

Dr. Catalona's Comments

to the Draft of USPSTF Recommendations

How could the USPSTF make this draft Recommendation Statement clearer?

- 1) The draft recommendation statement includes misinformation that needs to be corrected, not just for clarity but for accuracy.
- 2) Contrary to what Dr. Virginia A. Moyer, the pediatrician who chaired the USPSTF panel, has said in the popular media, the USPSTF should acknowledge the evidence that screening in certain patient groups, such as healthy patients and younger patients, reduced prostate cancer (PC) death rates.
- 3) The primary endpoint of the randomized clinical trials (RCTs) was PC-specific mortality, not all-cause mortality. The RCTs were neither designed nor powered to evaluate all-cause mortality. However, it is possible with longer follow-up, the all-cause survival will be significantly longer in these patient populations screened with PSA. The USPSTF therefore needs to acknowledge that PSA screening has been shown to reduce deaths from prostate cancer, and that follow-up was too short in the existing studies to adequately address all-cause mortality.
- 4) The USPSTF recommendation does not take into account the "number needed to treat" (NNT) to prevent 1 case of metastatic disease. This NNT is much lower than that to prevent 1 PC death. Preventing advanced disease causes a reduced financial burden on the healthcare system and an incalculable reduction in human suffering.
- 5) Data from the low-quality randomized clinical trials (RCTs) or RCTs designed with a different goal should not have been combined in metaanalyses with data from 2 higher quality RCTs that showed substantial PC mortality benefits. In this regard, Roobol et al called the metaanalysis by Djulbegovic et al "seriously flawed." In contrast, the ERSPC and Goteborg trials showed that PSA screening resulted in 20% and 44% reductions in PC mortality, respectively. This dilution of the mortality benefits by combining the data from these heterogeneous trials was foreseeable.
- 6) USPSTF should also acknowledge the 44% mortality benefit with a NNT to prevent 1 PC death of 5 in the healthier PLCO trial subgroup reported by Crawford et al.
- 7) USPSTF should explain that PSA screening as performed in these RCTs is not representative of the way PSA screening is currently practiced today, and thus the results are of limited current relevance.
- 8) USPSTF should acknowledge that high-risk populations, such as African-Americans, have not been adequately studied for PC mortality benefits.
- 9) USPSTF should acknowledge the > 40% PC mortality benefit in epidemiologic data from SEER (more than for any other cancer in men or

women) and similar patterns in the global World Health Organization (WHO) data during the PSA era.

What information, if any, did you expect to find in this draft Recommendation Statement that was not included?

- 1) Subgroup analysis of healthier PLCO men (44% mortality benefit with NNT= 5)
- 2) Epidemiologic evidence that screening decreases PC mortality; SEER data shows 75% decrease in metastases at diagnosis during PSA era and 40% decrease in the age-adjusted PC mortality; WHO data show similar trends where PSA has been adopted but not where it has not
- 3) Citing NCI modeling team study estimating 45-70% of the PC mortality benefit is attributable directly to PSA screening
- 4) Citing NCI modeling team's lower estimates of over diagnosis using U.S. statistical models with SEER data compared to the widely-quoted Rotterdam models and data
- 5) Citing published surgical series showing that under diagnosis is more common than over diagnosis in patients treated with radical prostatectomy. PC is still detected too late more often than too early.
- 6) Pointing out that men with a 10-year life expectancy would have more options and a better chance of avoiding metastases and death from PC by having a discussion of the benefits and risks of PSA screening and then proceeding according to NCCN guidelines
- 7) Pointing out that patients needing treatment can be informed about all of the options and seek expert doctors for treatment with fewest side effects

Based on the evidence presented in this draft Recommendation Statement, do you believe that the USPSTF came to the right conclusions? Please provide additional evidence or viewpoints that you think should have been considered.

I believe the USPSTF committee not only came to the wrong decision, but, if implemented, the resulting effects would be harmful, life-threatening and unconscionable.

- 1) They did not review all relevant literature, nor did they interpret it properly.
- 2) The AUA and the ACS have adopted positive recommendations for screening, and NCCN guidelines help implement screening.
- 3) USPSTF's recommendation polarizes the medical community and confuses patients and physicians.
- 4) Over diagnosis and over treatment are exaggerated in the literature and popular media.
- 5) I have prepared an article that provides evidence that should have been

considered in the recommendations: See www.drcatalona.com page 1 article:

Ramon Guiteras Lecture: Early Diagnosis of Prostate Cancer through PSA Testing Saves Lives

What resources or tools could the USPSTF provide that would make this Recommendation Statement more useful to you in its final form?

I don't believe this recommendation statement is helpful or accurate no matter what additional tools are provided. Instead, more accurate information would need to be provided.

- 1) Point out that high-risk men have not been adequately represented in studies, and avoiding PC death may be more important for them.
- 2) Include urologists and cancer specialist on the panel.
- 3) Point out that the NNT to prevent metastases and PC death is lower in younger, healthier men, in those trials that continue screening for many years, and in those that have longer follow-up.

The USPSTF is committed to understanding the needs and perspectives of the public it serves.

Please share any experiences that you think could further inform the USPSTF on this draft

Recommendation Statement.

- 1) Because the cancer begins on the prostate's outer edges, it produces no symptoms until it is far advanced and too late to cure. An apparently 'healthy' man may have a steadily climbing PSA, silently trumpeting the danger alarm.
- 2) African-American men were not included in studies used to make the guidelines and they are a group that benefit greatly from PSA screening.
- 3) USPSTF recommendation could result in insurance not covering screening; this would be disproportionately detrimental to men in the less affluent African-American community who are 50% more likely to be diagnosed with PC and 200% more likely to die of it. This would unnecessarily increase healthcare disparities in the U.S.
- 4) Side effects of prostate cancer treatment are greatly diminished with expert surgeons and ongoing improvements in treatment
- 5) Gann et al reported studies reflecting what would happen if all PSA screening were to stop. In a study of the relationship between PSA values in blood samples drawn before the PSA era from the Physician's Health Study, in men who subsequently were diagnosed with PC and died, the cause of death was PC in 75%.

Do you have other comments on this draft Recommendation Statement?

- 1) PSA is the best screening test available for the early diagnosis prostate cancer, and until there is a replacement for PSA, it would be unconscionable to stop it.
- 2) The risk of possible side effects should not be used as a fear tactic to discourage life-saving PSA screening and treatment.
- 3) When I first started my prostate surgery practice more than 30 years ago, I would too often have to stand at the bedside of a patient and his family and tell them the operation went well, but the cancer had spread beyond the prostate and the prognosis was not good. Even with the development of nerve-sparing surgery in the early 1980s, I had to say the same thing. Soon after the beginning of the PSA era in the early 1990s, there were far fewer patients with advanced disease. Because of early detection through PSA testing, the radical prostatectomy allowed for a cure in most patients, and the PC death rates plummeted. Now, I am concerned, with the USPSTF's recent misinterpretation of studies and ill-advised recommendation, we will see a return to patients with advanced prostate cancer. It is a sad occasion for surgeons, patients, and patients' families. The outcry against the USPSTF recommendation resonates --- nobody wants to go back there.