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Screening for Prostate Cancer among Men 75 Years of Age or Older

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Prostate-cancer screening with the prostate-specific–antigen (PSA) test remains one of the most controversial issues in modern medicine. The U.S. Preventive Services Task Force (USPSTF), an independent group of experts supported by the Agency for Healthcare Research and Quality under a mandate from Congress, recently revised its recommendations regarding prostate-cancer screening. The USPSTF concluded that "the current evidence is insufficient to assess the balance of benefits and harms of prostate cancer screening in men younger than age 75 years," but it now "recommends against screening for prostate cancer in men age 75 years or older."[1] In its 2002 statement, the task force did not recommend for or against screening in either age group. The implication of the new recommendation for medical practice is that clinicians should discuss the potential benefits and known harms of screening with men between 50 and 74 years of age, but not necessarily with older men.

Why change the recommendation for men 75 or older, at least given the continuing dearth of evidence from randomized trials that addresses the tradeoff between the benefits and harms of prostate-cancer screening in men of any age? The task force believes that at least a moderate amount of evidence now makes it possible to conclude that the known harms of screening outweigh the possible benefits for this age group.

This statement does not imply that prostate cancer is an unimportant problem among men 75 or older; in fact, as the statement acknowledges, 71% of deaths due to prostate cancer — almost 20,000 annually in the United States — occur after the age of 75. Moreover, it does not mean that no men 75 or older could possibly benefit from screening. After all, there are relatively healthy men in their late 70s and even early 80s harboring high-grade cancers that are likely to kill them; early detection and attempted curative treatment might prevent these men from dying from prostate cancer. So why not continue to offer screening after the age of 74?

First, the effectiveness of attempted curative treatment for prostate cancer among men 75 or older appears to be low or negligible. In the only published randomized trial comparing the effect of radical prostatectomy with a strategy of "watchful waiting" for men with clinically localized prostate cancer, the benefit of radical prostatectomy was statistically significant but small, with an absolute difference of 5.4 percentage points in the rate of death due to prostate cancer at 12 years (which has not widened with continued follow-up). This difference means that about 18 radical prostatectomies would have to be performed to prevent a single death from prostate cancer over a 12-year period.[2] However, in subgroup analyses at both 10 and 12 years of follow-up, even this level of effectiveness appeared to be confined to men 65 years of age or younger. Men 75 or older were not enrolled, presumably because they were considered less likely to benefit from surgery.

It is important to note that less than 10% of subjects in this Scandinavian trial had their prostate cancer diagnosed through screening. The long average lag time between a detectable increase in the PSA level — 5 to 10 years — and the development of clinical cancer, as well as the possibility of overdiagnosis associated with PSA screening, suggests that an even smaller benefit may be seen in the U.S. Prostate Cancer Intervention versus Observation Trial (PIVOT), in which about three quarters of participants had their cancer diagnosed through PSA screening.

Results from PIVOT are expected in 2010. As in the Scandinavian trial, men 75 or older were not enrolled.

The effect of competing hazards would also attenuate the benefit of screening and attempted curative treatment for men 75 or older. Given the slow growth of most prostate cancers and the resultant long lead times between detectability and clinical disease, men may need to live much longer than 10 years to reap the benefits of PSA screening — and of course, preventing a death from prostate cancer does not bestow immortality. For example, out of 1000 75-year-old male nonsmokers, 19 would be expected to die of prostate cancer over the next 10 years, whereas 430 would be expected to die of other causes.[3] Even if a few of the deaths from prostate cancer could be prevented within this time frame, the effect on overall mortality would be small. And fewer older men than younger men would still be alive beyond 10 years to reap any delayed benefits of screening; for example, life expectancy for men surviving to the age of 85 is about 6 years.

Whereas the benefits of screening attenuate with age, the harms increase. PSA levels are strongly age-dependent, so at any given PSA threshold, older men will have substantially higher risks of both requiring a prostate biopsy and being diagnosed with prostate cancer. For example, about 6% of men in their 60s, 21% in their 70s, and 28% in their 80s would be expected to have a PSA level above 4.0 ng per liter,[4] a common threshold for considering a prostate biopsy. Regular PSA screening roughly doubles the risk that men will have to face a diagnosis of prostate cancer over the next 10 years, but many of these cancers would never present clinically. Given that the risk of prostate cancer is also age-related, this effect will be greatest among older men. And finally, the risks of both postoperative death and complications of radical prostatectomy are age-related, escalating after the age of 75.[5]

Given the unfavorable trade-off between the possible benefits and known risks of prostate-cancer screening after the age of 74, I believe the USPSTF recommendation is sound. As with all guidelines, clinical judgment should be used in its application. For example, given the relationship between self-rated health and life expectancy, a clinician might consider having a discussion about PSA screening with (not simply testing) men in their late 70s who rate their own health as "excellent" but discontinue screening discussions at the age of 75 if self-rated health is "good," at the age of 70 if self-rated health is "fair," and at the age of 65 if self-rated health is "poor." These thresholds roughly correspond to a remaining life expectancy of 10 years, a threshold below which other guidelines — for example, those from the American Cancer Society — have recommended against screening. Any threshold, of course, is inevitably somewhat arbitrary.

Considering the ongoing controversies surrounding prostate-cancer screening, evidence from randomized trials about benefit and harms would be welcome indeed. The large, ongoing trials of PSA screening in the United States (the Prostate, Lung, Colorectal, and Ovarian, or PLCO, Cancer Screening Trial), Europe (the European Randomized Study of Screening for Prostate Cancer, or ERSPC), and the United Kingdom (Prostate Testing for Cancer and Treatment, or Protect) will eventually help to resolve some of these controversies — the first two trials should produce results over the next 5 years. However, none of the findings from these trials will bear directly on the question of whether screening is appropriate for men 75 or older, since men in this age group were excluded from all three.

Population-based studies of PSA testing in the United States have shown fairly high levels of screening among men in their late 70s and even in their 80s. The new recommendations from the USPSTF should prompt clinicians and patients to think twice, or even three times, before ordering PSA tests for cases in which screening is especially likely to do more harm than good.

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