



U.S. Preventive Services Task Force: Draft Prostate Cancer Screening Recommendation (April 2017)

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Disclaimer

This presentation is being made on behalf of the U.S. Preventive Services Task Force (USPSTF). Some views expressed by the presenter, however, may not reflect the process and recommendations of the USPSTF. For the current findings and recommendations of the USPSTF, please see: www.uspreventiveservicestaskforce.org.

Goals

- Explain the general methods used by the U.S. Preventive Services Task Force (USPSTF) in making recommendations
- Understand the recent draft recommendation statement from the USPSTF about prostate cancer screening
- Discuss the basis for the change from a “D” to a “C” recommendation for prostate cancer screening
- Assess potential implementation issues associated with the 2012 and 2017 recommendations

What is the Task Force and what does it do?

Learn about the USPSTF



General USPSTF Methods

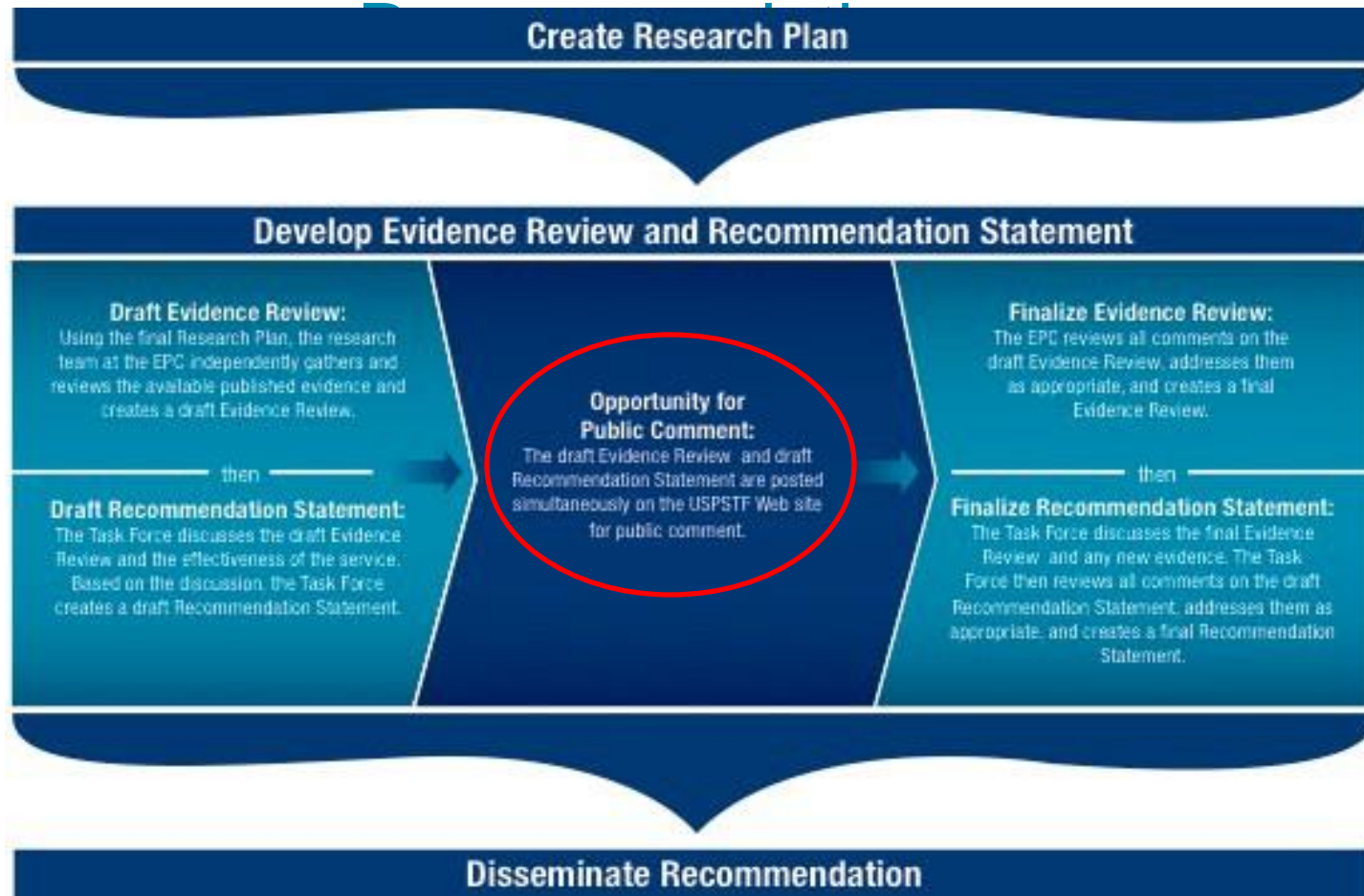
The U.S. Preventive Services Task Force...

- Makes recommendations on clinical preventive services to primary care clinicians
- The USPSTF scope for clinical preventive services include:
 - Screening tests
 - Counseling
 - Preventive medications
- Recommendations address only services offered in the primary care setting or services referred by a primary care clinician.
- Recommendations apply to adults & children with no signs or symptoms

USPSTF Members

- 16 volunteer members from primary care including family medicine, internal medicine, nursing, obstetrics/gynecology, pediatrics, and behavioral medicine
- Led by a Chair & Vice Chairs
- Serve 4-year terms
- Appointed by AHRQ Director with guidance from Chair & Vice Chairs
- Complete a rigorous review of potential conflicts of interests
- Consult with external subject matter experts through Evidence-based Practice Centers and Partners

Steps the USPSTF Takes to Solicit Public Input and Make a



The USPSTF Steps: Brief and Generic

- The USPSTF assesses the evidence across the analytic framework:
 - Judges the ***certainty*** of the estimates of the potential benefits and harms
 - Judges the ***magnitude*** of the potential benefits and harms
 - The ultimate goal is to judge the ***balance*** of the benefits and harms, or the ***magnitude of the net benefit*** of the preventive service
- When evidence is insufficient (low certainty), the USPSTF *does not* use “expert opinion”

Basic USPSTF Methods for Developing Recommendations: The Letter Grades

Certainty of Net Benefit	Magnitude of Net Benefit			
	Substantial	Moderate	Small	Zero/Negative
High	A	B	C	D
Moderate	B	B	C	D
Low	I—insufficient evidence			

Which
preventive services
does the **Task Force**
recommend and why?

Search recommendations



Prostate Cancer Draft Recommendation Statement April 2017

Prostate Cancer in the United States

- 2.5 million American men diagnosed and living with prostate cancer
- Many men with prostate cancer never experience symptoms, and without screening, would never know they have it
 - 20% of men 50-59 years who died of other causes had prostate cancer on autopsy, and over 50% for men over 80 years
- Prostate cancer is the third leading cause of cancer deaths among men in the U.S.
- In 2016, 26,000 men died from prostate cancer

Higher Risk Populations

- African American men are twice as likely as white men to die from prostate cancer (44.1 vs. 19.1 per 100,000)
 - This is due to onset at a younger age, more advanced cancer stage at diagnosis, and higher rates of advanced cancer
- Men with a family history are more likely to develop prostate cancer
 - From the Finnish ERSPC site, men with a first degree relative with prostate cancer were 30% more likely to be diagnosed with cancer
 - But with high screening rates for prostate cancer in the U.S., more men have a father, brother, or son with a history of prostate cancer

History of USPSTF's Prostate Cancer Recommendations

- Prior to 2012: “I” recommendation – insufficient evidence to recommend for or against prostate cancer screening
- 2012-current: “D” recommendation – recommends against PSA-based prostate cancer screening
 - “Although the USPSTF discourages the use of screening tests for which the benefits do not outweigh the harms in the target population, it recognizes the common use of PSA screening in practice today and understands that some men will continue to request screening and some physicians will continue to offer it. The decision to initiate or continue PSA screening should reflect an explicit understanding of the possible benefits and harms and respect patients' preferences.”

Draft Recommendation Statement April 2017

Draft: Recommendation Summary

Population	Recommendation	Grade (What's This?)
Men ages 55 to 69 years	<p>The USPSTF recommends that clinicians inform men ages 55 to 69 years about the potential benefits and harms of prostate-specific antigen (PSA)-based screening for prostate cancer.</p> <p>The decision about whether to be screened for prostate cancer should be an individual one. Screening offers a small potential benefit of reducing the chance of dying of prostate cancer. 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 impotence. The USPSTF recommends individualized decisionmaking about screening for prostate cancer after discussion with a clinician, so that each man has an opportunity to understand the potential benefits and harms of screening and to incorporate his values and preferences into his decision.</p> <p>Please refer to the Clinical Considerations sections on screening in African American men and men with a family history of prostate cancer for more information on these higher-risk populations.</p>	C
Men age 70 years and older	The USPSTF recommends against PSA-based screening for prostate cancer in men age 70 years and older.	D



Key Elements of the April 2017 Draft Recommendation

- Men age 55 to 69 – clinicians inform men ages 55 to 69 years about the potential benefits and harms of prostate-specific antigen (PSA)–based screening
 - Decision about whether to be screened... an individual one
 - Small potential benefit of reducing chance of dying of prostate cancer
 - Many men will experience potential harms... false positives... overdiagnosis... overtreatment
 - Each man has an opportunity to... incorporate his values and preferences into his decision
- Men age 70 and older – recommends against PSA-based screening

Key Elements of the April 2017 Draft Recommendation

- No specific interval to discuss screening stated, but we highlight that in ERSPC (the positive trial), screening was no more frequent than every 2 years, and some every 4 years
- No specific recommendation for African American men or men with a family history of prostate cancer
 - “C” recommendation applies to these groups
 - Language to help guide clinicians and patients in making decisions
 - Specific call for research on screening in these groups

What a “C” Recommendation Means

	<p>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.</p>	<p>Offer or provide this service for selected patients depending on individual circumstances.</p>
	<p>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.</p>	<p>Discourage the use of this service.</p>

- A “C” means to **SELECTIVELY** offer or provide the service
- It includes both (a) professional judgement and (b) patient preferences
- It does not mean to *routinely* screen men
- Community-based or population screening should not be done in the absence of shared decision-making

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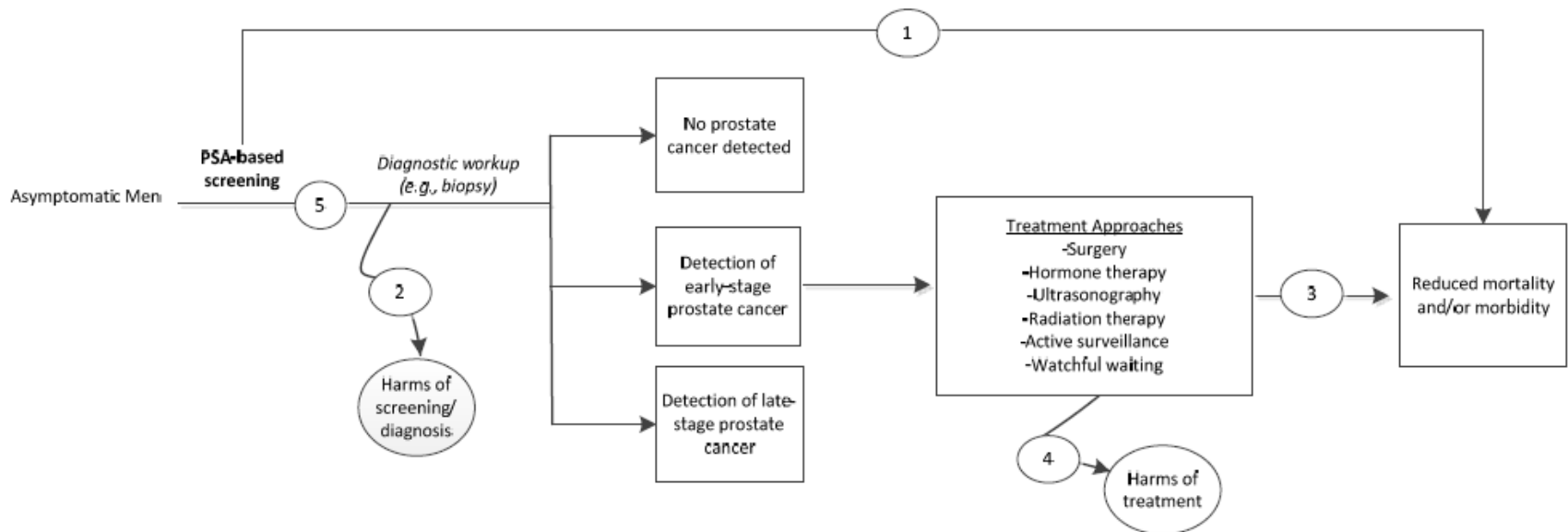


So Why the Change?

Basis for Change from “D” to “C” Recommendation

- Extended follow-up ERSPC trial increased the confidence in the benefits of screening, which continued to show a reduction in prostate cancer mortality
 - Also, new evidence that 3 men per 1,000 screened may avoid metastatic disease
- An increase in the use of Active Surveillance as a treatment for prostate cancer may mitigate some of the harms of screening and subsequent treatment
- What has not changed is that the balance of benefits and harms remains close, requiring individualized decision-making

Analytic Framework for the Systematic Evidence Review and Two Contextual Reviews



- Contextual Review 1 – Overview of Prostate Cancer Screening Decision Models
- Contextual Review 2 – Overdiagnosis in Prostate Cancer Screening Decision Models

Key Decision Considerations

- Evidence was largely influenced by two KQ1 RCTs – PLCO and ERSPC
 - PLCO (n=76,693) may be viewed as a trial of organized versus opportunistic screening due to high rate of screening in the control group
 - ERSPC (n=182,160) has heterogeneous protocols and treatments – even between intervention and control groups (which may inflate differences)
- A key decision point was how to balance benefits versus harms
- Historically, enthusiasm for screening has outweighed the evidence on the value for screening
- The benefits of screening may be proportional to the aggressiveness of screening and thus the potential for harm.
 - Screening strategies that mitigate harms, may diminish potential benefits

Direct Evidence (KQ1) Was Central to USPSTF Recommendation

Characteristic	PSA Screening Trial	
	PLCO	ERSPC
Sample size	N=76,693 (ages 55-74 y)	N=162,388 (ages 55-69 y, "core" age group) N=182,160 (ages 50-74 y)
Setting, Years	10 U.S. Centers, 1993-2001	8 European countries, 1993-2003
Interval	Annual (up to 6 rounds)	4 y (2 y in Sweden)
PSA threshold	4 ng/mL	Varied by site/year, usually 3 ng/mL
Biopsy after abnormal screen	44.8%	88.8%
Median followup	14.8 y (mortality) 13.0 y (cancer incidence) (vs. 7 y in prior review)	13.0 y (vs. 9 y in prior review)
Quality rating	Fair	Fair

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Outcomes with Extended Follow-up

ERSPC

- 2009 (9 years) – 0.71 death averted per 1000 men randomized
- 2012 (11 years) – 1.07 deaths averted per 1000 men randomized
- 2014 (13 years) – 1.28 deaths averted per 1000 men randomized
 - And 3 cases of metastatic cancer averted per 1000 men randomized

PLCO

- No reduction in mortality

Active Surveillance

- From three KQ3 trials comparing radical prostatectomy vs. active surveillance or watchful waiting:
 - No difference in mortality
 - More metastatic disease with active surveillance compared to radical prostatectomy in 1 trial (ProtecT), but need additional studies with longer term follow-up to verify
- Active surveillance may be a means to mitigate or delay harms
- Increase in the use of active surveillance in the U.S. from 10% of low grade prostate cancer cases in 2005-2009 to 40% of cases | 2010-2013 (JAMA 2015;314(1):80-82)

Harms

- False-positive screening: 10-18% of men undergoing ≥ 1 screening
- 44% of men having a positive test underwent biopsy (PLCO); $>80\%$ in ERSPC
- Biopsy associated with moderate/severe pain or fever in 5-7% of men
- At 13 years, 21-50% of screen-detected cancers are likely to be overdiagnosed
- One third of men have erectile dysfunction or incontinence from radical prostatectomy or radiation therapy

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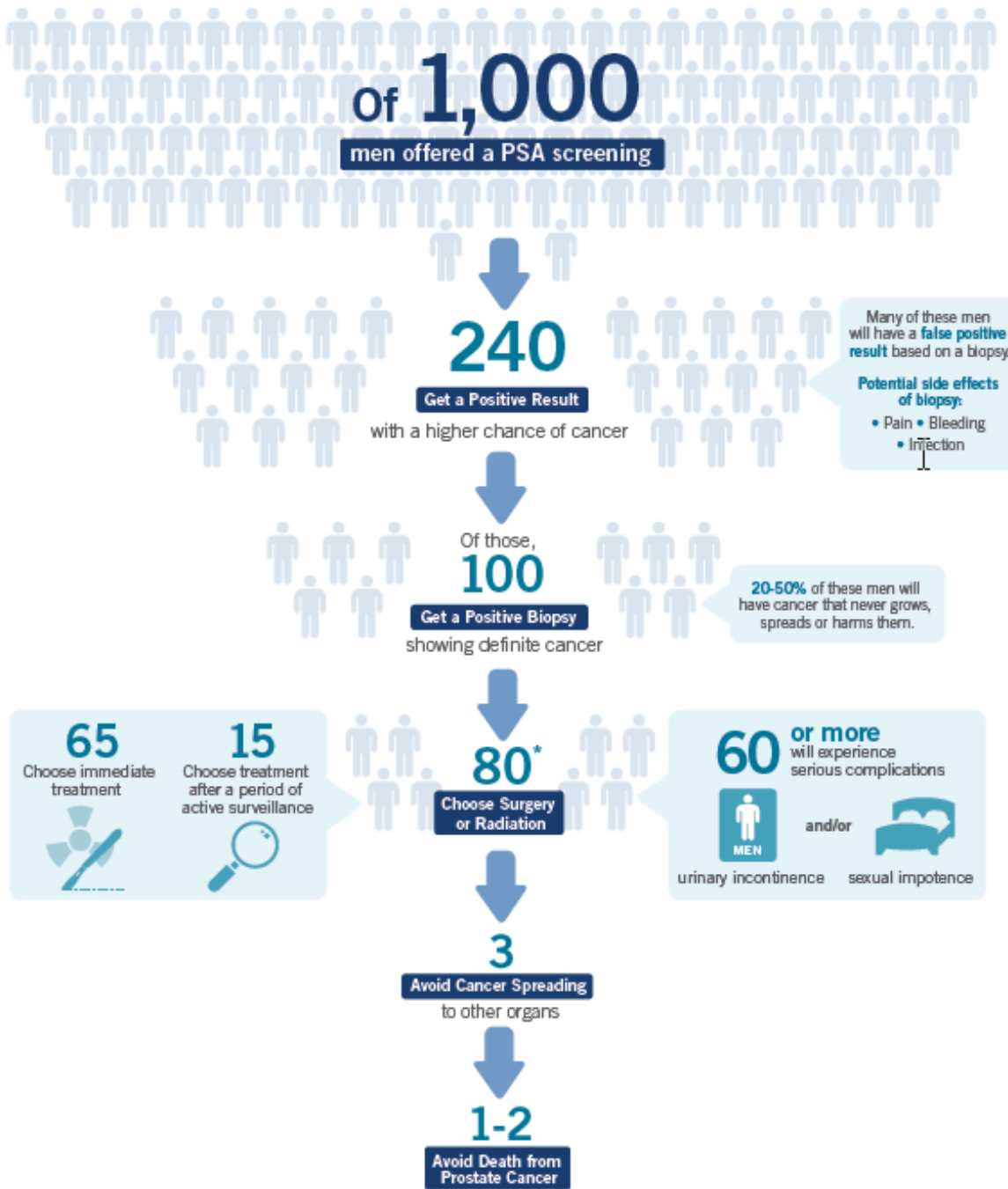
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Implementation Issues

Why No Recommendations for High Risk Groups

- No significant interaction of screening impact by age (PLCO, ERSPC) or comorbidity (PLCO)
- No analysis on differential effects by race/ethnicity
 - Low numbers of non-whites in PLCO (n=3,370 non-Hispanic black men, 4.4% of sample)
 - Not reported in ERSPC, but suspect low numbers of blacks
- Family history (PLCO, n=4,833 white men with a family history)
 - HR for prostate cancer death = 0.49, 95% CI: 0.22-1.10
 - No formal test for interaction and likely underpowered



Putting it all together
(for patients)

Implementation Challenges

- Some may INCORRECTLY interpret a change from a “D” to a “C” as implying that all men should be screened
- Doing shared decision-making is difficult
 - Allen Brett, *Journal Watch*, 5/15/17, “...conveying the probabilities and combinations and permutation of all the downstream events that happen when one initiates PSA screening – and somehow assimilating those probabilities into a patient’s “values and preferences” (the USPSTF’s language) – is a daunting, if not an impossible task during primary care office visits.”

Identified Evidence Gaps

- Comparing different screening strategies, including different screening intervals
 - Screening for and treatment of prostate cancer in African American men and men with a family history of prostate cancer
 - How to better inform men with a family history of prostate cancer about the benefits and harms of PSA-based screening
 - How to refine active prostate cancer treatments to minimize harms
 - How to better understand patient values about the known benefits and harms of screening for and treatment of prostate cancer
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