Clinical Practice Guidelines and Shared Decision Making for Prostate Cancer Screening

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Disclosures

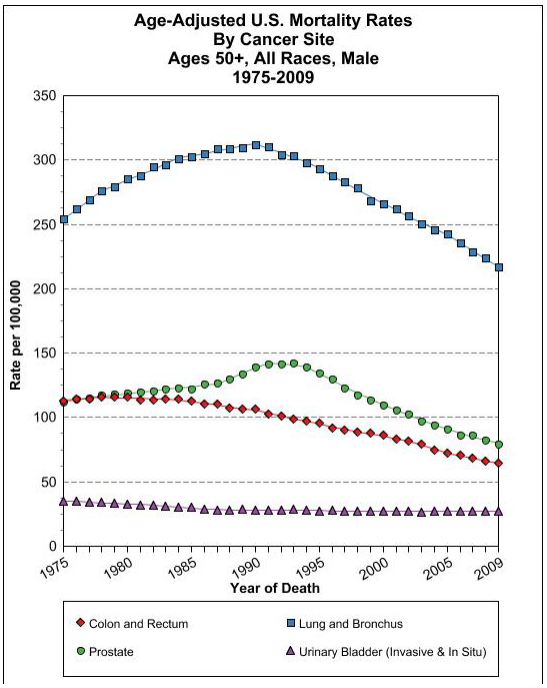
"I have no conflicts of interest to disclose."

Overview

- Prostate Cancer Epidemiology
- The Massachusetts Guideline Panel Process and Recommendations
- Other Organizations' Recommendations
- The Controversy: Summary of the Evidence
- Mitigating Harms and Optimizing Benefits
- Shared Decision Making and Decision Aids
- Shared Decision Making Exercise
- Feedback

Prostate Cancer Incidence and Mortality

- Prostate cancer is the most common cancer in men in the United States.
- In 2012, est. U.S.:
  - 241,740 new cases
  - 28,170 prostate cancer deaths
- 16.5% : Lifetime risk of prostate cancer diagnosis in era of PSA screening (About 10% before PSA)
- 2.8%: Lifetime risk of prostate cancer death in recent years



Prostate Cancer Risk Factors

- Age: Increased risk with age
- Race: Higher risk in African Americans and lower risk in Asians
- Family history: Higher with 1st degree relative

Prostate Cancer Incidence and Mortality In Men by Race/Ethnicity

Race/Ethnicity	New PrCA Cases Per 100,000 /year	PrCA Deaths Per 100,000 /year
White	**144.9**	**21.2**
Black	**228.5**	**50.9**
Asian/Pacific Islander	81.8	10.1
Hispanic [b]	125.8	19.2

http://seer.cancer.gov/statfacts/html/prost.html#incidence-mortality (accessed 11/05/14)

Direct Engagement of Stakeholders in Translating Clinical Effectiveness Research into Clinical Guidelines

- Two year UMass Med School project
- Contract with Patient-Centered Outcomes Research Institute (PCORI)
- Translating research on screening for prostate and lung cancer, into patient-centered guidelines for Massachusetts
- Guidelines to adhere to IOM principles
  1. **Transparency**
  2. **Management of conflict of interest**
  3. **Multidisciplinary, balanced guideline panel**
  4. **Evidence from systematic reviews when possible**
  5. **Document evidence for and strength of recommendations**
  6. **External review**
  7. **Updating**

The Panel Members

With the assistance of MHQP we recruited 21 panel members:

- 6 PCPs
- 6 patients (2 African American men, 4 white men)
- 3 urologists
- 2 health care systems representatives
- 2 payer representatives
- 2 public health representatives

The Panel Process

Evidence Team (ET):

- Reviewed and summarized studies on prostate cancer (PrCA) screening, diagnosis, natural history, epidemiology, and treatment
- Facilitated modeling of Panel screening strategies through relationship with Gulati and colleagues
- Advised Panel on strength of evidence related to proposed recommendations

Professional mediators:

- Facilitated meetings
- Worked on building consensus

Issues Addressed by the Panel

1. Estimated balance of benefits/harms based on review of key RCTs of treatment and screening
2. Process for educating men about possible benefit, harms, uncertainties related to PSA screening
3. Screening strategy (start/stop criteria, PSA level to consider biopsy, screening interval)
   - Minimizing harms
   - Preserving reasonable benefit
4. Implementation issues

Panel Conclusions on Benefits and Harms

- Reasonable to conclude that PSA screening does or does not reduce PrCA mortality
- Given the potential significant benefit, men should have the option of choosing screening
- Potential harms related to early and overdiagnosis with possible early and overtreatment as well as harms directly related to treatment are significant, but will be viewed differently by different individuals

Summary of Panel Recommendations

MHQP PSA Guideline Language

18-49 Years
• Screening and routine discussion of screening are not recommended except for patients at high risk for prostate cancer. • High risk men should be provided with the same screening education and options as men age 50-69, but starting at age 40 or above depending on individual risk. Risk factors include African American ancestry and having a family history* of prostate cancer. **Family history of prostate cancer indicates either a brother or father diagnosed with prostate cancer before age 65.*

MHQP PSA Guideline Language

50 – 69 Years
• Screening for prostate cancer with the prostate specific antigen (PSA) should not be performed or offered routinely without patient education and informed consent. • PSA screening may be offered to men who express a clear preference for screening after demonstrating an understanding of the harms and benefits (e.g. through a shared decision making process) and who have a life expectancy >10 years. For men who express a clear preference for screening after shared decision making: - Screen with PSA every 2 years - For confirmed PSA>4.0 assess/refer for possible prostate biopsy. • Providers are encouraged to make men aware that PSA screening is controversial and associated with a significant risk of harm, but that screening is an option available to them. Providers are also encouraged to facilitate access to information on harms and benefits for men who may be interested in PSA screening.

MHQP PSA Guideline Language

>=70 Years
• Screening and routine discussion of screening are not recommended.

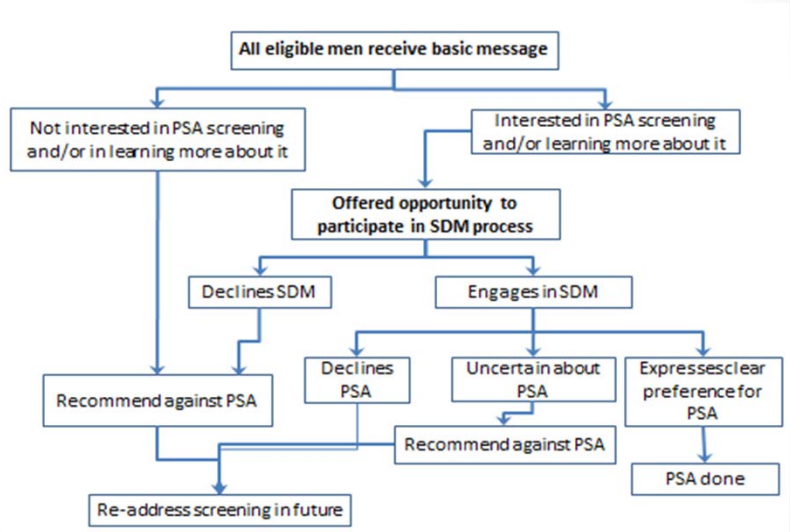
Panel Recommendations

1. All eligible men should be offered the opportunity to find out if they have a clear preference for PSA screening.
2. All eligible men should receive a basic message about PSA screening when they reach the age at which screening could begin or at the next available opportunity.
3. Men interested in learning more about PSA testing should be offered an opportunity to engage in a shared decision making (SDM) process leading to a personal decision for or against getting tested based on each man's values and preferences.
4. Men who are uncertain about PSA screening and/or do not express clear preference for PSA screening after participating in an SDM process should receive a recommendation that they NOT be tested with PSA.

The Basic Message Should Include:

- A brief description of the PSA test.
- Acknowledgment that experts disagree about whether men should get PSA screening.
- A brief explanation of the possible benefits/harms and related evidence.
- A statement about factors that increase the risk for PrCA (African American race, brother or father with prostate cancer) and their impact on benefit/harms.
- A recommendation that men interested in PSA screening engage in a shared decision making process.
- A statement about ongoing research that may in the future reduce potential harms and show which men may most likely benefit from screening.

Recommended Pathway to PSA Screening



Recommendations of Other Organizations

All organizations recommend:

- **Shared decision making and screening only if clear choice**
- **Against screening with < 10 year life expectancy**

	Starting/ Stopping Age Average Risk	Screening Interval	PSA Threshold for Biopsy	African American/ Family Hx
ACP	50/69	> 1 year OK unless PSA>2.5	PSA > 4.0	Earlier age
AUA	55/69	>=2 yrs. OK	No specific standard. Urologist discretion. Usually PSA >3-4	Individualize
ACS	50/69	PSA>=2.5 → 1 yr. PSA<2.5 →2 yrs	PSA >=4.0 "reasonable" Individualize if PSA = 2.5-4.0	Individualize
UPSTF	Screening not Recommended			

The Evidence

Treatment of Prostate Cancer

PIVOT RCT: Prostatectomy vs. Watchful Waiting

Median Years Follow-up	Inclusion Criteria and Study Population	PSA Detected (T1c) Tumors
10.0 years	• Age <75 • Tumor stage T1, T2 • Any grade • PSA<50 • 75% enrolled due to PSA level or change in PSA	50%

PIVOT RCT: Prostatectomy vs. Watchful Waiting

Relative Risk (RR) of Death from PrCA (Treat/Cntrl) (95% CI)	Risk Difference (RD) of Death from PrCA (Treat-Cntrl)	Number Needed to Treat (NNT) to Prevent 1 PrCA Death
All 0.88 (0.71 to 1.08) **PSA>10** 0.36 (0.15 to 0.89) **PSA<=10** 0.92 (0.44 to 1.91)	-2.9/100 (p>.05, Not significant) (2.9 fewer deaths per 100 men treated over 10 years)	34.5 over 10 yrs.

Swedish (Bill- Axelson) RCT: Prostatectomy vs. Watchful Waiting

Median Years Follow-up	Inclusion Criteria	PSA Detected (T1c) Tumors
13.4	• Age <75 • Tumor stage T1b, T1c or T2 • Well/Mod. Differentiated • PSA<50	12%

Swedish (Bill-Axelson) RCT: Prostatectomy vs. Watchful Waiting

Relative Risk (RR) of Death from PrCA (Treat/Cntrl) (95% CI)	Risk Difference (RD) of Death from PrCA over 13.4 yrs. (Treat-Cntrl) (95% CI)	Number Needed to Treat (NNT) to Prevent 1 PrCA Death over 13.4 yrs.
0.56 (0.41 to 0.77) Age<65 0.45 (0.29 to 0.69) Age >=65 0.75 (0.47 to 1.19)	-11/100 (-4.5 to -17.5) (11 fewer PrCA deaths per 100 men treated	8 Age<65 4

Treatment: Conclusions

- Strong evidence for clinically significant PrCA mortality reduction with prostatectomy for cancers that are palpable
- Preliminary evidence for possible mortality reduction with prostatectomy for some PSA detected cancers
- Inconsistent evidence that the benefits of prostatectomy may be limited to subgroups with PSA>10 and/or age <65
- Selecting patients for treatment remains challenging

Harms of Prostate Cancer Treatment

Harms	Likelihood of Harm Occurring
• Perioperative complication/death	• 1-2/1000 deaths within 30 days • Up to 5/1000 deaths <=30 days • 22% - 30 day complication
• Erectile dysfunction (ED)	• Prostatectomy: 37—57% • Radiation – 26-50%
• Urinary Incontinence	• Prostatectomy - 12-16% • Prostatectomy – 8-9% need surgery
• Stricture of urethra	• Prostatectomy - 5-14%
Bowel dysfunction • Increased frequency BMs • Rectal bleeding	 • 4% (Radiation) • 4% (Radiation)

Harms of Prostate Cancer Treatment

Harms	Likelihood of Harm Occurring
• Quality of life effects	Limited evidence suggests major negative effects on quality of life are related to physical adverse effects of treatment and that many men appear to adjust to these effects. However, some studies identify other domains of social and emotional functioning that may be affected by treatment.

The Evidence

Screening for Prostate Cancer

Screening: PLCO (U.S.) RCT of Prostate Cancer Screening

Inclusion	Screen Interval	Biopsy Threshold	Follow-up	Received >= 1 Screen
Age 55-74	Every year	PSA>=4.0	13 years	Int. - 85% Cntrl. -52%

PLCO Mortality Outcomes

PrCA Mortality Comparisons			
Mortality Rate (per 10,000 py)	**Relative Hazard (RH) (Int./Cntrl)**	**Risk Difference (Int. – Cntrl.)**	**Number Needed to Diagnose with PrCA to Cause 1 Excess PrCA Death**
Int. - 3.7 **Cntrl. – 3.4**	**1.09** (0.87 to 1.36) **(9% relative risk increase)**	**+0.39 PrCA deaths/ 1000 over 13 years**	**37 over 13 yrs.**

PLCO: Alternative Interpretations

Pro Screening

- Statistically consistent with up to 13% relative mortality ***reduction***
- Moderate probability contamination caused finding of increased PrCA mortality in screened
- >50% of control group received screening
- Interpretation: Neither supports nor refutes screening effectiveness
- Interpretation: Shows more intense screening in screened population is not effective

Against Screening

- Imperfect trial, but best point estimate suggests harm, not benefit.
- The best study we have with a US population and the US health care system.

ERSPC (European) RCT of Prostate Cancer Screening

Inclusion	Screen Interval	Biopsy Threshold	Follow-up	Received >= 1 Screen
Age 55-69 (7 countries)	q. 2-4 yrs.	PSA >=3	11 years	Int. - 83% Cntrl. - 20%

ERSPC RCT vs. PLCO RCT of Prostate Cancer Screening: Mortality Outcomes

PrCA Mortality Comparisons			Number Needed to Diagnose with PrCA to Prevent 1 PrCA Death
Mortality Rate (per 100,000 py)	Relative Hazard (RH) (Int./Cntrl)	Risk Difference (Int. – Cntrl.)	
Int. - 3.9 Cntrl. - 5.0	0.79 (0.68 to 0.91) (21% Relative Risk Reduction)	-1.1 PrCA Deaths/1000 over 11 years	37 over 11 yrs

ERSPC : Alternative Interpretations

Pro Screening

- Limited contamination
- Consistency across sites
- No reason to believe PrCA biology, treatments delivered different from U.S. men and health care system

Against Screening

- Only 2 of the 7 sites had statistically significant findings
- Largest site (Finland) did NOT have a significant benefit
- Different protocols/eligibility in different countries
- Non-U.S. populations and care systems. Risky to generalize to the U.S.
- Much higher mortality (total & prostate-specific) than in PLCO population, unclear why

Harms Specific to Screening

Overdiagnosis and Overtreatment:

- Diagnosis and possible treatment of cancer that would never have caused symptoms during a man's lifetime

Early diagnosis without mortality benefit:

- Diagnosis and possible treatment of PrCA earlier than would occur without screening such that a man may live longer with knowledge of cancer and possibly harms of treatment than would occur without screening

Harms of PSA Testing and Prostate Biopsy

Harms	Likelihood of Harm Occurring
Psychological harm of + PSA tests	**• Higher short/long term prostate specific anxiety than men with - PSA results**
False positive PSA	
• Moderate anxiety	**• 49%**
• Severe anxiety	**• 6%**
Complications of prostate biopsy	
• Hematuria	**• 6-13%**
• Urinary tract infection	**• 0.3-4%**
• Serious urinary tract infection	**• <2%**

Mathematical Models of Screening Strategies

- Allow testing of different screening strategies (combinations of age to start/stop, interval, biopsy threshold)
- Quantification of benefits and harms

PrCA Screening Models by Gulati et al.

(*Ann Intern Med. 2013;158:145-153.*)

- Mortality component calibrated using data from ERSPC
- Mortality reduction 29% after 11 years
- 35 screening strategies modeled with different combinations of:
  - Starting/stopping age
  - PSA threshold for biopsy
  - Screening interval

Can we trust this model?

Strengths:

- Produces estimates of incidence and mortality that compare favorably to same measures in epidemiologic and clinical studies
- Produces output estimates similar to those other prostate cancer models with different structure
- Multiple layers of review by modeling experts

Weaknesses:

- Complexity and number of assumptions decrease transparency and may increase opportunity for errors in inputs
- Extrapolating risk reduction beyond the time interval of the source RCT may not be justified
- Based on ERSPC findings only; no role for PLCO

Lifetime Model-based Outcomes for 1000 Men Screened Annually from Age 55 to 74

Result	N	Comment
Never diagnosed with prostate cancer • Die from some other cause	784.6	
Diagnosed with prostate cancer • Would have been diagnosed if not screened • Die of other cause • Life not prolonged by screening	115	Live average 5.4 years longer with the diagnosis of prostate cancer and any effects of its treatment than if not screened.
Diagnosed with prostate cancer • Would have been diagnosed if not screened • Die from prostate cancer • Life not prolonged by screening	18.9	Live average 7.0 years longer with the diagnosis of prostate cancer and any harm from its treatment than if not screened
Diagnosed with prostate cancer • Overdiagnosed (Never clinically diagnosed in life) (48% of all cancers diagnosed) • Die from some other cause	71	Live average 10.7 years longer with their diagnosis and any treatment harms than if not screened
Lives prolonged by screening	10.5	Average prolongation is 8.6 years.
Total	1000	

Lifetime Model-based Outcomes for 1000 Men Screened Annually from Age 55 to 74

Result	N	Comment
Never diagnosed with prostate cancer • Die from some other cause	784.6	No harm
Diagnosed earlier than without screening or overdiagnosed and receive no benefit from screening	204.9	Harms: Anxiety of living with diagnosis and/or adverse effects of treatment
Lives prolonged by screening	10.5	Average prolongation is 8.6 years.
Total	1000	

As many as 20 men possibly harmed physically and/or psychologically for every prostate cancer death avoided and life prolonged

Model Outputs for Selected Screening strategies

Policy	Screen Age, y	Screening Interval (A=annual; B=biennial)	PSA Criterion for Biopsy Referral (µg/L)	Mean Screens, n	Prob of ≥ 1 FP Results, (n/1000)	Prob of Overdiag, (n/1000)	Prob Life Saved, (n/1000)
1	40-74	A (every 5 y if <50 yo & PSA <1)	>2.5 or Vel >0.35/yr	21.8	440	60	8.5
25	40-69	B	>2.5	13.6	240	22	5.2
26	50-69	A	>4.0	17.3	170	18	5.1
35	50-69	B	>4.0	8.7	140	13	4.1

Strategies for Reducing Harms of Screening and Related Treatment

- Active Surveillance: Just in time treatment avoids overtreatment of low risk cancer that progresses slowly or not at all
- Higher PSA threshold for biopsy: Reduces diagnosis of indolent cancers but misses from significant cancers
- Longer intervals between screens: Reduces overdiagnosis, number of false positives, and number of PSA tests
- Basing stopping age on PSA level sometime at age 50 or older reduces overdiagnosis and overtreatment

Active Surveillance

- Some observational studies support active surveillance for low risk cancers
- One RCT underway
- Consensus on defining risk and surveillance protocol may be emerging
- Serious psychological impact of living with low risk, untreated cancer documented
- Significant percentage of men switch to active treatment before it is recommended

10 Year Prostate Cancer Mortality Among Untreated Men: PIVOT Study

10 year prostate cancer mortality:

Low risk :	4/147	**(2.7%)**
Intermed. risk :	13/120	**(10.8%)**
High risk:	14/80	**(17.5%)**

Stopping Age

- Population-based case-control study from Malmo, Sweden 1167 men provided a blood sample at age 60, followed to age 85
- For the 50% of men with PSA <1.0 ng/mL at age 60, lifetime risk of prostate cancer death 0.2% (2/1000)
- BLSA cohort 849 men followed over time with PSA
- Predicted lifetime risk of prostate cancer death for ~60% of men with PSA <3.0 ng/mL at age 75 is 0.2% (2/1000)

Shared Decision Making

What is Shared Decision Making?

Shared decision making (SDM) is a collaborative process that allows patients and their providers to make health care decisions together, taking into account the best scientific evidence available, as well as the patient's values and preferences.

SDM honors both the provider's expert knowledge and the patient's right to be fully informed of all care options and the potential harms and benefits. This process provides patients with the support they need to make the best individualized care decisions, while allowing providers to feel confident in the care they prescribe.

(From: Informed Medical Decision Making Foundation website)

Characteristics of Shared Decision Making (USPSTF)

The patient should:

1. Understand the **risk or seriousness of the disease** or condition;
2. Understand the **preventive service** (screening test, follow-up testing, disease treatment), including the **risks, benefits, alternatives, and uncertainties**
3. Have **weighed his or her values** regarding the potential harms and benefits associated with the service;
4. Have **engaged in decision-making** at the level at which he or she desires and feels comfortable.

Shared Decision Making Steps

1. Invite patient to participate
2. Present options
3. Provide information on benefits and harms
4. Assist patient in evaluating options based on their goals, values and concerns
5. Facilitate deliberation and decision making
6. Assist with implementation

Decision Aids

Tools that help people become involved in decision making by:

- Providing information about the options and outcomes and
- Clarifying personal values.

They are designed to complement, rather than replace, counseling from a health practitioner

(From: http://decisionaid.ohri.ca/index.html)

Decision Aids: Cochrane Review

- Improve knowledge and realistic expectations;
- Enhance active participation in decision making;
- Lower decisional conflict;
- Decrease the proportion of people remaining undecided, and
- Improve agreement between values and choice.

UMass PSA Informed Decision Making Study

- Patients referred by PCPs
- Mailed Decision Aid (Booklet)
- 95% read booklet before call
- Telephone counseling call
  - About 30 minutes
  - Review of material in Decision Aid
  - Values Clarification
- Decision at end of call and at 3 months

Is Getting the Prostate Cancer Test the Right Decision for Me?

Read this booklet to learn why there is no right or wrong answer to this question.

Please save this booklet for the telephone call.

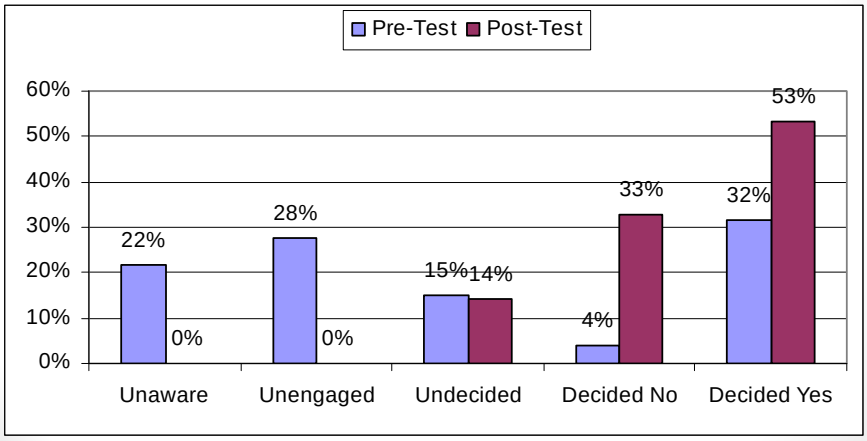
Your Health Educator can help you decide if getting tested is the right decision for you.

SHOULD YOU GET THE PSA TEST?

How much do the reasons listed below matter to you in making a decision about the PSA test?

Reasons you have FOR getting the PSA test		Reasons you have AGAINST getting the PSA test	
Worry less about prostate cancer	*****	Other health problems that are more important	*****
Prostate cancer could hurt or kill me	*****	Prostate cancer may never cause me any problems	*****
Better chance for a cure	*****	Treatment could ruin my sex life	*****
I want know it if I have prostate cancer	*****	Treatment could cause me to leak urine	*****
May help me live longer	*****	May not help me live longer	*****

Decision Stage Pre-Test and Post-Test (n=92) 63% Change Stage



Shared Decision Making (SDM) Exercise

Part 1: Patient Perspective

- Assume the role of a patient
- You are at average risk for prostate cancer
- Clinic visit for routine periodic health assessment
- Receives and reads previsit Decision Aid on PSA testing before the visit
- What do you understand about PSA testing based on reading?
- What questions and concerns do you want to address with your PCP?

Patient A:

- **50 years old, married with 2 children ages 15 and 18**
- **Very health conscious in recent years:**

  Quit smoking 5 year ago, moderate alcohol use, regular exercise, colonoscopy to screen for colon cancer at age 50, overweight but losing weight on diet
- **Cousin died from prostate cancer at age 60, 2 years ago**
- **Likes to make his own decisions on health matters**

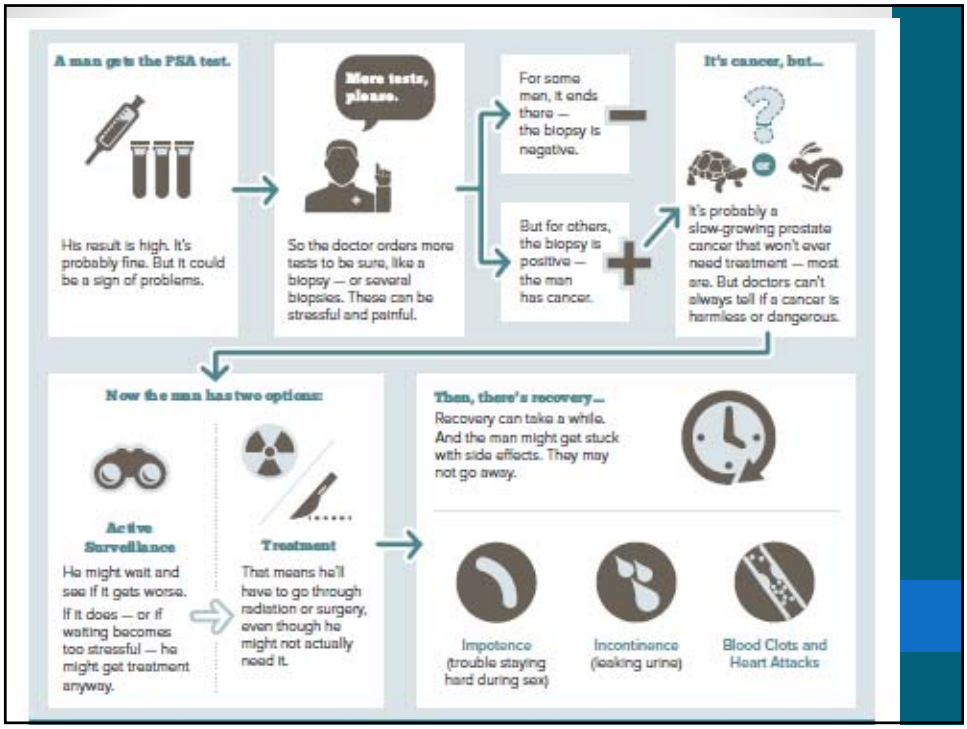
Patient B:

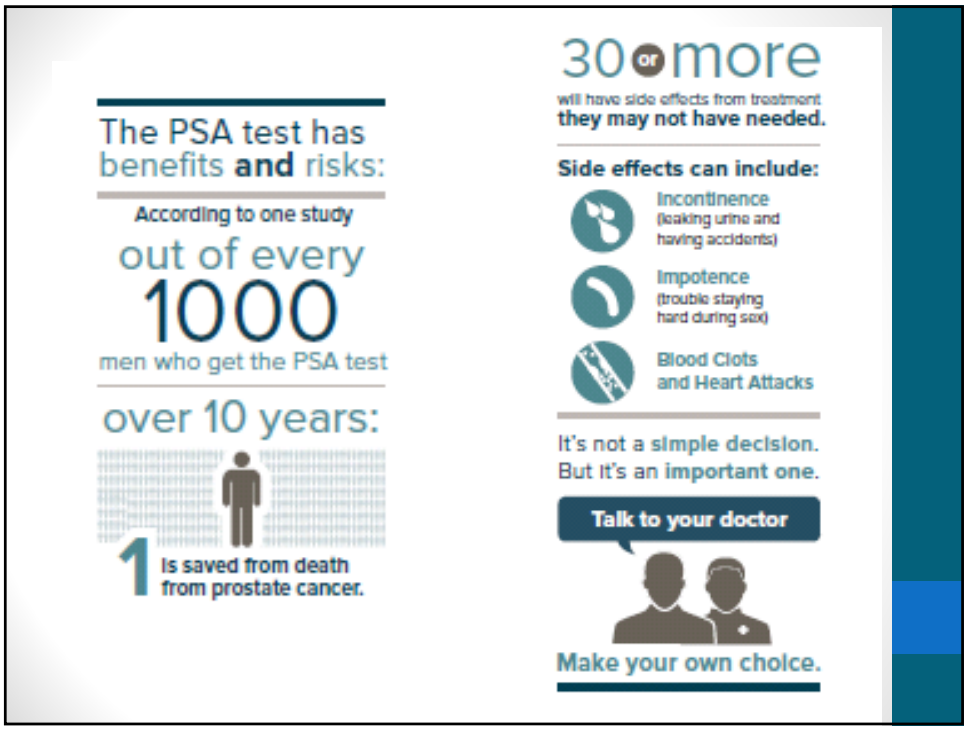
- **New patient, 63 years old, unemployed, widower with 2 grown children**
- **Post-MI at age 60 with no CHF or angina, adheres to CAD preventive medications, current smoker with intention to make 5th quit attempt soon, overweight, sedentary**
- **Is used to having PCP provide clear advice on health matters and complies to the best of his ability, has done annual FIT testing for last 5 years**
- **Previous PCP never mentioned prostate cancer screening**

Part 2: Provider Perspective

- You have 10-15 minutes to engage your patient in shared decision making about PSA testing
- Assume he has read the previsit Decision Aid
- What are the most important things you want him to understand about PSA screening?
- How could you use the Decision Aids in your discussion?
- How would your address the questions your patient may ask?

Questions?


A man gets the PSA test.
His result is high. It's probably fine. But it could be a sign of problems.
More tests, please.
So the doctor orders more tests to be sure, like a biopsy — or several biopsies. These can be stressful and painful.
For some men, it ends there — the biopsy is negative.
But for others, the biopsy is positive — the man has cancer.
It's cancer, but...
It's probably a slow-growing prostate cancer that won't ever need treatment — most are. But doctors can't always tell if a cancer is harmless or dangerous.
Now the man has two options:
Active Surveillance
He might wait and see if it gets worse.
If it does — or if waiting becomes too stressful — he might get treatment anyway.
Treatment
That means he'll have to go through radiation or surgery, even though he might not actually need it.
Then, there's recovery...
Recovery can take a while. And the man might get stuck with side effects. They may not go away.
Impotence (trouble staying hard during sex)
Incontinence (leaking urine)
Blood Clots and Heart Attacks


The PSA test has benefits and risks:
According to one study
out of every
1000
men who get the PSA test
over 10 years:
1 is saved from death from prostate cancer.
30 or more
will have side effects from treatment they may not have needed.
Side effects can include:
Incontinence (leaking urine and having accidents)
Impotence (trouble staying hard during sex)
Blood Clots and Heart Attacks
It's not a simple decision. But it's an important one.
Talk to your doctor
Make your own choice.