

## **Rebuttal**

### **Otis Brawley, MD**

Note that the decline in prostate cancer mortality started in 1992, and Dr. Catalona's very good article was published in 1991 to start PSA screening. Yet when we talk about the trials, we can't look at five or six-year survival. We need to look at ten or twelve-year survival. To say that the mortality decline in the United States is due to PSA screening but that we have to look at the trials long term doesn't jive together. We do need to look at the trials long term, but there is another possible reason for the decline in mortality in the United States. It is a problem that is seen in the European screening studies—advances in treatment once diagnosed whether diagnosed through screening, symptoms or other things.

An important element about the Goteborg trial and the European randomized study is that the European randomized study was actually eight trials in different areas of Europe. One was in Goteborg, and the men in the Goteborg trial who were born between 1930 and 1939, which was over 7%, are included in the European study. They are one of the eight parts. Six of the eight parts of the European study have an important difference from the American trial, which is that the men in the control arm still don't know they are in the do-not-screen arm. They were randomized without ever being informed, and they are being watched through death registries. What that creates is in the six arms of the European trial you have men who are being screened and if diagnosed get treated in one of the specialized centers for treatment of prostate cancer. If you are in the control arm and you happen to get diagnosed with prostate cancer, you get the treatment that is normally given in Europe, which is very passive and not nearly up to the U.S. standards of treatment. That is one reason why the mortality rises are continuing in the parts of Europe that do the old style passive treatment. Finally, in terms of survival data, in schools of public health we teach our graduate students not to look at survival. It's like counting people who didn't have cancer in the five-year survival statistic. Mostly importantly with regard to screening is what the three organizations all said. There is a debate, and men need to make an informed decision about screening. That philosophy carries over to making a treatment decision as well.

### **William Catalona, MD**

There have been improvements in treatment. Radiation has improved, and surgery has improved. When the statistical teams analyzed to what extent early detections or PSA testing affects the mortality rates, the results came out 40 to 70%. The PSA has contributed greatly to the reduction in prostate cancer mortality rates.

As far as the Goteborg study being part of the European randomized study, it was an independent study and started before the European randomized study. It can stand on its own two feet and is actually better than the other parts of the European randomized study. The results are robust and fully stand on their own.

### **Virgil Simons**

When you look at the number necessary to screen, 293 on one side and 1,410 on the other, and the number necessary to treat, what do these things mean?

### **William Catalona, MD**

I don't think number needed to screen data is that important. I think number needed to treat is, however, important. The number needed to treat of 12 from the Goteborg study means, for example, if we treat 12 men with localized disease, one of the twelve's, and we don't know which one, life will be saved. The other 11 get treatment that is not necessary either because they did not need to be cured or unfortunately the treatment that we currently have cannot cure them. They either died from prostate cancer or never would have died from prostate cancer. We desperately need to do studies to get better answers.

### **Participant**

The number needed to treat may be 12, but for example, maybe the number needed to treat to prevent someone from suffering from metastatic disease and being treated with hormonal therapy, radiation therapy or secondary therapy would come into that. If one is screened for prostate cancer and the cancer is detected early, it might prevent you from actually having to die from prostate cancer. It might prevent you from developing metastatic prostate cancer and having you and your family go through the inconveniences of having advanced cancer. A number needed to treat of 12 is considered very acceptable. The other statistic that often bothers me is they say that one in six men are diagnosed with prostate cancer, but only one in thirty die of it. Why is that? Maybe a lot of the other 24 were diagnosed early and cured by surgery and radiation therapy.

### **Virgil Simons**

All of the recommendations suggest that a man should have an informed conversation with his healthcare professional. Right now we have something like 37 million men who are uninsured in the United States, and we have seen that less than half of men go to the healthcare system to be checked compared to women. How do we address these issues from a public health standpoint?

### **Otis Brawley, MD**

This is one of the reasons why the American Cancer Society was a supporter of health care reform, and we need to reform not just how we pay for health care and who has health insurance to get health care paid, but we also need to reform our entire approach to health care to include preventive services and counseling about blood pressure, diet, weight and other things. We currently have a third-world health care system.

### **William Catalona, MD**

One of my real fears is that PSA testing, which is now paid for by Medicare and Medicaid, will be removed with health care reform. Realistically, the only way you can decrease health care cost is to decrease the amount of health care delivered. They could never get away with that for breast cancer.

### **Participant**

The American Cancer Society is out there sucking a lot of money off of the American public. From a prostate cancer research standpoint on a scale of one to ten, where are we? You have really painted a very bleak picture.

### **Otis Brawley, MD**

First off, the American Cancer Society is the largest private funder of cancer research in the United States. Eighty percent of our money is spent on young investigators, but because these people are early in their careers it is sometimes hard to figure out if they are a prostate cancer researcher, a breast cancer researcher, or a colon cancer researcher. We have some estimates that prostate cancer is the number two cancer that we support among cancers. Breast cancer is number one.

Sometimes it is difficult and wrong to play disease Olympics—how much money is for prostate cancer versus breast cancer? For instance, Lupron was developed for prostate cancer in the 1980s, but by 1990 it had been FDA approved not just for prostate cancer but also for pre-menopausal breast cancer and for treatment of precocious puberty in children. There are other examples of this type of thing, and I don't know when money stops being called, for instance, breast cancer research money and starts being called prostate money. We need to support all research and all leads.

### **Participant**

With respect to the statistics that you have shown us, most of them seem to be based on the financial cost to the society of screening. If that is the case, is there any medically adverse effect from screening?

### **Otis Brawley, MD**

None of my data is based on cost. The adverse side effects of screening include men who have abnormal PSAs and end up stuck in their jobs because they have been offered a new great job but they have to change health insurance. There is also a paper to show that there is a higher suicide rate amongst men who are obsessed with their PSA level. We also know for a fact that at least half of all Americans who are treated for localized disease and consequently have all of the side effects of treatment for localized disease be it impotence, incontinence, bowel pain, and other things do not need to be treated. The problem is that right now I can't tell you which half.

### **Virgil Simons**

We have to be our own advocates. We have to understand what our expectations are for the quality of life that we want to have and what our expectations are for the quality of life we want our family to have. Will this treatment ultimately provide benefit for me?

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