Men's Health Network
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April 23, 2012

The Honorable Kathleen Sebelius
Secretary
Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

RE: Prostate cancer early detection and the USPSTF

Dear Secretary Sebelius,

Under the provisions of the ACA, the U.S. Preventive Services Task Force (USPSTF) has the ability to make life-or-death decisions for the health care system. It determines which potential life saving prevention and early detection services are covered by insurance, and by extension, Medicaid and possibly even Medicare.

The USPSTF posted a draft recommendation on the use of the PSA test for prostate cancer screening and opened the web site for comments on October 11, 2011. The comment period was open until November 8, 2011. Due to a web site malfunction that caused the loss of some of the public comments, the comment period was reopened until December 13, 2011.

MHN submitted comments on November 8, 2011 and, based on additional information about the process used by USPSTF to reach its conclusion, MHN posted additional comments on December 13, 2011. Both comments are attached to this letter.

We expressed concern that special consideration was not given to high-risk men, African American men, men with a family history, and those men exposed to Agent Orange. We are also concerned about low-incidence groups whose cancer, because of lack of screening, is diagnosed at late stage, resulting in a high mortality (American Indian and Alaska Native men). Other men may not know that they are at high risk, because they do not know their family history or because of exposure to various chemicals in the workplace, and other factors.

As can be gleaned from MHN's latest comments, we are concerned that critical data were left out of the decision-making process and flawed data were used. This is not to say that the USPSTF has intentionally avoided critical data. To the contrary, we suggest that the USPSTF followed current procedures to the letter, but that those procedures are in need of substantial revision to reflect the important role that the USPSTF serves under the Affordable Care Act.

The USPSTF is a panel consisting of highly credentialed volunteers who offer their time and expertise to examining health issues that are key to the health and well-being of the

nation. Apparently it is the policy of the USPSTF to exclude specialists who might benefit from a recommendation from the panel. Currently the USPSTF initiates a review of the research literature, issues a draft recommendation based on a review of the literature, and opens the recommendation for public comments. This comment period is a new addition to the process.

We feel this process is critically flawed, but can be dramatically improved.

What is lacking under current procedures?

- Agencies and organizations listed as partners by the USPSTF were not actively engaged.

- Representatives of patient groups, with their vast store of individual case stories, are not involved in the process.

- Specialty medical organizations that could provide critical information about identification of prostate cancer, treatments options and outcomes are excluded from the decision-making process, nor are they placed in an advisory role.

The PSA draft recommendation process highlighted these shortcomings.

While the USPSTF relied heavily on meta analysis of published studies, it did not look to more current data, nor did it consider the current and past data available at CDC, NCI, NIH, the VA, Medicare, and other agencies that collect, either intentionally or in the course of everyday operations, information that is critical to determining the prevention initiatives that best serve the American public. Just as important, current procedures apparently do not include consideration of ongoing studies at those sister agencies.

These are faults of the procedures used, not the individuals involved who have tried their best to make sense of a plethora of confusing and seemingly contradictory data.

To put it quite simply, by relying almost entirely on one study that is critically flawed, and by not having the benefit of data from other federal agencies and non-governmental organizations, the USPSTF has reached a preliminary decision that does not reflect the needs of men at risk for prostate cancer. For instance, heavy emphasis was placed on the PLCO (Prostate, Lung, Colorectal, Ovarian) study, a study whose prostate data seem to generate headlines with each public update. But as has been recently revealed, the prostate arm of the PLCO study is critically flawed, with over half of the men in the control (not screened) group having been screened for prostate cancer (opportunistic screening) and only 85% of those in the screened group were ever screened.

The other study often cited, the European Randomized Study of Screening for Prostate Cancer (ERSPC), has followed 182,000 men for 11 years. While preliminary data were less clear (prostate cancer is usually a slow-growing cancer), the latest data, released since the USPSTF draft recommendation, indicate a reduction in prostate cancer-specific mortality of 29% at 11 years follow-up. This indicates a significant, life-saving

benefit. ERSPC is the largest study of screening effectiveness and compliance has been significantly better than that of the PLCO study.

At the very least, the USPSTF should be required to throw out it's current draft recommendation, start again, initiating a procedural process that actively engages all elements of the field, including federal agencies that are funded to investigate prostate cancer detection, decision making, treatments and outcomes, professional organizations that identify, advise patients, and treat prostate cancer, and patient representatives who are the ones who have first hand knowledge of the positives and negatives (if any) of early detection.

Sincerely,

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December 13, 2011

Dr. Robert Cosby
c/o USPSTF
540 Gaither Road
Rockville, MD 20850

Re: USPSTF Proposed Recommendation Statement on Screening for Prostate Cancer

Dear Dr. Cosby,

Men's Health Network (MHN) welcomes the opportunity to offer additional comments on the United States Preventive Services Task Force (USPSTF) draft recommendation statement concerning PSA screening for prostate cancer. Please accept the following as our additional comments for the record.

"President Obama is in 'excellent health,' his doctor reports"

Published: Monday, October 31, 2011, 9:32 PM
The Associated Press

"The new report says he was also screened for prostate cancer using a PSA blood test. That's a test that the U.S. Preventive Services Task Force recommended against earlier this month, saying it can do more harm than good in part because many tumors found are too slow-growing to be a threat. The report cites "informed patient request" in giving Obama the screening. His PSA level, or prostate-specific antigen, was found to be low."

"Obama, who turned 50 in August, seems to have improved his health on some fronts since his last physical, which Kuhlman conducted in February 2010."
(*Found at:*
www.nola.com/politics/index.ssf/2011/10/president_obama_is_in_excellen.html)

Under the draft recommendation from the USPSTF, men other than the President may be denied the opportunity to receive the welcome news that their "…PSA level, or prostate-specific antigen, was found to be low."

As mentioned in our earlier comments, we oppose a "D" rating for PSA screening for prostate cancer and would suggest a rating that encourages a discussion between a man and his physician about when he should be screened for prostate cancer.

We are also concerned that the USPSTF recommendation process did not involve patient and research organizations at an early stage, groups who are very likely to know about recent discoveries and trends that might affect the final recommendation. We are also concerned that while certain other agencies and organizations are mentioned as

partners in the process, their input is not actively pursued. Some of these partner agencies have important ongoing research programs that are critical to a well-thought-out decision. Partners like:

- Centers for Disease Control and Prevention, which has established an excellent ongoing research program into informed decision making for prostate cancer. (Synopsis presented at the Prostate Cancer Roundtable meeting on November 28, 2011 in Washington, DC.)

- National Institutes of Health (National Cancer Institute), which has determined: "Models suggest between 45% and 70% of the mortality decline (from prostate cancer) observed in the 1990s could be attributed to the stage-shift induced by screening" (A presentation at the 7th Annual African American Prostate Cancer Disparity Summit (Washington, DC, September 2001) by Kathy Cronin Ph.D. MPH and Angela Mariotto Ph.D. of the Surveillance Research Program at the National Cancer Institute.)

- Veteran's Health Administration, which could have provided critical information that men exposed to Agent Orange, and possibly other chemicals, are at significantly high risk for prostate cancer.

- Department of Defense / Military Health System (Congressionally Directed Medical Research Program), which could have provided critical information from the cutting-edge research funded by this program.

- Indian Health Service, which could have provided information about the lack of screening among American Indians / Alaska Natives and the resultant excessively high mortality rate.

The USPSTF process would also have benefited from engaging top researchers such as Dr. Chiledum Ahaghotu of Howard University who presented an excellent critique of the two 'studies" mentioned above at the recent (December 7, 2011) Congressional Men's Health Caucus, Prostate Cancer Task Force briefing "Prostate Cancer Screening: Dangerous or Life Saving?"

We suggest that the USPSTF reopen the recommendation process for use of the PSA to screen for prostate cancer and actively engage other entities in an open discussion of the advisability of placing the health of men in the preliminary results of the two universally criticized "studies" referenced by the USPSTF. (Those studies are the Prostate, Lung, Colorectal and the Ovarian Cancer Screening Trial and European Randomized Study of Screening for Prostate Cancer.)

We also believe that the recent NIH State-of-the-Science Conference: Role of Active Surveillance in the Management of Men With Localized Prostate Cancer revealed important options that should be offered to men who are found to have elevated PSA levels. An elevated, or accelerating PSA need not result in invasive treatment, but careful observation so that proactive treatment can be initiated if and when the cancer becomes aggressive or appears ready to spread to other parts of the body.

The Consensus Statement from the conference echoes what we already know: "Prior to the adoption of PSA screening, the majority of prostate cancer was detected because of symptoms of advanced cancer or a nodule found on digital rectal examination. The symptomatic tumors were usually high grade, advanced, and often lethal. Other tumors were found incidentally at the time of surgery for benign enlargement of the prostate. These were often low grade and localized." (*page 3*)

While acknowledging that "…there are many unanswered questions about active surveillance strategies and prostate cancer," the Statement concludes that "Active surveillance has emerged as a viable option that should be offered to low-risk patients." (*page 18*)

Elaborating on our earlier comments, discouraging use of the PSA puts certain men at needless high risk for early death from prostate cancer:

- *African-American men*: African-American men are 1.6-times as likely as white men to develop prostate cancer, but over 2.4-times as likely to die from prostate cancer. *Found at: http://seer.cancer.gov/statfacts/html/prost.html*

- *Men with a Family History*: The Centers for Disease Control and Prevention (CDC) reports that men with a brother, father, or son who has been diagnosed with prostate cancer are 2- to 3-times more likely to develop prostate cancer. *Found at: http://www.cdc.gov/cancer/prostate/basic_info/risk_factors.htm*

- *Men exposed to Agent Orange*: Giri et al. (2004) found that Vietnam veterans exposed to Agent Orange were more than 2-times as likely to develop prostate cancer and that when diagnosed the cancer was more aggressive.

  > "…twice as many exposed men were diagnosed with prostate cancer (OR=2.19), they developed the disease at a younger age, and they had a more aggressive variant of prostate cancer." *Found at*: *www.atsdr.cdc.gov/toxprofiles/cdds_addendum.pdf*

- *American Indian / Alaska Native men*: Have the lowest incidence rate of prostate cancer, but are twice as likely as Asian/Pacific Islanders (who have a higher incidence rate) to die from it. *Found at: http://seer.cancer.gov/statfacts/html/prost.html*

  This scenario can only be the result of identifying prostate cancer at a later stage, when treatment is minimally effective.

- Men not in any of the above categories who are initially diagnosed with aggressive, life-threatening prostate cancer.

In conclusion, we suggest that the USPSTF scratch its draft recommendation, reopen the process, and start from the beginning in an effort to reach a decision that best serves men and their families.

# # #

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November 8, 2011

Dr. Robert Cosby
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Rockville, MD 20850

Re: USPSTF Proposed Recommendation Statement on Screening for Prostate Cancer

Dear Dr. Cosby,

Men's Health Network (MHN) welcomes the opportunity to offer comments on the United States Preventive Services Task Force (USPSTF**)** draft recommendation statement concerning PSA screening for prostate cancer. Please accept the following as our comments for the record.

According to the Surveillance Research Program at the National Cancer Institute: "On January 1, 2008, in the United States there were approximately 2,355,464 men alive who had a history of cancer of the prostate. This includes any person alive on January 1, 2008 who had been diagnosed with cancer of the prostate at any point prior to January 1, 2008 and includes persons with active disease and those who are cured of their disease." (http://seer.cancer.gov/statfacts/html/prost.html#survival)

We contend that the data indicate that a significant number of those men are alive because they were diagnosed before their cancer had spread, and that the diagnosis is most often facilitated with a PSA test, or a series of such tests. In its statement recommending against use of the PSA in men "…that do not have symptoms that are highly suspicious of prostate cancer," the USPSTF appears to acknowledge that the PSA has benefits under certain circumstances, but only when a person's prostate cancer has spread.

In making a recommendation that PSA screening be graded a "D", the USPSTF is looking for evidence from studies that almost everyone agrees are critically flawed. We contend that stage of diagnosis and survival rates should be a determining factor when making a recommendation.

Further, the USPSTF has taken a path that moves away from an examination of whether a screening test is life-saving or not. The draft recommendation on PSA screening seeks to save people from themselves; from possibly making unfortunate treatment decisions when they find they have cancer, taking the decision away from the person before he has a chance to make a decision he may later regret – or – before he has a chance to make a decision that may save his life.

Even more distressing is the message this sends men, their families, and the broader cancer community. Is the cancer community to believe that early detection harms lives? Difficult and sometimes tragic decisions are faced by most who find they have cancer, from breast cancer, to lung cancer, to brain cancer. Would we tell those unfortunate individuals that they should not have been diagnosed until their cancer had spread beyond any hope of cure?

There are also far reaching statutory implications for the "D" recommendation. The Affordable Care Act (ACA) gives the USPSTF responsibilities it had not enjoyed before, and while in the past it played a purely advisory role, it now finds itself square in the middle of health reform and the Affordable Care Act. USPSTF recommendations have moved beyond advisory, they are now mandates to the entire country, determining many of the preventive services that a nation will receive.

As an example of the far-reaching statutory influence the USPSTF now enjoys, the ACA gives the Secretary of Health and Human Services (HHS) the authority to deny payment for any service that is rated a "D" by the USPSTF.

> Sec. 4105. Evidence-Based Coverage of Preventive Services in Medicare.
>
> (a) Authority To Modify Or Eliminate Coverage Of Certain Preventive Services.—Section 1834 of the Social Security Act
>
> (42 U.S.C. 1395m) is amended by adding at the end the following new subsection:
>
> ''(n) Authority To Modify Or Eliminate Coverage Of Certain Preventive Services.—Notwithstanding any other provision of this title, effective beginning on January 1, 2010, if the Secretary determines appropriate, the Secretary may—
>
> ''(1) modify—
>
> ''(A) the coverage of any preventive service described in subparagraph (A) of section 1861(ddd)(3) to the extent that such modification is consistent with the recommendations of the United States Preventive Services Task Force; and
>
> ''(B) the services included in the initial preventive physical examination described in subparagraph (B) of such section; and
>
> *''(2) provide that no payment shall be made under this title for a preventive service described in subparagraph (A) of such section that has not received a grade of A, B, C, or I by such Task Force.''.*
>
> (b) Construction.—Nothing in the amendment made by paragraph (1) shall be construed to affect the coverage of diagnostic or treatment services under title XVIII of the Social Security Act.

Further, while private insurers (and arguably Medicaid) once looked to the USPSTF and other entities for guidance, they are now required to follow the recommendations of the USPSTF, providing coverage for all those USPSTF recommendations graded A and B, and certain breast cancer screenings, and are responding, as expected, to the other grades issued by this newly empowered panel. Some insurers are already notifying their clients that PSA screening will no longer be covered, even those clients at high risk for prostate cancer.

While statutory weight should not influence evidence-based findings, the USPSTF must be very careful in making decisions about a screening for cancer based on what a patient might do with the information from the test. That goes beyond the effectiveness of the test, but to the doctor-patient relationship and decision-making. Basing a recommendation on a fear that a patient might make a regrettable decision about treatment (or non-treatment) could, and in this instance probably will, deny other patients' access to a potentially life-saving screening.

The question of PSA screening raised by the USPSTF seems to come down to this, "Does early detection of cancer, any form of cancer, save lives?" Yes.

"Does cancer always require active treatment?" No.

"Do people with cancer, practically any cancer, who choose active treatment sometimes make unfortunate treatment decisions, though those decisions, at the time they are made, may appear to be the correct ones?" Yes.

We do know that if we do not identify clinically significant cancer early, it is very likely to spread and prove fatal. There seems to be no argument that the PSA can help identify clinically significant prostate cancer that otherwise would otherwise go undetected until it has spread.

As flawed as the PSA is as an identifier of cancer, it is the only tool we presently have to identify possible cancer in men "…that do not have symptoms that are highly suspicious of prostate cancer." Waiting to use this tool until a man presents with "…symptoms that are highly suspicious of prostate cancer" is to condemn that man to a slow and painful death. And, why should he be required to wait – because other men may make poor decisions? Because some make poor decisions is no reason to deny a potentially life-saving diagnosis. However, it is cause to call for better patient and physician education, better diagnostic tools, and better decision-making tools.

The USPSTF recommendation against use of the PSA for early detection of prostate cancer (PCa) provides no differentiation between the general population and men at high risk. This places high risk men (African-Americans, those exposed to Agent Orange, and those with a family history of PCa) in danger of being diagnosed with advanced prostate cancer. It also places at high risk those men not in one of those three categories who may have aggressive prostate cancer. Let's examine what we know of these special categories of men:

***African-American men*:** African-American are 1.6-times as likely as white men to develop prostate cancer, but 2.38-times as likely to die from prostate cancer.

Further, the 5-year relative survival rate among African-Americans is 96%, compared to approximately 100% among whites. Prostate cancer is diagnosed at the local or regional stage in 90% of African Americans and 92% of whites.

The 5-year relative survival rate among African-Americans who are diagnosed with early stage prostate cancer is close to 100%, but drops to 29% when the cancer has spread to distant sites.

The American Cancer Society states that the steady decline in African American prostate cancer death rates since a peak in 1993 is possibly due to improved treatment "and early detection by PSA." However, they also point out that "a major U.S.-based randomized trial" (also referenced by the USPSTF) failed to show any benefit, and that two European trials showed a modest benefit." (American Cancer Society. Cancer Facts and Figures for African Americans 2011-2012. pages 10,12,14.).

MHN would propose that early detection is in part responsible for the improved treatment outcomes, and that the PSA is in great part responsible for the early detection.

***Men exposed to Agent Orange*:** Giri et al. (2004) found that Vietnam veterans exposed to Agent Orange were more than 2-times as likely to develop prostate cancer and that when diagnosed the cancer was more aggressive.

> "…twice as many exposed men were diagnosed with prostate cancer (OR=2.19), they developed the disease at a younger age, and they had a more aggressive variant of prostate cancer."
>
> (Addendum to the Toxicological Profile for Chlorinated Dibenzo-P-Dioxins (CDDs): Part I. Human Studies. U.S. Department Of Health And Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry. April 2011. Page 14.)
> *Found at*: www.atsdr.cdc.gov/toxprofiles/cdds_addendum.pdf)

***Men with a Family History*:** The Centers for Disease Control and Prevention (CDC) reports that men with a brother, father, or son who has been diagnosed with prostate cancer are 2- to 3-times more likely to develop prostate cancer.

> Risk Factors
> Family history: Certain genes (the functional and physical units of heredity passed from parent to offspring) that you inherited from your parents may affect your prostate cancer risk. Currently, no single gene is sure to raise or lower your risk of getting prostate cancer. However, a man with a father, brother, or son who has had prostate cancer is two to three times more likely to develop the disease himself.

(Bostwick DG, Burke HB, Djakiew D, Euling S, Ho SM, Landolph J, Morrison H, Sonawane B, Shifflett T, Waters DJ, Timms B. Human prostate cancer risk factors. Cancer 2004; 101(10 Suppl):2371–2490.)
As cited at: www.cdc.gov/cancer/prostate/basic_info/risk_factors.htm#1

Next, let's examine the effect that early detection of prostate cancer (and use of the PSA) has on mortality.

A presentation at the African American Prostate Cancer Disparity Summit (a prelude to the Congressional Black Caucus annual meeting) in the Fall of this year (2011) by National Cancer Institute researchers was informative in providing data on the use of PSA and its effect on mortality.

In a presentation titled, *Understanding Prostate Cancer Disparities Through NCI SEER Data,* presenters Kathy Cronin Ph.D. MPH and Angela Mariotto Ph.D. of the Surveillance Research Program at the National Cancer Institute provided information demonstrating the effect that early detection using the PSA has had on prostate cancer mortality. Exact language from that presentation is below:

(*slide 25*)

Modeling the Impact of Screening on Incidence and Mortality Rates

> Cancer Intervention and Surveillance Modeling Network (CISNET)

NCI sponsored consortium of modelers

> Model the impact of cancer control interventions (Screening, Treatment, Primary Prevention) on current and future cancer trends in the U.S. population

Inform optimal cancer control planning

CISNET prostate models have been used to evaluate benefits and harms of PSA screening

http://cisnet.cancer.gov

(*slide 26*)

Modeling the Mortality Decline Attributable To Prostate Cancer Screening

> Mortality for prostate cancer has declined nearly 40% between 1994 and 2007, from 38.5 to 23.5 deaths per 100,000

> Two CISNET models projected prostate cancer mortality in the presence and absence of PSA screening

> Models suggest between 45% and 70% of the mortality decline observed in the 1990s could be attributed to the stage-shift induced by screening

Etzioni et al. Cancer Causes and Control 2008

This last point is worth repeating, and is critical to the USPSTF final recommendation:

> Models suggest between 45% and 70% of the mortality decline observed in the 1990s could be attributed to the stage-shift induced by screening

A closer look at SEER data provides the following, found at:
http://seer.cancer.gov/statfacts/html/prost.html

Surveillance Research Program at the National Cancer Institute, Surveillance Epidemiology and End Results data

Survival & Stage

Survival can be calculated by different methods for different purposes. The survival statistics presented here are based on relative survival (A measure of net survival that is calculated by comparing observed (overall) survival with expected survival from a comparable set of people that do not have cancer to measure the excess mortality that is associated with a cancer diagnosis.), which measures the survival of the cancer patients in comparison to the general population to estimate the effect of cancer. The overall 5-year relative survival for 2001-2007 from 17 SEER geographic areas was 99.4%. Five-year relative survival by race was: 99.7% for white men; 96.2% for black men.

Stage Distribution and 5-year Relative Survival by Stage at Diagnosis for 2001-2007, All Races, Males

Stage at Diagnosis	Stage Distribution (%)	5-year Relative Survival (%)
Localized (confined to primary site)	81	100.0
Regional (spread to regional lymphnodes)	12	100.0
Distant (cancer has metastasized)	4	28.7
Unknown (unstaged)	3	69.9

The stage distribution (Stage provides a measure of disease progression, detailing the degree to which the cancer has advanced. Two methods commonly used to determine stage are AJCC and SEER Summary Stage. The AJCC method (see Collaborative Staging Method) is more commonly used in the clinical settings, while SEER has strived to provide consistent definitions over time with their Local/Regional/Distant staging.) is based on Summary Stage 2000.

While we agree that the PSA is an imperfect test to determine if someone has PCa, it is the only test available and should not be abandoned until a better test is approved for general patient use.

Screening is just the first step in a journey to possible diagnosis or cancer and treatment decisions. The American Urological Association recommends a baseline PSA test for all men at age 40, in consultation with their physician. This seems a reasonable recommendation as the change in PSA level over years, and the velocity of that change are important considerations in determining a person's options.

Screening of high risk men is particularly important and should be encouraged using the best available tools, including the PSA.

# # #