

Prostate Cancer 101: Testing and Treatment

PSA Screening

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There are three primary tests for screening for prostate cancer. First, you need to know what you want in a screening test to indicate which subjects have a condition. A good screening test has a high sensitivity and a high specificity, and must be acceptable to the population being screened, ideally rapid, and noninvasive. One also must take into account the issue of what you are preventing, what the side effects are, what the costs are in terms of routine population level decisions for an individual, and whether you can get access to the test.

The digital rectal exam, or DRE, is a mainstay of prostate cancer screening since the entire prostate cannot be palpated, and a small lesion may not be detected. Transrectal ultrasonography is used particularly in many research studies and for follow-up, but it has limited value for screening in and of itself. A history of symptoms, physical exam, and laboratory findings such as elevated PSA may indicate a need for evaluation by TRUS. DRE alone clearly could never be expected to detect all indolent prostate cancers. Once prostate cancer advances, there is a large solid rock which penetrates through and is then palpable; we would like to be able to detect it at an earlier stage. Risks and benefits of screening should be weighed; the value of screening can only be proven by showing a reduction in the chance of dying from prostate cancer and in terms of quality of life. You can't look at simply incidence or prevalence numbers and make judgments; you need to have mortality data. The average time from detection from a screening test of prostate cancer to when it would normally have been detected varies according to different studies, but in general, it is probably a decade or slightly more. This also means that in order to evaluate the results of any of these screening tests, you should follow-up for an excess of a decade.

For prostate cancer, the economics of screening yet have not been proven, but we are still early in the course of looking at the data. Screening does offer the possibility to diagnose early impressive prostate cancer that can lead to suffering and death from the disease. Screening may detect cancers that do not pose a threat to the patients; there are many people who are diagnosed with prostate cancer, and a large proportion of them die of other causes.

When screening the general population, over 50% of prostate cancers detected will be minimal cancers. The issue becomes what do you do about them. Watchful waiting is an option and one that is usually chosen. There has been no demonstrated benefit for the active treatment of early stage cancers, and there are side effects which help justify why watchful waiting makes sense.

A large European randomized study screening for prostate cancer from over ten years ago showed a 20% reduction in the rate of death from prostate cancer, which is statistically significant. There is no known safe way to separate those whose cancer will not progress from those requiring any treatment.

We have a large trial published at the same time, which was a prostate, lung, colorectal, and ovarian cancer screening trial based in the U.S.; it hopes to provide some answers about the effect of prostate cancer screening. It is designed as a 17-year project of the National Cancer Institute. If you look at the U.S. study, these two curves are nearly superimposable. There is a bit of difference here at the ten-year endpoint, but in fact, it is not statistically significant. This study is really saying we are in our infancy; we don't have any data yet that is meaningful. There is not much difference with the European data at ten years except that screening seems to be faring a little bit better, and at routine years of follow-up, there is survival advantage of about 20%, which is statistically significant. Even the European study is still relatively in its infancy in terms of

knowing the long-term benefits. The conclusions which were made which talked about ultimate benefit and economic benefits are clearly premature; we need more time. Note that the U.S. study includes the use of a PSA cutoff point which is too high; the European study used a lower cutoff. Also, the study is underpowered and cannot detect statistically significant differences that were anticipated when patients enrolled.

Getting people to participate in trials is often very difficult, and if common practice is followed, more physicians will get to goal. Ultimately, this becomes self-defeating of the study design. There were a limited and variable number of biopsies, ultimately leading to underdetection of disease, which could lead to an understaging of disease in Gleason score. People may not get appropriate therapy; one would not expect them to do as good a job as compared to standard modern practice. This is relatively short follow-up, variable care. One center was enrolled specifically because they stated they could get a large number of African-Americans enrolled. Therefore, this study has absolutely no useful information to contribute to tell us whether or not PSA testing and screening in African-Americans is of benefit or not.

Looking at the European study, which showed a 20% decrease in mortality, the initial findings show screening and subsequent treatment to be expensive and require a significant amount of treatment to be able to save just one life out of 50, or 2%. It appears this type of screening should not be done because it is so expensive. If this information is sustained over a later time, then the conclusion that it may not economically make sense may be correct; we just don't know.

We have screening guidelines that have been put out by the American Urological Association and the American Cancer Society. There is still the general feeling by those societies that education about prostate cancer is needed. The organizations have tended to back off from a stance towards screening.

The United States Public Health Task Force has recommended to not screen routinely over age 75; I believe that is a mistake because all 75- or 80-year-olds are not alike. Some are active; some are bedridden. They are not physiologically identical; their life expectancy is not the same. To use a mere age cutoff makes no sense; we reach the point of individualized care and individualized guidelines with respect to patient and physician. No clear guidelines exist whether younger people should be screened.

One question to consider when screening is what is the best way to screen? There are prostate specific antigens on blood tests. There are age cutoff issues in the design of the U.S. prospective study; it is simplistic to use a single cutoff value. Should clinical findings be incorporated in testing algorithms? The U.S. study did not do so; that may be an error. We know that PSA rises with BPH, and we know the trend is to rise with acute prostatitis. If you have these conditions with DRE and a big prostate, that is not the same as a man who has a small prostate with no nodules in terms of what their baseline value should be. All types of information must be incorporated when making treatment decisions.

Regarding PSA velocity, some studies show a clear advantage in using PSA velocity others show absolutely no advantage. It is not totally clear why there are different results. Also, we have very little data regarding the use of PSAs in the early 40s, outside of a few studies of limited size. A risk calculator nomogram can be compiled online. An individual can enter their own data, including race, age, PSA level, family history, DRE findings, prior prostate biopsy, and use of finasteride. A calculation is performed and a prototype obtained. The supplemental slides have specific data which address rates of prostate cancer existing at different PSA values. At low PSA values, a small fraction of people will have cancer and some even advanced cancer; at high PSA values, it may be due to BPH and no cancer. False positive/false negative readings relate to sensitivity and specificity.