

Prostate Cancer and the PSA Test

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CANCER SURVIVOR DAY

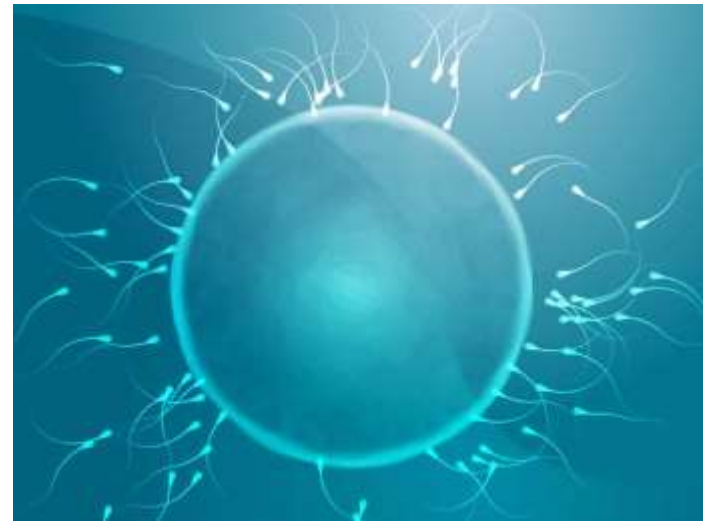
What are we going to talk about today?

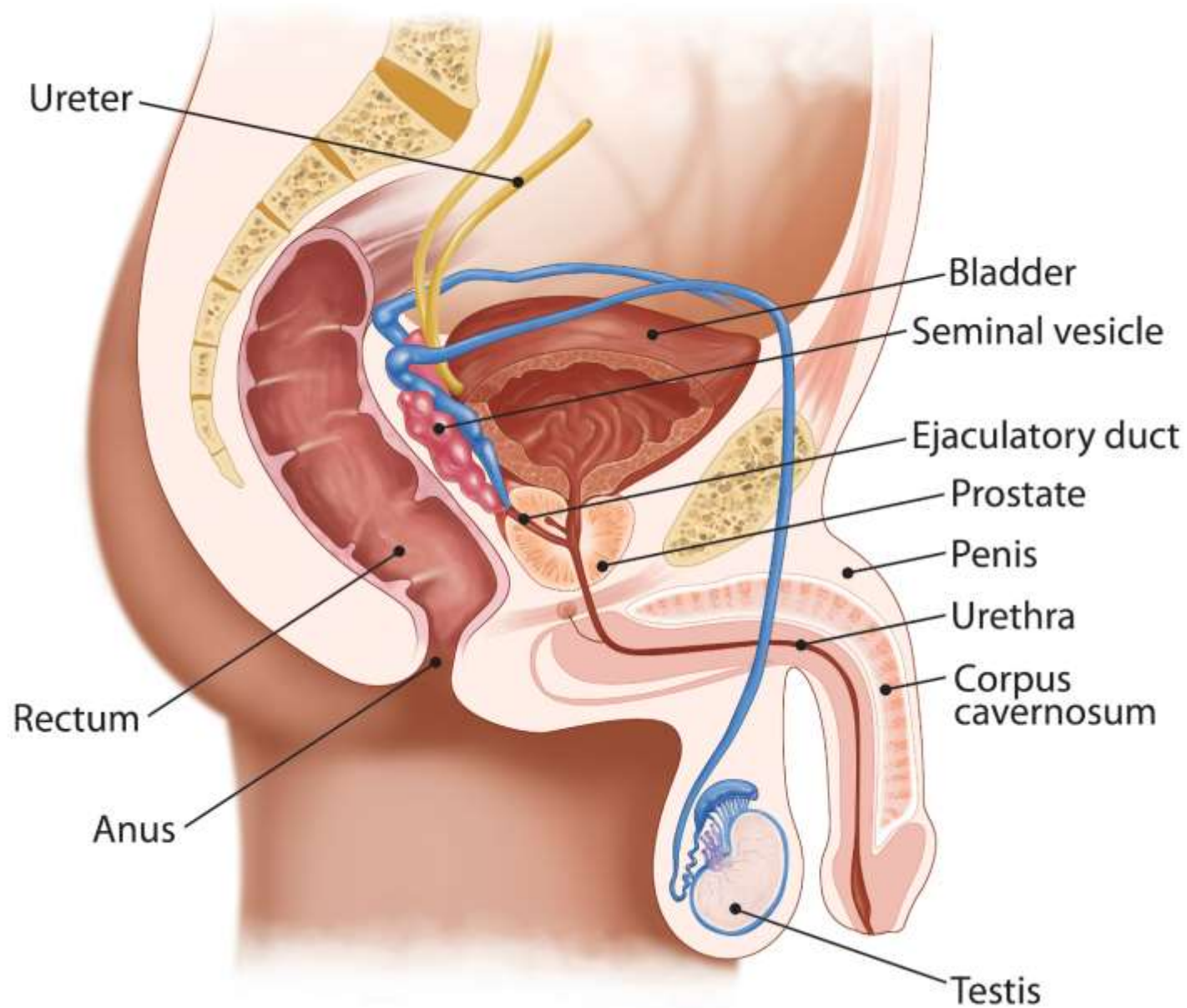
- **Understand the role of the PSA test in the world of Prostate Cancer**
- A lot of confusion about the PSA test.
 - Is it useful?
 - Is it dangerous?
 - Am I supposed to be getting a PSA test?
- PSA serves in two functions:
 - Screening: Initial detection of prostate cancer
 - Surveillance: Checking for recurrence after prostate cancer treatment



What is the Prostate?

- The prostate is a reproductive organ. Without the prostate, a man is sterile
- It produces several chemicals and enzymes that assist sperm
- One of these enzymes, is the PSA





Tell me about Prostate Cancer

In 2018:

- ~ 164,690 new cases of prostate cancer - most common cancer in men (non-skin)
- ~ 29,430 deaths from prostate cancer
- SECOND leading cause of cancer death among men
- ~ 1 in 9 men will be diagnosed with prostate cancer during his lifetime (higher risk in African American men)
- ~ 1 in 41 men will die of prostate cancer.

What is this PSA test you speak of

PSA = Prostate Specific Antigen

It is an enzyme produced by the prostate to liquefy semen so sperm can swim freely.

It is a blood test.



History

- Before 1990, prostate cancer deaths were on the rise. The only blood test detected prostate cancer too late and many men had advanced disease.
- PSA was discovered in the early 1980s
- It started to be used for prostate cancer screening by the early to mid 1990s
- Prostate cancer deaths went DOWN



How the PSA Test *WAS* used

If the PSA test is high, then prostate cancer may be present.



Many men were being diagnosed with prostate cancer - including early and insignificant prostate cancer.



Over-diagnosis and over-treatment of low risk (clinically insignificant) prostate cancer



Men suffered side effects from unnecessary treatment

Concept: Sensitivity and Specificity

- All medical tests rely on this concept.
- A sensitive test will tell you if the disease is present:
 - All patients with Disease X will have a positive test
- A specific test will tell you that you have the disease you are testing for:
 - If Test Y is positive, then you must have Disease X and nothing else.

Sensitivity and Specificity

		DISEASE	
		+	-
T E S T	+	True + (a)	False + (b)
	-	False - (c)	True - (d)
		Sensitivity = $a / a + c$ = $TP / TP + FN$	Specificity = $d / b + d$ = $TN / FP + TN$




The PSA is a sensitive test, but not very specific.

This means you can get a lot of false positives.



What makes this more difficult is determining which prostate cancers are **CLINICALLY SIGNIFICANT** (and which ones you don't need to worry about right now)

You might have cancer, but you don't necessarily need treatment.



Where are you on this spectrum?

What can else cause an elevated PSA (false positives)?

- Infection and/or Inflammation
 - Prostatitis
 - Urinary tract infection
- BPH
- Urinary symptoms
 - Incomplete bladder emptying
 - Slow stream
 - Urinating at night
- Prostate size enlargement
- Age



The problem that occurred with PSA

Too many men were being treated for prostate cancer unnecessarily.

OVER-TREATMENT

Men were suffering possible side effects of treatment:

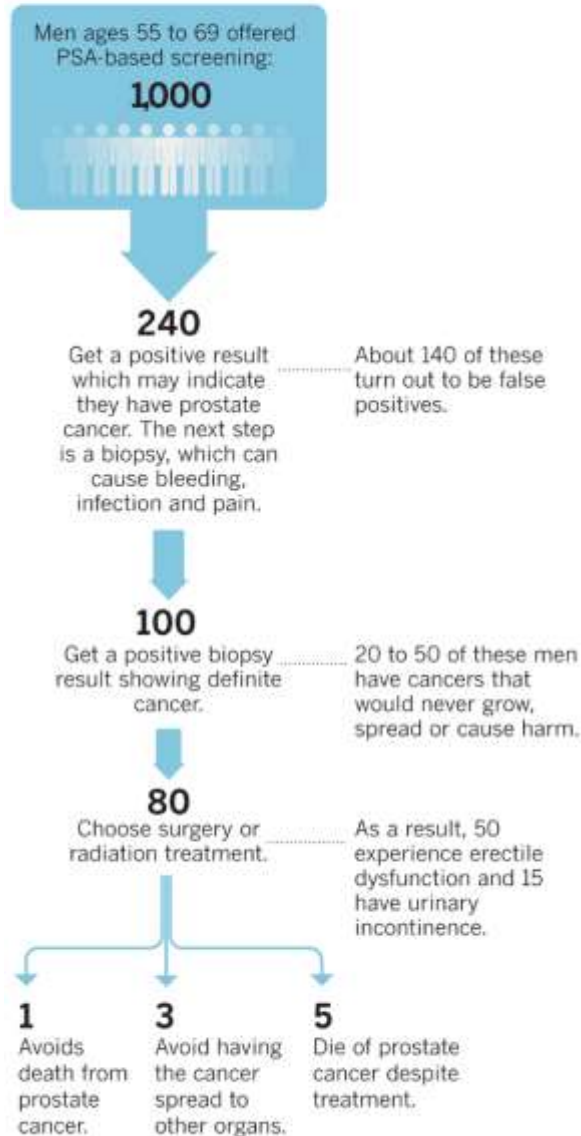
- Urinary Incontinence
- Erectile dysfunction
- Surgical and radiation side effects
- Decreased quality of life

Treating men who may not have needed treatment.



Balancing benefits and harms of prostate cancer screening

The PSA test can catch prostate cancer in its early stages, but for many men it leads to unnecessary medical procedures that have significant side effects. Here's a look at what happens to 1,000 men invited to take the PSA screening test:



LANDMARK EVENT!!!

In 2012, the US Preventive Services Task Force (USPSTF) gave prostate cancer screening a D recommendation.



USPSTF Grades

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.

What did urologists think about the USPSTF recommendations?



The Response: American Urological Association

USPSTF recommendations on clinical preventive health services **have created confusion among patients and the primary care community for years.**

This decision counters the informed opinion of expert physicians, as well as decades of data and research showing early detection of prostate cancer...saves lives.



American
Urological
Association

The Fallout

JAMA, 5/23/2017

Prostate Cancer Diagnoses Fall as Use of PSA Test Declines

“It’s not that there’s less cancer - there’s the same amount of cancer - it’s just being diagnosed less.” - Meir Stampfer, MD, DrPH, Brigham and Women’s Hospital

JAMA[®]

The Journal of the American Medical Association

The Fallout

Washington Post, 5/22/2018

After long decline, death rates from prostate cancer stop falling

“After falling for two decades, the death rate for prostate cancer has stopped decreasing, and the incidence of advanced disease is rising...”

The Washington Post

The Fallout

Medscape 3/27/2018

More Men Presenting With Higher-Grade, More Invasive Prostate Cancer After USPSTF's 2012 Recommendations, Evidence Indicates.

“As predicted by urologists in 2012 after the recommendations were released, there has been a consistent, stepwise increase in cancers of higher Gleason score, as well as... the median level of PSA, in the 4 years after the USPSTF recommendations were released compared to the 4 years prior to the recommendations.”

But...is it real?

Did the USPSTF recommendations actually make prostate cancer worse for men?

Probably. Maybe.

- A decline in prostate cancer screening did happen (~18% reduction)
- 5 years is a small amount of time to detect significant change in a disease that takes years to progress
- We may not know the answer for another 5-7 years
- What definitely did happen: CONFUSION

6 year of debating and studies...



The Update

May 2018: USPSTF updates its PSA screening recommendations to a grade C for men ages 55-69

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AUA Guidelines for the Early Detection of Prostate Cancer

1. The Panel recommends against PSA screening in men under age 40 years.

- In this age group there is a low prevalence of clinically detectable prostate cancer, no evidence demonstrating benefit of screening and likely the same harms of screening as in other age groups.



American
Urological
Association

AUA Guidelines for the Early Detection of Prostate Cancer (2018)

2. The Panel does not recommend routine screening in men between ages 40 to 54 years at average risk.

- For men younger than age 55 years at higher risk, decisions regarding prostate cancer screening should be individualized. Those at higher risk may include men of African American race; and those with a family history of metastatic or lethal adenocarcinomas (e.g., prostate, male and female breast cancer, ovarian, pancreatic) spanning multiple generations, affecting multiple first-degree relatives, and that developed at younger ages.

AUA Guidelines for the Early Detection of Prostate Cancer (2018)

3. For men ages 55 to 69 years the Panel recognizes that the decision to undergo PSA screening involves weighing the benefits of reducing the rate of metastatic prostate cancer and prevention of prostate cancer death against the known potential harms associated with screening and treatment. For this reason, the Panel strongly recommends shared decision-making for men age 55 to 69 years that are considering PSA screening, and proceeding based on a man's values and preferences.

- The greatest benefit of screening appears to be in men ages 55 to 69 years.
- Multiple approaches subsequent to a PSA test (e.g., urinary and serum biomarkers, imaging, risk calculators) are available for identifying men more likely to harbor a prostate cancer and/or one with an aggressive phenotype. The use of such tools can be considered in men with a suspicious PSA level to inform prostate biopsy decisions.

AUA Guidelines for the Early Detection of Prostate Cancer (2018)

4. To reduce the harms of screening, a routine screening interval of two years or more may be preferred over annual screening in those men who have participated in shared decision-making and decided on screening. As compared to annual screening, it is expected that screening intervals of two years preserve the majority of the benefits and reduce overdiagnosis and false positives.

- Additionally, intervals for rescreening can be individualized by a baseline PSA level.

AUA Guidelines for the Early Detection of Prostate Cancer (2018)

5. The Panel does not recommend routine PSA screening in men age 70+ years or any man with less than a 10 to 15 year life expectancy.

- Some men age 70+ years who are in excellent health may benefit from prostate cancer screening.

The PSA test as it is today

Still remains a good screening test for prostate cancer.

We don't need to get rid of it. We need to use it smarter.

There is no cut-off value for PSA.

be smart.

The PSA test as it is today

We DO NOT use the PSA test alone in deciding how to screen men for prostate cancer.



The other puzzle pieces

- A combination of factors are used to assess a man's risk of having clinically significant prostate cancer:
 - Age
 - Physical Examination
 - Race
 - Family History
 - Medical History
 - PSA kinetics
 - PSA variants

What happens in my office

- Three patients
 - James
 - Sylvester
 - Arnold

ALL OF THEM HAVE A PSA OF 4.8

James - PSA 4.8



- 58 years old, African American
- Good health
- No urinary symptoms
- His father was diagnosed with prostate cancer in his 60s
- PSA detected on routine screening by his primary care doctor
- Prostate feels normal with digital rectal exam
- PSA for the past 3 years has been around 1.0

Should James have a prostate biopsy to check for prostate cancer?

Strongly suggest yes.

Sylvester - PSA 4.8



- 69 years old, caucasian
- Has had urinary symptoms for more than 10 years
 - wakes up at night to urinate
 - urinates frequently
 - doesn't feel like he empties his bladder all the way
- Is taking medications (Flomax) to help him urinate better
- Has had prostate infections in the past
- Prostate is enlarged on digital rectal exam
- PSA testing has been inconsistent. Has been as low as 2.5 and as high as 7.2 and fluctuates

Should Sylvester have a prostate biopsy to check for prostate cancer?

Probably not.

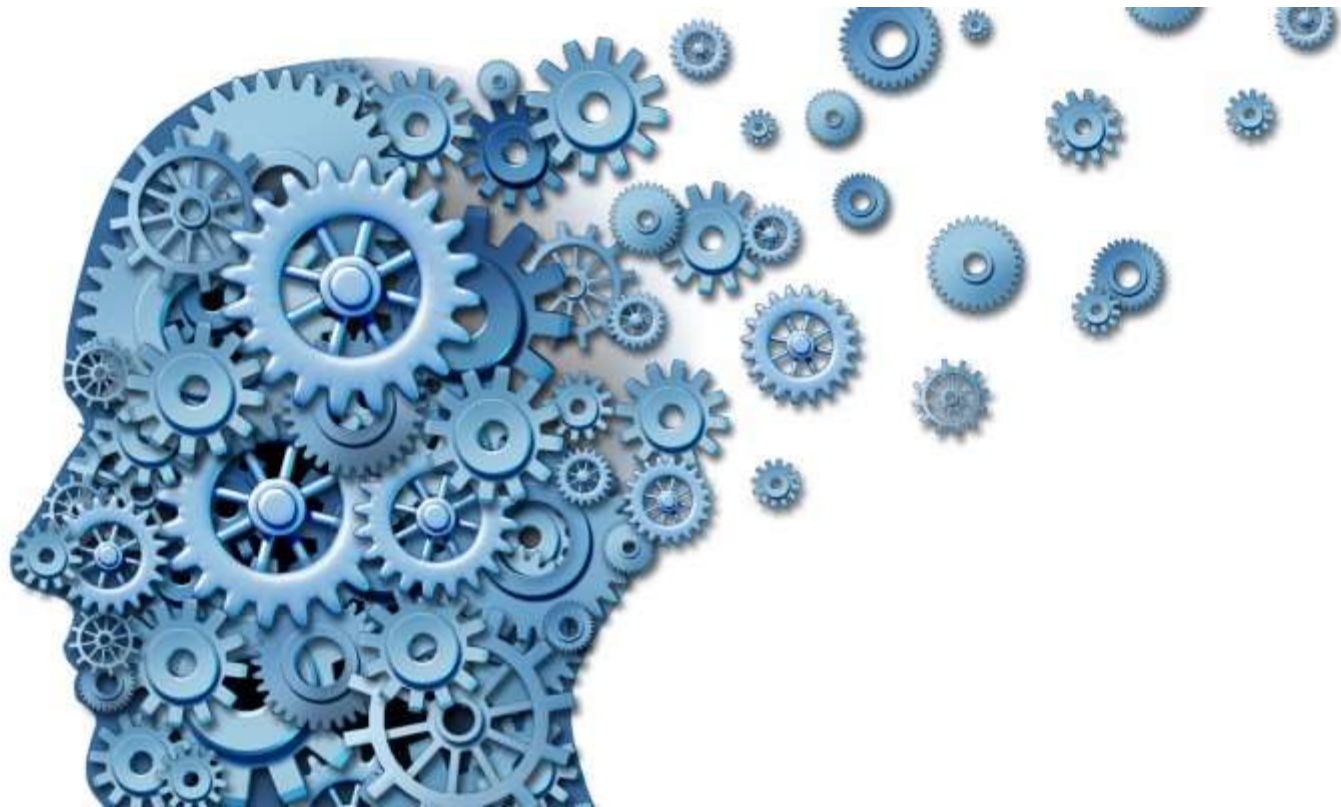
Arnold - PSA 4.8



- 65 years old, caucasian
- Mild urinary symptoms
 - wakes up 1 x a night to urinate
 - mostly urinates okay during the day
- No family history of prostate cancer
- Prostate is normal to slightly enlarged on digital rectal exam
- He has never had a PSA test before

Should Arnold have a prostate biopsy to check for prostate cancer?

We should have a shared decision making conversation.



PROSTATE CANCER SURVEILLANCE

- PSA used to detect prostate cancer recurrence after treatment.
 - Surgery (radical prostatectomy)
 - Radiation (External beam, cyberknife, brachytherapy)
- PSA terms
 - Biochemical Recurrence (BCR)
 - PSA nadir
 - PSA kinetics
 - Doubling time

After Radical Prostatectomy

- PSA should be near zero.
- <0.01 ng/mL

- Biochemical recurrence: >0.2 ng/mL
- Second confirmatory value



After Radiation

- PSA will go down, but will not reach zero
- PSA nadir: lowest PSA recorded
- Biochemical Recurrence: nadir + 2
- For example:
 - If lowest PSA is 0.11, then recurrence at 2.11



CONCLUSION

- PSA is a useful test for prostate cancer screening



- Prostate cancer screening is a shared decision making process
- PSA is useful in detecting prostate cancer recurrence



THANK YOU