

The Politics of Prostate Cancer Screening

Samuel D. Kaffenberger, MD^a,
David F. Penson, MD, MPH^{b,c,*}

KEYWORDS

- Prostate cancer • Localized • Screening • Prostate-specific antigen
- United States Preventive Services Task Force

KEY POINTS

- There is a perception among policymakers that effective screening programs that identify patients at high risk for a disease or diagnose a condition earlier in its disease course may result in reduced health care costs.
- Much disagreement exists among government agencies, payers, and policymakers concerning whether prostate cancer screening using the prostate-specific antigen test should be a component of routine preventive health care maintenance for American men.
- In the case of the United States Preventive Services Task Force (USPSTF), one can argue that politics plays a role in the development of guidelines, and that this has influenced their recommendation concerning prostate cancer screening.
- Efforts are currently under way to improve the efficiency and transparency of the USPSTF in the form of the USPSTF Transparency and Accountability Act of 2013.
- It is of particular importance that urologists have a voice in the creation of health policy for conditions that we directly diagnose and treat.

Preventive screenings are recognized as an important part of routine health care maintenance and are routinely promoted by governmental agencies, such as the Centers for Disease Control and Prevention, the Agency for Healthcare Research and Quality (AHRQ), and the National Institutes of Health. There is a general perception among policymakers that effective screening programs that identify patients at high risk for a disease or diagnose a condition earlier in its disease course may result in reduced health care costs down the line. In the case of cancer, while primary prevention through behavior modification or other interventions is most desirable, it is often not feasible and, as such, the goal of most cancer screening

interventions tends to be secondary prevention, identifying the malignancy earlier in the disease course and rapidly initiating effective therapies that affect outcomes. The last clause of this sentence is critical, as a screening program that identifies a disease at an earlier stage but does not ultimately reduce morbidity and/or mortality would be considered ineffective and a waste of limited health care resources. An example of an effective cancer screening intervention that has been widely endorsed by payers, government agencies, and policymakers is the regular use of the Papanicolaou (Pap) test to screen for cervical cancer. Because there is solid evidence that the Pap test identifies cervical cancer at an earlier stage and

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^a Department of Urologic Surgery, Vanderbilt University, 2525 West End Avenue, Nashville, TN, USA;

^b Department of Urologic Surgery, VA Tennessee Valley Geriatric Research, Education, and Clinical Center (GRECC), Vanderbilt University, 2525 West End Avenue, Nashville, TN, USA; ^c Center for Surgical Quality and Outcomes Research, Vanderbilt University, 2525 West End Avenue, Suite 1200, Nashville, TN 37203-1738, USA

* Corresponding author. Center for Surgical Quality and Outcomes Research, Vanderbilt University, 2525 West End Avenue, Suite 1200, Nashville, TN 37203-1738.

E-mail address: david.penson@vanderbilt.edu

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also that morbidity and mortality from the disease are reduced as a result of testing,¹ there is no controversy surrounding the use of or payment for this test in cervical cancer screening.

Inherent in any discussion concerning screening policies is a natural tension that develops between making population-wide recommendations concerning a health care intervention and advising individual patients in the setting of clinical decision making. As urologists, we are trained to view and treat each patient individually, and to consider unique preferences concerning outcomes when counseling patients regarding clinical decisions. By contrast, however, policymakers consider health care interventions at the level of the population, balancing the harms and benefits of a screening program in the aggregate. This approach can result in a population-level recommendation that may be in conflict with an individual patient's preferences and desires. This conflict holds particularly true in a situation where a screening intervention is shown to have a positive effect on disease-related morbidity and/or mortality, but is also associated with a set of harms that may outweigh the benefits of early detection. Such is the case in prostate cancer screening, where there is evidence that screening clearly allows us to detect the disease at an earlier stage and reduces mortality,² but where there exists great controversy regarding whether the morbidity and mortality benefits of screening outweigh the harms. In turn this has resulted in disagreement between government agencies, payers, and policymakers concerning whether prostate cancer screening, using the prostate-specific antigen (PSA) test, should be a component of routine preventive health care maintenance for American men.

The various organizations that generate guidelines regarding PSA screening have major differences in perspective (population vs individual) that are reflected in their approach to developing these guidelines. For example, organizations such as the National Comprehensive Cancer Network and the European Association of Urology use a consensus process for setting guidelines,^{3,4} based primarily on expert opinion and interpretation of the available literature. This approach is consistent with the fact that these organizations consist primarily of providers and the goal of their guidelines is to provide insight into the treatment of individual patients. By contrast, organizations such as the United States Preventive Services Taskforce (USPSTF), the American Urological Association, and the American Cancer Society use a different, evidence-based approach to the development of guidelines.^{5,6} In the particular

case of the USPSTF, however, one can argue that politics plays a role in the development of guidelines and that this influenced their recommendation concerning prostate cancer screening. This article discusses the history of the USPSTF and how it arrived at its recommendation, and suggests future advocacy efforts that will result in a more inclusive guidelines process.

THE HISTORY AND MISSION OF THE USPSTF

Originally formed in 1984, the USPSTF is a government-appointed panel of 16 volunteer members, each serving a 4-year term.⁵ Members of the panel are appointed by the director of the AHRQ (1 of 12 agencies under the auspices of the US Department of Health and Human Services) with the guidance of the Chair and Vice-Chair of the Task Force. Although the task force is funded by AHRQ, it operates quasi-independently of this agency, in that it receives funding and administrative support from AHRQ, but the agency has no further oversight in the decision-making process. The task force members are gathered from the fields of primary care and preventive medicine, including family medicine, internal medicine, pediatrics, obstetrics and gynecology, behavioral health, and nursing. Noteworthy is that no specialty fields are represented on the panel.

The stated mission of the USPSTF is "to evaluate the benefits of individual services based on age, gender, and risk factors for disease; make recommendations about which preventive services should be incorporated routinely into primary medical care and for which populations; and identify a research agenda for clinical preventive care."⁵ It is worth noting that the USPSTF is specifically prohibited from assessing the cost-effectiveness of the preventive services it evaluates. The services or topics that are evaluated are chosen by the USPSTF from public nominations (available at <http://www.uspreventiveservicestaskforce.org/ftopicnon.htm>) at 1 of 3 annual USPSTF meetings. The public can nominate a new topic for consideration or suggest reconsideration of a previously evaluated topic because of availability of new evidence, presence of novel screening tests supported by evidence, or changes in the public health status of a condition. Recommendations by the USPSTF are reviewed every 5 years if no instigating factor has caused them to be assessed at an earlier time point.

When USPSTF makes a recommendation regarding a clinical preventive service, it begins establishing key research questions and

commissioning a comprehensive systematic review of the literature around the topic. Although the task force weighs randomized clinical trials (level I evidence) most heavily, it does sometimes consider lower levels of evidence, such as observational studies or modeling studies. This area is one of those where politics can be injected into the task force recommendation through the inclusion or exclusion of certain types of studies based on the level of evidence. Once the systematic review of the literature is completed, the task force then meets in private, and usually does not consult disease-content experts to assist in its deliberations. The panel arrives at a draft recommendation that is then released for public comment. After the public comment period, the task force then reviews the comments and responds as it feels appropriate. It is not, however, obligated to respond to all comments. It then releases a final recommendation.

As shown in **Table 1**, the USPSTF assigns a letter grade from A to D to its recommendation regarding the particular service. Services graded an A or B are generally recommended, as there is at least a moderate certainty of net benefit. Services graded C are recommended to be selectively offered based on patient preference and/or professional judgment, owing to the likelihood of a small net benefit. Services graded D are not recommended because of a lack of net benefit, or because the benefits are outweighed by the harms. All services for which there is insufficient evidence to adequately evaluate the benefits or harms are graded an I.

The political ramifications of the USPSTF recommendations cannot be understated. Beyond the influence of the recommendations on individual patients and practitioners to commence or terminate a preventive service, the Patient Protection and Affordable Care Act (PPACA), as written, mandates full coverage with no copayment by Medicare for those preventive services that receive an A-grade or B-grade recommendation. Conversely, if a service is graded a C, D, or I, Medicare does not necessarily have to cover the service and, if it does, beneficiaries are expected to make a copayment. Obviously this has a significant impact on access to care, and may result in patients who might garner a benefit from a preventive service not receiving it.

THE USPSTF AND PROSTATE CANCER SCREENING

In May 2012, USPSTF concluded that the harms of PSA screening outweighed the potential benefits, and gave PSA screening for early detection of

Table 1
USPSTF grades for recommendations regarding clinical preventive services

Grade	Definition
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial
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
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
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
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

prostate cancer a grade D recommendation.^{2,7,8} This recommendation was based primarily on 2 randomized clinical trials: the Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer screening trial from the United States, and the European Randomized Study of Screening for Prostate Cancer (ERSPC).^{2,8} Although a discussion of the strengths and weaknesses of each of these studies is beyond the scope of this article, it bears mentioning that the task force: (1) did not consider modeling studies that document a greater benefit for screening than was seen in either of the clinical trials⁹; (2) likely overestimated the mortality and other harms associated with treatment through the use of older studies¹⁰; and (3) did not adequately weigh the results of the strongly positive Göteborg trial¹¹ in its deliberations.

The larger question is: why did the Task Force handle the evidence in this manner? It is the authors' opinion that, before even starting the literature review, the Task Force had decided that it was going to recommend against prostate cancer screening. Prostate cancer care represents a significant economic burden to Medicare.¹² In addition, already overworked primary care providers really do not have the time to adequately counsel patients regarding the benefits and harms of prostate cancer screening. To this end, it would be easier and politically expeditious for the Task Force to recommend against prostate cancer screening as opposed to keeping an I recommendation or giving it a C recommendation (which would require primary care providers to spend significant amounts of time counseling men regarding PSA testing). When one considers the USPSTF's prior actions around prostate cancer screening, this argument seems to be even more valid.

Before publication of the ERSPC and PLCO trial mortality results in 2009, there was little high-quality, randomized controlled trial data with which to inform USPSTF recommendations.^{2,8,13–15} That being said, the USPSTF still addressed the issue for the first time in 2002. The 2002 USPSTF report on PSA screening allowed data not only from randomized controlled trials but also from case-control studies and observational studies. Because study results were equivocal and contradictory, the Task Force concluded that there was insufficient evidence to provide a recommendation (grade I).^{13,16–19}

In the 2008 report, the Task Force restricted the evidence used to inform their recommendation with regard to assessing whether a morbidity or mortality benefit existed from PSA screening.^{20,21} This action would have been reasonable if there had been impactful new level I evidence on screening to inform the discussion, but at that time there were no new completed trials. Rather, the Task Force extrapolated early results from the Scandinavian Prostate Cancer Group Study 4 (SPCG-4), a trial comparing radical prostatectomy with watchful waiting, to recommend against screening for men older than 75 years (grade D).²² Interestingly the Task Force did allow the use of cross-sectional and observational studies to inform the key question assessing the harms of PSA screening (other than overtreatment) in the 2008 report. The presumed reasoning behind the inclusion of these lower levels of evidence was that there were no clinical trials available, and none planned to explore this issue. Still, the authors contend that one could have made the same argument for the key question regarding the benefits of screening.

Because there were few such randomized controlled trials available at that time for men younger than 75, a grade I was again assigned.^{14,15} The USPSTF acknowledged that they were waiting for the results of ERSPC and PLCO and, in the authors' opinion, implied in their report that unless these trials were strongly positive, the Task Force would issue a D recommendation after their release.

When the results from the ERSPC and PLCO trials were published in 2009, the USPSTF immediately began a new evidence review, which was published in 2011 ahead of the new USPSTF recommendations for PSA screening in 2012.²³ This maneuver was an unusual one that likely resulted from the backlash the USPSTF had recently received after publication of the clinical recommendations for screening mammography for early detection of breast cancer.²⁴ It is worth considering the USPSTF decision on prostate cancer screening in the context of the public response to the USPSTF decision on mammography and the political backlash that occurred as a consequence. Simply put, if the USPSTF had released its recommendation on prostate cancer screening concurrently with its recommendation on mammography (which likely was its original plan, given the publication date of the evidence review), it is entirely possible that there would have been congressional action to defund the USPSTF and, possibly, its parent agency AHRQ.

THE USPSTF AND BREAST CANCER SCREENING

In November 2009, the USPSTF released a recommendation statement on screening for breast cancer. Differing from common practice at that time, routine mammography for women aged 40 to 49 years was not recommended and was given a grade D recommendation, despite the confirmation of a mortality benefit in the USPSTF evidence review of screening mammography in this age group. Biennial screening mammography was recommended for women aged 50 to 74 years (grade B). The rationale for this was presumably attributable to the decreased magnitude of effectiveness of mammography screening in the younger age group (number needed to invite for screening mammography to extend one patient's life: 1904 patients for those aged 40–49 and 1339 patients for those aged 50–59).²⁴ It is interesting to consider how the USPSTF arrived at these estimates. The Task Force used simulation models that were developed by researchers from the CISNET breast cancer group.²⁵ The models assessed the cost-effectiveness of screening for breast

cancer, which is surprising given that the USPSTF specifically states on their Web site that they do not consider economic costs in their decision-making process.²⁵ Critics of the USPSTF recommendation on breast cancer screening even contend that the Task Force did not accurately estimate the number needed to invite when they made their final recommendation.²⁶

Although it is unclear whether this is definitively the case, there is certainly some merit to the claim and it begs several questions. First, why is the USPSTF using cost-effectiveness models when it explicitly states it is not going to consider cost; second, are their estimates of effect accurate; and third, why are they even using models in the first place if they state that they only will allow level I evidence to document a benefit? Their own meta-analysis of the trials for mammography in women aged 40 to 49 documents that there is a benefit, so it seems that additional modeling would only be needed if the results of the meta-analysis did not fit with the Task Force's political agenda. Of note, there are similar models for prostate cancer screening that document a benefit,²⁷ but in the case of PSA screening the USPSTF established a different set of rules for reasons unclear.

Regardless, the outcry from professional organizations, patient advocacy groups, the media, and the public at large to the mammography decision was strident and defiant. Elected officials were pushed into action and indeed, Secretary Sebelius of the Department of Health and Human Services advised that screening mammography continue to start at age 40 years. Within a month, the USPSTF altered the language of the recommendation for women aged 40 to 49 to reflect the individual nature of the decision to undergo screening mammography without recommending against screening (but maintained a grade D recommendation).

Unfortunately, there was no similar public outcry with the release of the prostate cancer recommendations. Although the American Urological Association (AUA) expressed "outrage" at the decision, this carried little weight, presumably because, as specialists who may stand to gain professionally and financially from prostate cancer screening, we are viewed as irreversibly biased. Had there been a strong response from the patient advocacy community and the media, however, things might have been different, as these stakeholders have considerably more political clout. Unfortunately, although there was pushback from the patient advocacy groups it was somewhat muted compared with the response to the mammography decision, and ultimately it had little effect.

POLITICAL NEXT STEPS IN THE PROSTATE CANCER SCREENING DEBATE

The discussion around prostate cancer screening is far from over. Since the release of the USPSTF recommendation, numerous other organizations have issued guidelines on the topic. The American College of Physicians,²⁸ The European Association of Urology,²⁹ the National Comprehensive Cancer Center Coalition,³⁰ and the AUA³¹ have all issued guidelines that endorse informed decision making around prostate cancer screening, in direct contrast to the USPSTF recommendation. The new AUA guidelines, in particular, have important political ramifications in the debate. Specifically, the guidelines do not recommend routine PSA screening in men at average risk for prostate cancer ages 40 to 55 years, which is a change from the 2009 AUA best practice panel statement. This updated statement, which does not specifically recommend against prostate cancer screening but is evidence based and acknowledges that the clinical trials do not support population-wide screening in this setting, helps re-establish urology's credibility in the debate. Similarly, the guidelines do not recommend screening in men older than 70, which is in line with the evidence and with other organizations' recommendations. Importantly the guidelines specifically discourage mass screening events, such as testing at health fairs, where shared decision making is unlikely to occur.

A second key political initiative is to encourage the USPSTF to review its decision using existing mechanisms. The USPSTF reviews its recommendations at regular intervals, when new evidence becomes available and when there are enough public stakeholder requests. Interested parties are encouraged to go to the USPSTF Web site (available at: <http://www.uspreventiveservicestaskforce.org/tftopicnon.htm>) and submit an electronic request to review the recommendation on prostate cancer screening.

Finally, efforts are currently under way to improve the efficiency and transparency of the USPSTF in the form of the USPSTF Transparency and Accountability Act of 2013 (HR 2143, <https://www.govtrack.us/congress/bills/113/hr2143>), introduced by Marsha Blackburn (R-Tn), which has bipartisan support. This bill also includes provisions for decreasing the USPSTF impact in the PPACA and for increased inclusion of specialists, and also is endorsed by the AUA. The Act is a key priority on the AUA's legislative agenda, and is having an effect. Specifically, the USPSTF and AHRQ have already volunteered to incorporate some of the recommendations in the bill into the

process, potentially obviating the legislation. While the changes that have been made are promising they are by no means adequate, and there is still a need for this legislation.

SUMMARY

It is of particular importance that urologists have a voice in the creation of health policy for conditions that we directly diagnose and treat. Although there is no danger yet for denial of coverage of PSA screening by Medicare, it will be important to urge the USPSTF to review their recommendation against PSA screening for men of all ages so that well-informed patients who might potentially benefit from the early detection of prostate cancer by PSA screening can continue to do so. Urologists must become more politically active on this issue in an effort to advance the health of their patients and reduce the public health burden of prostate cancer in the United States.

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