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Dr. Robert Cosby
United States Preventive Services Task Force
540 Gaither Road
Rockville, MD 20850

Re: Comments on the October 11, 2011 USPSTF Draft on PSA Screening

Dear Dr. Cosby:

I am writing both on behalf of myself and on behalf of the Proton Pals, Ltd., of which I am a director. Proton Pals, Ltd. is an organization of prostate cancer survivors across the United States who have undergone proton radiation treatment. We urge the United States Preventive Services Task Force ("USPSTF") to withdraw its October 11, 2011 Draft Recommendation Statement [1] (hereinafter "draft") for the following reasons:

1. The recent randomized prospective trials conducted without bias confirm that the PSA screening test reduces deaths from prostate cancer.

Goeteborg Trial. The trial conducted in Goeteborg, Sweden [2] published in 2010 produced the most favorable results for PSA screening of the recent studies. The death rate from prostate cancer of the men in the PSA screening group who actually showed up to take the PSA test was only 44% of the prostate cancer death rate of the men in the non-PSA group as a whole. The median follow up after randomization in the Goeteborg Trial was 14 years. The results suggest that most of the benefit of PSA screening occurs 10 years or more after randomization.

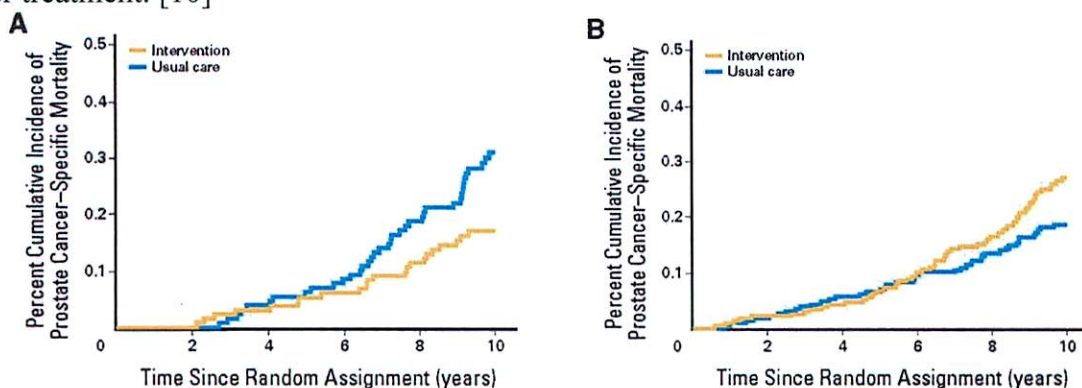
ERSPC Trial. The European Randomized Study of Screening for Prostate Cancer (ERSPC) Trial [3] published in 2009 also produced favorable results for PSA screening. The death rate from prostate cancer of the men who took the PSA test was 73% of the prostate cancer death rate of the men in the non-PSA group as a whole. However, the median follow up from randomization was only 9 years in the ERSPC Trial. Indeed, Goeteborg's results paralleled the ERSPC's for the first 10 years, but thereafter, Goeteborg's results exceeded those of the ERSPC.

PLCO Trial. By contrast, in the Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) Screening Trial [4] published in 2009, more of the participants in the PSA screening group died than in the non-PSA group. The reason for this outlier result is that the study was biased enough so that the biases understated the benefits of PSA screening:

- *There was high cross contamination in the PLCO study.* During the study, 52% of the *non-PSA group* underwent PSA screening, thus creating a bias in the study that understated the efficacy of the PSA screening test. Additional bias occurred at randomization, where 44% of both the non-PSA group and the PSA screening group had previous PSA tests. [4]
- *The median follow-up after randomization of the PLCO study (11.5 years) was not long enough to give a true picture of the benefit of PSA screening.* As discussed above, most of the benefit from screening occurs after ten years. [4]
- *The overall biopsy rate in the PLCO Trial for men with a positive screening was relatively low (about 30-40%) [5], compared to 85.8% in the ERSPC study and 93% in the Goeteborg study.* Without a biopsy after a positive PSA test, it is impossible to determine whether the PSA test reveals prostate cancer or not. PLCO's low biopsy rate thus understates the efficacy of PSA screening.

The Goeteborg and ERSPC studies confirm the findings of observational studies that PSA testing are associated with reduced prostate cancer deaths (Seattle area - a 62% reduction [6]; Austria – a 33% decrease [7]; and a 37% relative reduction comparing Rotterdam where PSA screening was used, with Northern Ireland, where only 6% of men were screened. [8].) The task force should pay no attention to the overall PLCO Trial results, or to the two meta-analyses cited in the task force draft, because they combined both a relatively high and relatively low quality of evidence. [9]

2. In recommending against PSA screening for all ages, the task force irresponsibly and recklessly ignores favorable results for men with minimal comorbidity or who are younger. Results from the PLCO study reported in 2011 show PSA screening for healthy men is associated with a reduced risk of prostate cancer deaths, with minimal over treatment. [10]



After 10 years, men with no or minimal comorbidity in the PLCO study who received PSA testing (gold line on chart A from [10]) were only 56% as likely to die from prostate cancer as those who received no PSA testing (chart A, blue line) k -sample $P = .03$; the additional number needed to treat (NNT) to prevent one such death at ten years was only

five. By contrast, men with at least one significant comorbidity who took the PSA test (gold line on chart B) did worse than men in that study not taking the test (blue line).

In another study with implications for healthy or younger men, the prospects of indolent cancers progressing to lethal ones greatly increase after 15 years of follow up. The *prostate cancer mortality rate* during the first 15 years increases to *triple* that rate for the period beyond 15 years. These findings support early radical treatment in men whose life expectancy exceeds 15 years. [11] They are also consistent with the 2011 PLCO results and those of the Goeteborg study, the only major trial to report results for men under 55 and where the median age was 56.

Some question the utility of reducing prostate cancer mortality, asserting that “it enables survivors to die of something else.” For younger men or healthy men, this argument is as false as it is cruel, because it ignores the shifts in the competing risk of death in this country. Cancer in all of its forms is now by far the leading cause of death in American men ages 60-79 with 152,231 deaths, compared to 119,209 from heart disease, and 30,237 for chronic lower respiratory diseases which is the third leading cause. Only for men age 80 or more is cancer second behind heart disease. [12]

By discouraging use of PSA for younger men or those with minimal comorbidity in the face of these results, the task force is willfully breaching the duty it owes to these men.

3. The PSA test is only a screening test in which blood is drawn. It is not associated with significant physical or psychological harm to patients. In the study of Carlsson et al [13], no anxiety was reported for 66% of Swedish men awaiting PSA results; although 2% reported high levels of anxiety, this group was susceptible to anxiety in any event. The study of Macefield et al [14] reports similar results.

In another study on the same issue, American patients with false positives were asked:
“Looking back on your experience, even though you had a result that required further testing, are you glad you had that test?”

Answering “yes” were 102 out of 103 of patients having a false positive “pap test”, 104 out of 108 having a false positive mammography test and 10 out of 10 having a false positive PSA test, though the experience of having had the false positive ranged from “a little scary” to the “scariest time of my life.” [15]

The task force mentioned none of these studies. Instead, it based its physical and psychological harm arguments on the reactions to the *biopsy* following the PSA test compared to men’s reactions to a screening test without a subsequent biopsy. [16, 17] This is absurd. Biopsy pain can occur whether or not preceded by a PSA test.

4. The PSA test by itself does not cause costly over treatment, because it is used for screening, not treatment. Over treatment is, by definition a problem of treating people who don’t need treatment, but treatment occurs *after* the PSA test. The solution to over treatment is more use of conservative management, not discouraging PSA screening.

5. The foregoing reflects the fact that in the nearly 25 years that it has been used, the PSA screening test has diagnosed many thousands of men with prostate cancer before it spreads, thereby saving countless lives. The death rate from prostate cancer has dropped, [18] the mix of patients presenting has shifted dramatically from high risk to low risk [19] and they now present at earlier stages of the disease than when the PSA test was introduced. [20]

6. The USPSTF would do far more good in the fight against prostate cancer by working with the ERSPC and other groups to develop a risk stratification method of testing, instead of discouraging the use of PSA testing for all men. In a study published last year, results from the ERSPC risk stratification approach using PSA, DRE, and ultrasound, “unnecessary” biopsies were reduced, and the predictive value of the PSA test was increased. [21] This approach to risk stratification is discussed by Schroeder in a recent article [9]. Risk stratification, rather than stopping PSA screening would implement the USPSTF’s avowed goal of enabling clinicians to “understand the evidence but individualize decision making to the specific patient or situation.”

Sincerely yours,



David O. Stevens

DOS/d

cc: Members of the Proton Pals, Ltd. (via website)

P. S. I am a 65 year old prostate cancer patient survivor who probably owes his future to the PSA test. Without it, I would not have had last year’s biopsy which disclosed a small but aggressive T1cN0M0 tumor with a Gleason score of 9 (4+5), nor underwent proton radiation therapy plus my current two year stint of leuprolide hormone therapy. This letter is but one product of my extensive reading in the medical literature about my disease.

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