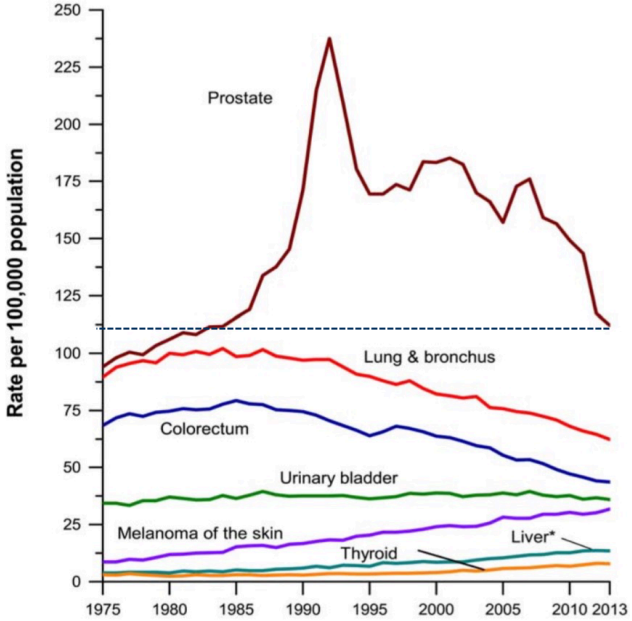
This is (mostly) our fault.

Prostate cancer is highly heterogeneous

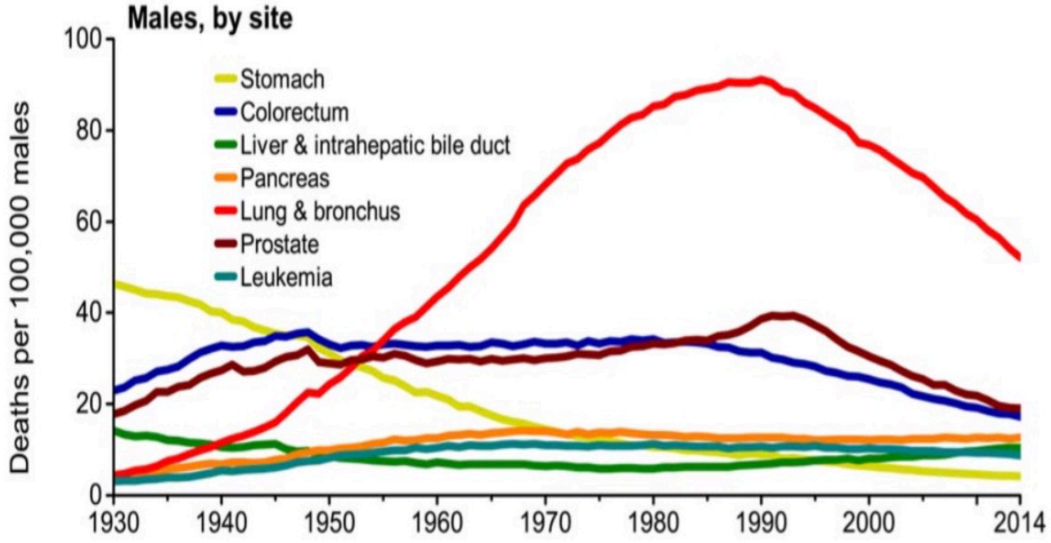


The Impact of the USPSTF "D" Recommendation

Incidence

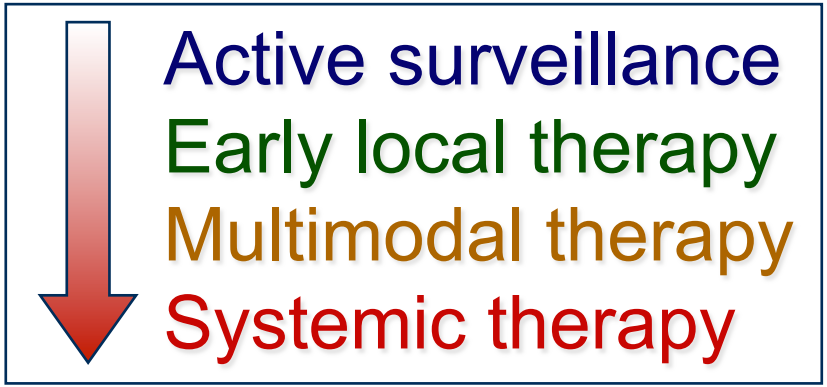


Mortality



Prostate cancer must be risk stratified

Goal: inform physician-patient decisions about optimal initial treatment approach and timing



Active surveillance 2017: finally standard of care

JOURNAL OF CLINICAL ONCOLOGY

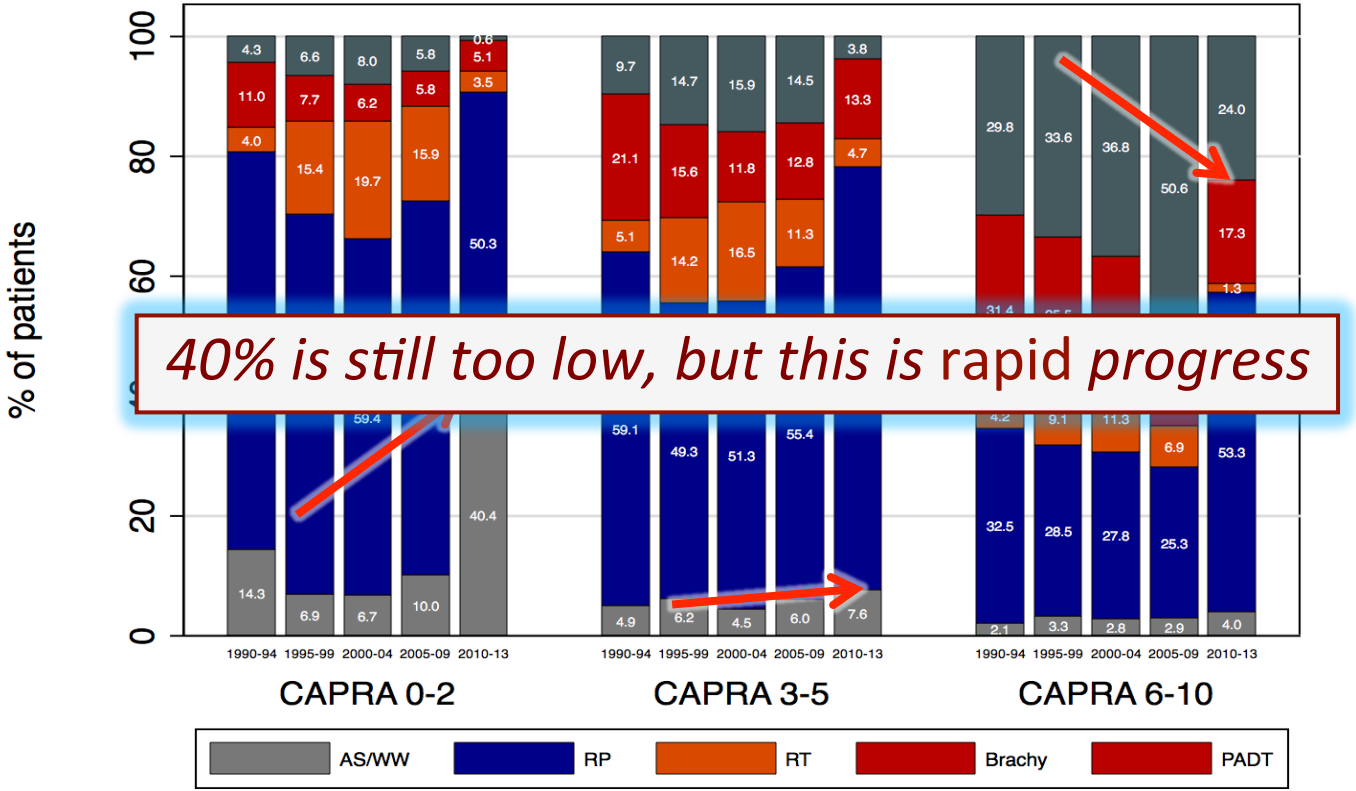
ASCO SPECIAL ARTICLE

Active Surveillance for the Management of Localized Prostate Cancer (Cancer Care Ontario Guideline): American Society of Clinical Oncology Clinical Practice Guideline Endorsement

Ronald C. Chen, R. Bryan Rumble, D. Andrew Loblaw, Antonio Finelli, Behfar Ehdaie, Matthew R. Cooperberg, Scott C. Morgan, Scott Tyldesley, John J. Haluschak, Winston Tan, Stewart Justman, and Suneil Jain

And AUA guideline now also endorses AS for all “very low risk” and most “low risk” disease

Times are changing – *fast!*



Risk stratification works

The UCSF-CAPRA score

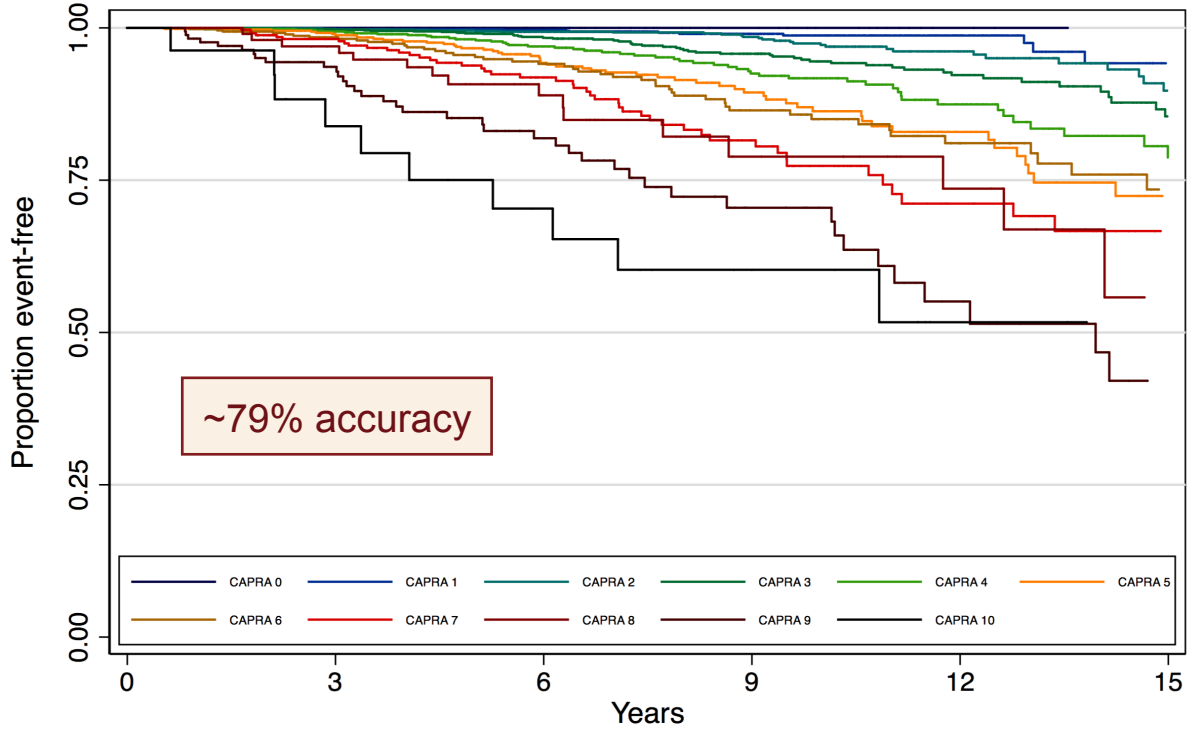
Variable	Level	Points	Variable	Level	Points
PSA	2.0-6	0	**T-stage**	T1/T2	0
	6.1-10	1		T3a	1
	10.1-20	2			
	20.1-30	3	**% pos bx**	<34%	0
	>30	4		≥34%	1
Gleason	1-3/1-3	0			
	1-3/4-5	1	**Age**	<50	0
	4-5/1-5	3		≥50	1

Sum of points from each variable for 0-10 score

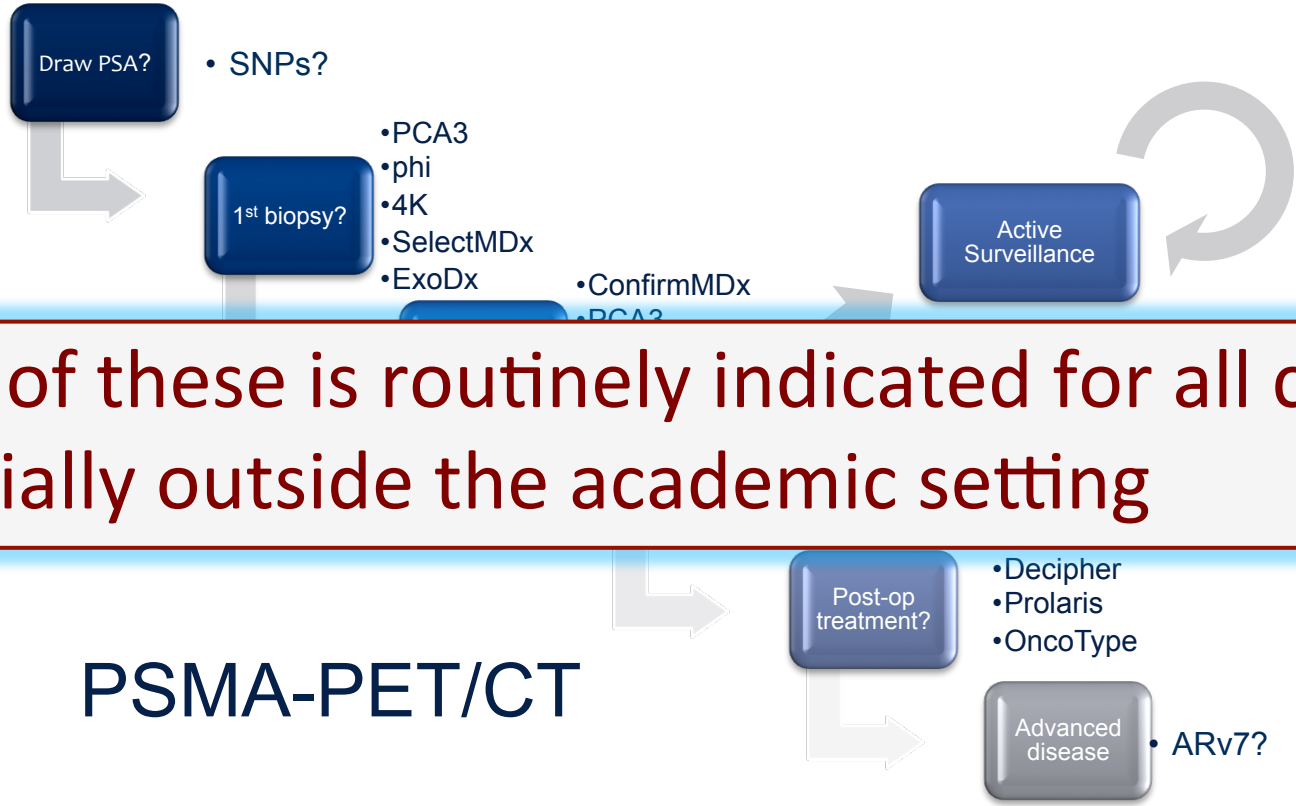
Validated in 14 studies on 4 continents, N>20,000

http://urology.ucsf.edu/capra.html

…so the bar is high for improved accuracy



Prostate Cancer 2017: Decisions, decisions…



Pre-diagnosis principles

1. Any candidate marker (including imaging) has to improve on an existing multivariable gold standard (not just PSA).
   Risk calculators: e.g. PCPT, ERSPC, Sunnybrook

2. High-quality methodology is absolutely critical, especially for retrospective studies.

3. The goal is *not* identification of prostate cancer. The goal is identification of potentially lethal prostate cancer.

Tests to *consider* before a first biopsy

PCA3

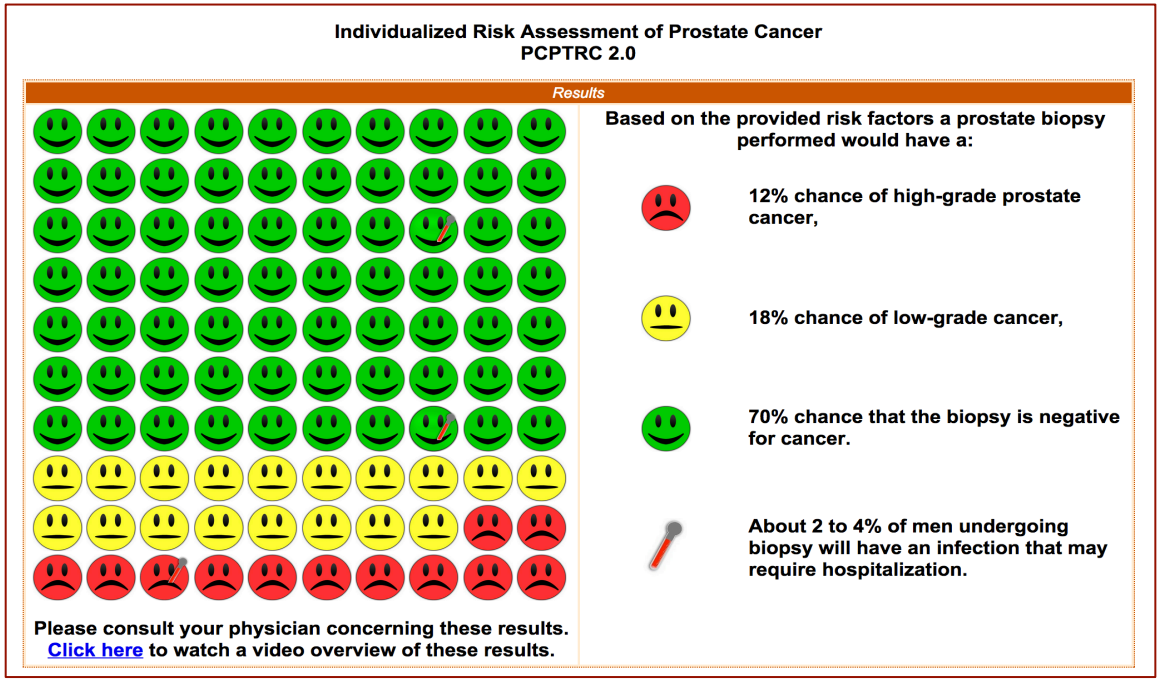
4K

phi

SelectMDx

ExoDx

mpMRI



Post-diagnosis principle

A putative biomarker (including imaging) must improve on an existing, *multivariable* clinical model, ideally a previously validated one

Nomograms
CAPRA / CAPRA-S

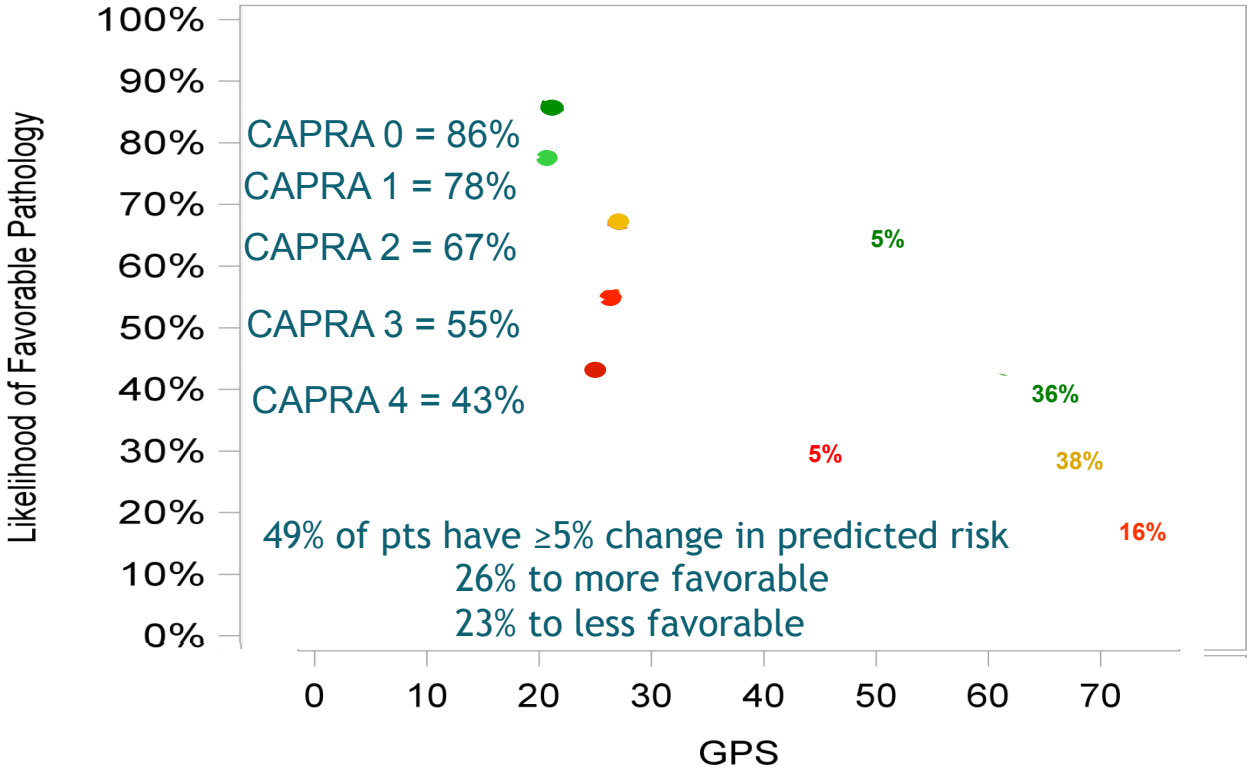
Not just Gleason score alone or the D'Amico / NCCN risk groups

Prognostic tests for newly dx'ed "low-risk"

Prolaris cell cycle progression score (Myriad)
OncoType Genomic Prostate Score (Genomic Health)
Decipher genomic classifier (GenomeDx)

- Based on RNA expression of gene sets derived from FPE biopsy tissue
- All shown and validated to improve multivariable model performance for post-treatment endpoints (adverse pathology, recurrence, metastasis, cancer mortality)

Adding GPS to CAPRA: predicting pathology



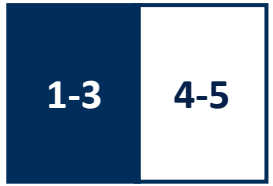
No prostate cancer test is truly binary

PIRADS: information loss

mpMRI exam

PACS

PIRADS



Dichotomized

Major opportunity for improvement through machine learning

mpMRI: The interobserver variation problem

Opinion: in 2017 mpMRI should have little to no role outside academic centers and other centers of excellence

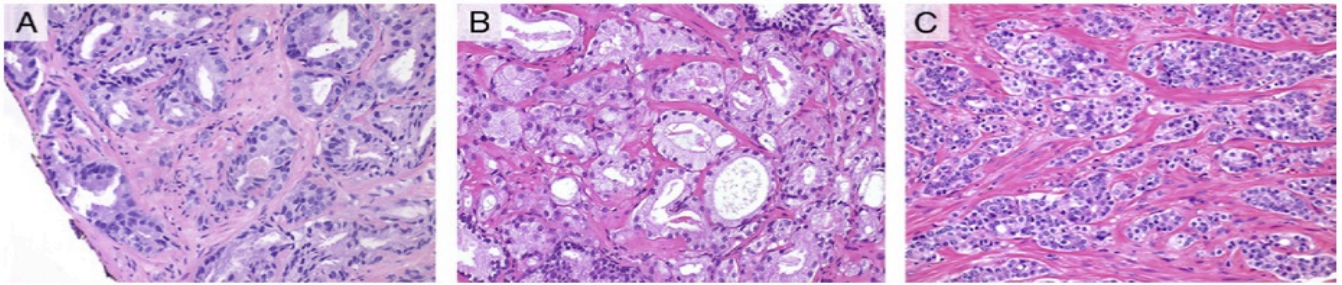
NCI analysis: 3 body radiologists, 2 prostate specialists

		Overall	H-H	H-M	M-M
All Lesions	PIRADS scoring	0.58 (0.04)	0.70 (0.04)	0.58 (0.04)	0.53 (0.04)
	Lesion detection	0.74 (0.03)	0.75 (0.04)	0.74 (0.03)	0.75 (0.03)
	PIRADS≥4	0.72 (0.03)	0.81 (0.04)	0.72 (0.04)	0.68 (0.04)
Index Lesions	PIRADS scoring	0.85 (0.04)	0.92 (0.03)	0.86 (0.04)	0.79 (0.05)
	Lesion detection	0.93 (0.02)	0.92 (0.03)	0.93 (0.02)	0.92 (0.04)
	PIRADS≥4	0.90 (0.03)	0.95 (0.03)	0.91 (0.03)	0.88 (0.04)

(by the way, pathology is not much better)

The Potential Impact of Reproducibility of Gleason Grading in Men With Early Stage Prostate Cancer Managed by Active Surveillance: A Multi-Institutional Study

Jesse K. McKenney,* Jeff Simko,† Michael Bonham, Lawrence D. True, Dean Troyer, Sarah Hawley, Lisa F. Newcomb, Ladan Fazli,‡ Lakshmi P. Kunju, Marlo M. Nicolas, Funda Vakar-Lopez, Xiaotun Zhang, Peter R. Carroll,§ James D. Brooks and the Canary/Early Detection Research Network Prostate Active Surveillance Study Investigators



N=17 “easy” cases: κ=0.76 (0.59-0.90)
N=17 “controversial” cases: κ=0.27 (0.15-0.42)

2017 Standard of Care still includes TRUS-Biopsy

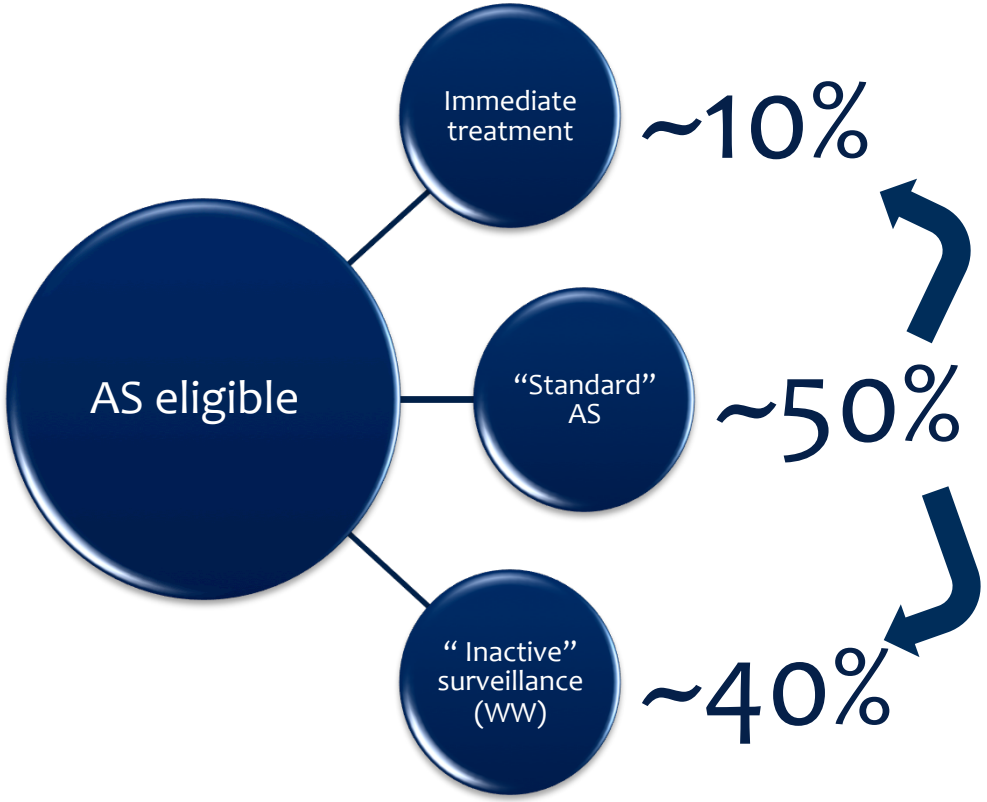
- mpMRI is not required for all, and should only be done in high-volume centers
- Negative MRI does not obviate need for at least a first mapped biopsy

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: Low-Risk Cancer, Gleason 6	Low-Risk Cancer, Gleason 3+4 Low Volume[a]	Intermediate-Risk Cancer, Gleason 3+4 High Volume[b]	High-Risk Cancer, Gleason ≥4+3	Totals	
	No cancer	439	74	12	12	5	542	5.3%
Low-Risk Cancer	Gleason 6	38	84	12	10	3	147	17%
Low-Risk Cancer	Gleason 3+4 Low volume[c]	17	14	9	19	7	66	47%
Intermediate-Risk Cancer	Gleason 3+4 High volume[d]	14	21	7	29	4	75	39%
High-Risk Cancer	Gleason ≥4+3	26	13	12	19	103	173	46%
	Totals	534	206	52	89	122	1003	29%

Siddiqui et al. JAMA 2015; 313:390

Future goal: tailored active surveillance

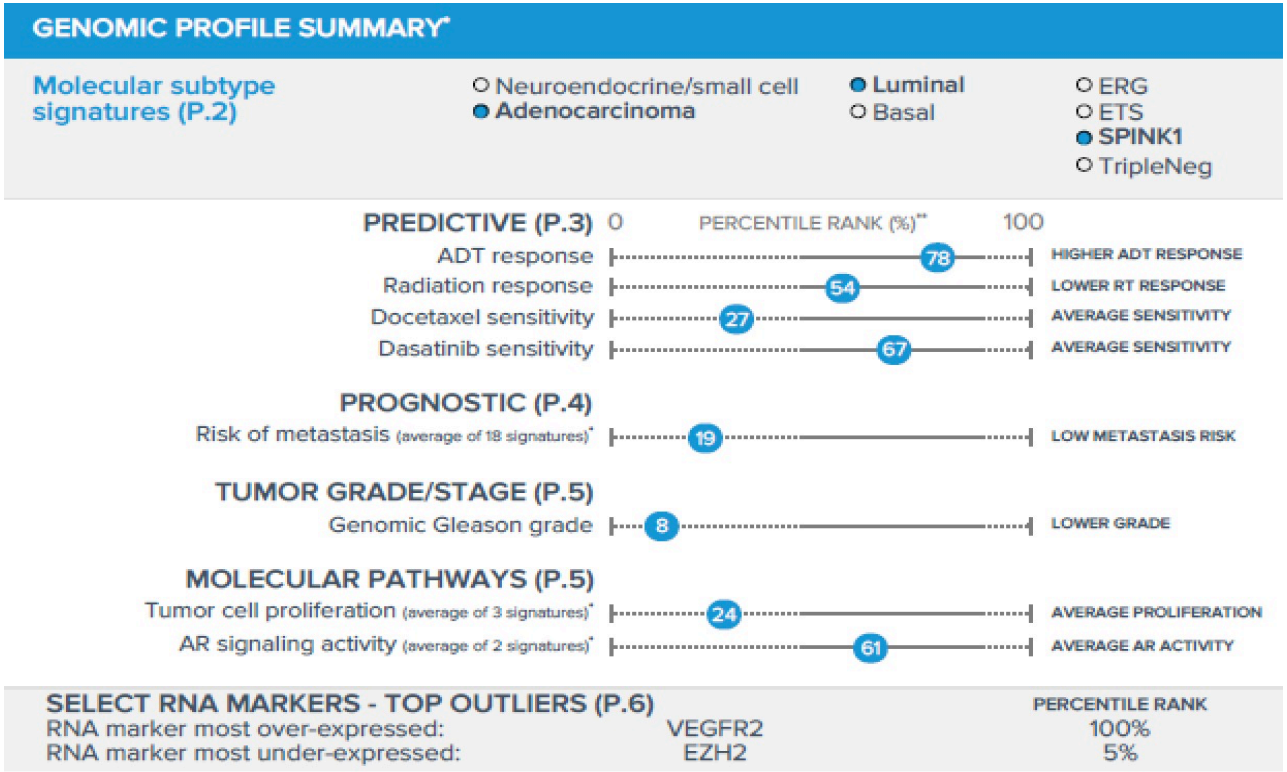


Better imaging

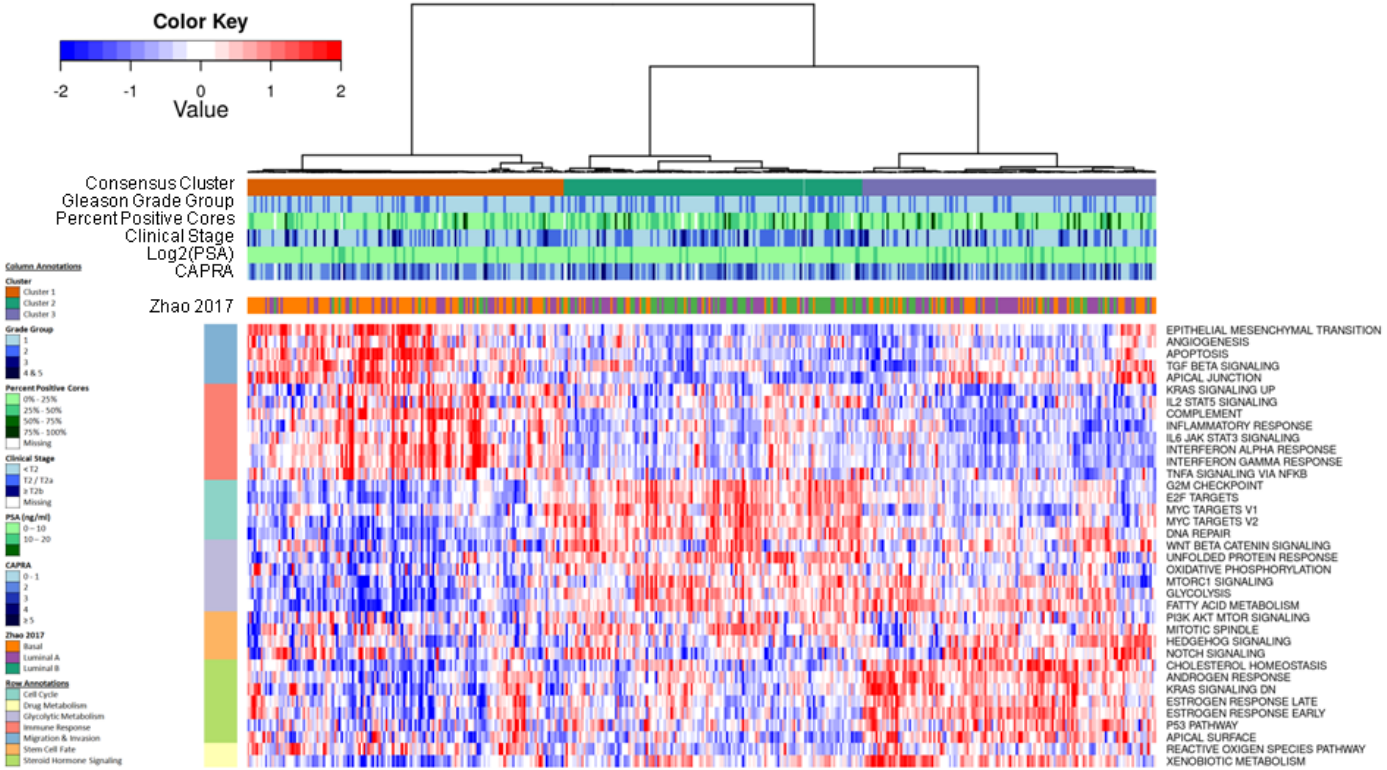
Better biomarkers

Can we "undiagnose" a subset of men?

Decipher GRID

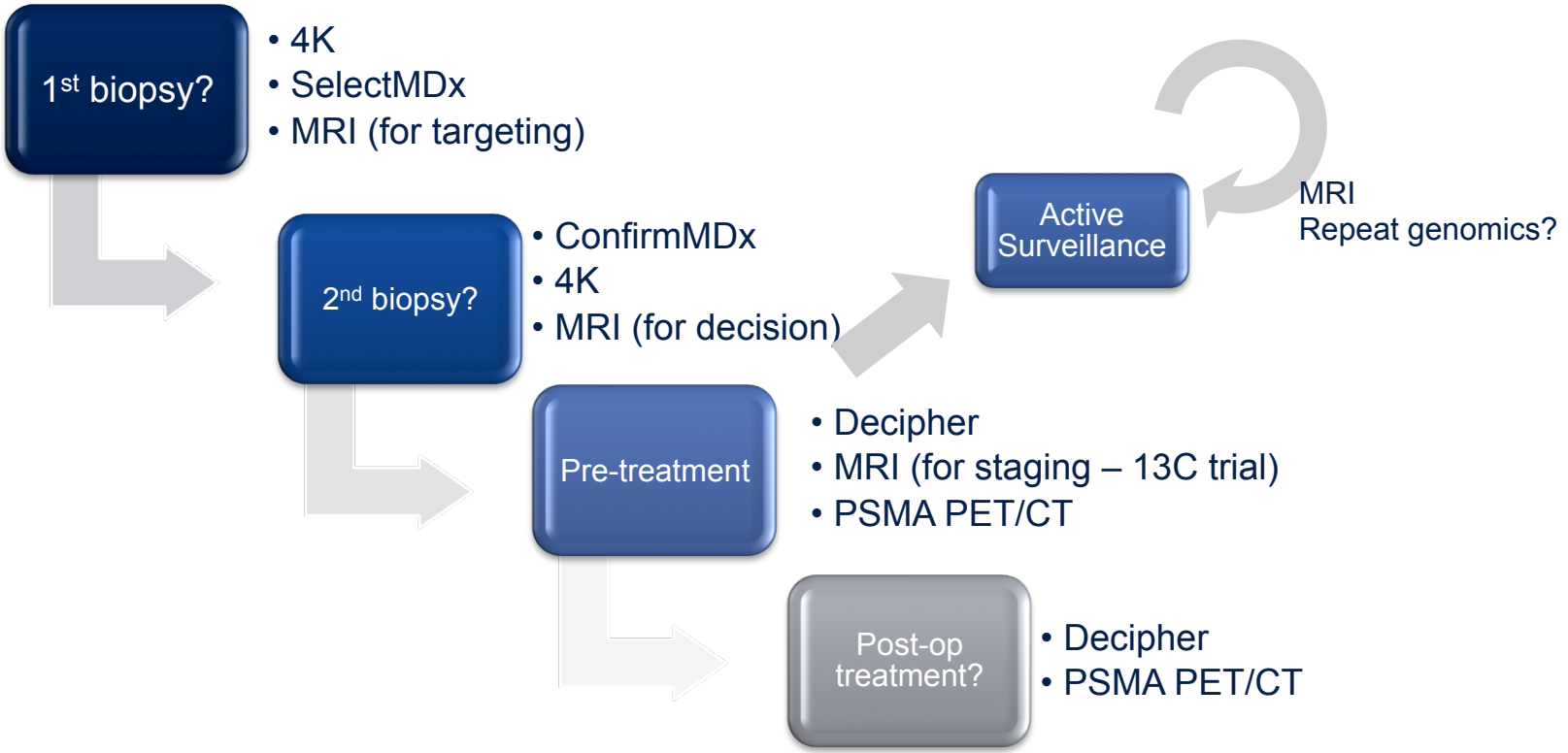


Why I’m bullish on genomics



Cooperberg et al. AUA 2017

Prostate Cancer 2017: UCSF practice



Summary and future directions

- Prostate cancer management decisions must be risk stratified —and standard variables set a high bar for accuracy.
- Novel biomarker and imaging tests can improve accuracy further, but how to use them in *routine* clinical practice is not yet clear, especially outside academic settings.
- Next generation genomics and imaging will yield far richer insights into individual cancer biology and heterogeneity.
- We are barely even at the “end of the beginning”.