Virtual Mentor
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ETHICS CASE
Is More Screening Always Better?
Commentary by Michael LeFevre, MD, MSPH

Andrew, a fourth-year medical student, applied for a residency in family medicine. While on a rotation at his top-choice program, he noticed something interesting. During the family medicine rotation at his medical school, residents and attending physicians had recommended biopsy if a patient's prostate-specific antigen (PSA) levels were above 4 nanograms per milliliter (ng/mL). In the program that Andrew hoped to become part of, however, residents and attending physicians often recommended biopsies if the patient's PSA levels were above 2.5 ng/mL, a practice Andrew had not seen before.

When Andrew asked the resident about this, he was told that this lower PSA threshold for biopsy allowed doctors not only to catch more cases of prostate cancer but to catch those cancers earlier, when they were more treatable. This made sense to Andrew, and he wondered why the family medicine department at his medical school did not do the same.

He approached the chair of family medicine at his school, who told him there was not enough evidence that biopsies at lower thresholds actually improved patient outcomes and, in fact, they could lead to overuse of resources and overdiagnosis of prostate cancer.

Andrew was confused. Both approaches seemed reasonable to him, and, given his lack of experience and his respect for both institutions, he was unsure which was better. He decided to talk to the dean of curriculum at his medical school about his dilemma. After their discussion, the dean wondered how many of his students encountered similar variations in care on rotations at other hospitals and how those variations should be discussed in the medical school curriculum.

Commentary
Why did Andrew encounter different approaches to the PSA threshold for recommending biopsy? What should he learn from the experience? When he becomes a family medicine resident and takes care of his own panel of patients, what should he recommend? Finally, what, if anything, should Andrew's dean of curriculum do?

All medical care should seek to achieve one or more of three goals: to prevent future suffering, to relieve suffering, or to prolong life. Preventive services, by definition, are used to prevent future suffering or prolong life. Prostate cancer is a logical target

for a preventive service; much public discourse about prostate cancer prevention today focuses on screening. Cancer screening seeks to identify cancers in asymptomatic people with the hope of altering the natural history of those cancers destined to cause suffering without doing too much harm in the process.

What do we know about the relationship between PSA level and the presence of either low-grade or high-grade prostate cancer? The control group in the Prostate Cancer Prevention Trial (PCPT) [1], i.e., those not receiving finasteride, provided a unique opportunity to examine how common prostate cancer is in a population of men eligible for screening, as well as the relationship between PSA level and the presence of prostate cancer. During the study, prostate biopsies were offered to all men (in both the intervention and control groups) who had abnormal screening results, either an abnormal digital rectal exam or a PSA above 4.0 ng/ml. In addition, men who had not had a biopsy for cause were offered an end-of-study biopsy. Almost 25 percent of men in the control group had cancer diagnosed with a biopsy; 85 percent of those cancers were in the low-grade category. Of the men whose PSA was consistently below 4.0 ng/ml and who had end-of-study biopsies, 15.2 percent had prostate cancer. The PSA distributions were very similar for those whose end-of-study biopsy showed no cancer, low-grade cancer, and high-grade cancer. This study allows us to draw three important conclusions: (a) prostate cancer is very common; many more men have prostate cancer than will ever suffer from the disease, (b) there is no clear PSA threshold that provides an optimal sensitivity for high-grade cancer while minimizing both the false positive rate and detection of low-grade cancer, and (c) most cancers detected by screening are low-grade. The harder you look for prostate cancer, the more you will find. What this study could not tell us is whether looking hard for prostate cancer serves medicine's goals, either by preventing future suffering or prolonging life.

What do we know about the benefits of prostate cancer screening? The multicenter Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial [2] conducted in the US showed a non-statistically significant increase in prostate cancer mortality in the screening group, though the European Randomized Study of Screening for Prostate Cancer trial [3] showed a statistically significant absolute reduction of 0.10 prostate cancer deaths per 1,000 person-years after a median follow-up of 11 years. All-cause mortality was 19.1 percent in the screened group and 19.3 percent in the control group, a difference not statistically significant. Screening frequency and the threshold for referral for biopsy differed by screening location, but differences in outcomes between countries could not be clearly linked to screening protocol.

The small reduction in prostate cancer mortality in the European trial occurred in the context of a significant increase in the number of cancers diagnosed and treated in the screened group. Much of the morbidity resulting from prostate cancer is a consequence of the diagnosis and management of the disease, rather than the disease itself, and many screen-detected cancers would never become apparent—never cause suffering—in the lifetime of the patient without screening. Screening for prostate cancer may prevent future suffering or prolong life in a few men, but the detection

and treatment of indolent disease may actually harm more men than it helps. This overdiagnosis and overtreatment is the principal source of harm in PSA screening for prostate cancer. It was the judgment of the US Preventive Services Task Force (USPSTF) that the potential benefit of screening does not outweigh the harms [4].

Andrew's dilemma will be played out over and over about many forms of screening, diagnosis, and treatment as he progresses through his medical education and training. Several ethical questions arise in this situation. How good should the evidence of benefit and harm be before we offer or recommend a medical intervention to a patient? Are we obliged to offer services we hope, but don't know, will help? Should we focus primarily on benefit, or are harms of equal importance? Preventive services are offered to people who feel well; we are leveraging a real possibility of causing suffering in people who feel well against a possibility of avoiding future suffering or prolonging life. Should the evidence bar be higher for preventive services than for those that aim to relieve current suffering? If we do offer services about which evidence is unclear, what do we owe our patients to enable an informed decision?

The principles of beneficence and nonmaleficence often come into conflict. When faced with a risk of future suffering, "don't just stand there, do something" is often in direct conflict with "first, do no harm." All medical care has the potential to cause harms. A case can be made that benefits and harms must hold equal sway and that, particularly for preventive services, the evidence should be clear that across the population served we do more good than harm. If clear evidence favors action, then we act. Science must trump hope.

Should Andrew continue to pursue training at his top-choice program? A critical component of residency training should be learning how to think about clinical decisions, not just learning what to do. Good doctors who are recent residency graduates can easily become bad doctors in a decade if they are not continually questioning what they do and why they do it and assimilating new information into clinical care. Good clinical decisions incorporate the best science available, individual patient circumstances, and patient preferences. Faculty should be open to learners who challenge their thinking in the interest of learning. If Andrew's sense is that the faculty are not thinking critically about the care they provide, another program may prepare him better for the future.

How should Andrew's dean of curriculum respond? Medical students should graduate with an understanding of the significant variations in care that exist both across and within institutions. Students should be taught to use the variations as a stimulus to learn how decisions are being made, and to pursue for themselves the science that informs those decisions. One of our major responsibilities in medical education should be to promote intellectual curiosity and lifelong learning.

What should Andrew do about PSA screening when gets his own panel of patients? It is difficult to make the case that we have an ethical imperative to offer PSA screening, but the balance of benefit and harms does not preclude a physician

offering or a patient requesting the service. Patient autonomy and patient preferences and values must be respected, but a clear understanding of what the science tells us about the benefit and harms of PSA screening for prostate cancer should precede testing.

It's not "just a blood test"; a cascade of testing and treatment that is hard to stop begins with the PSA test. Prostate cancer is very common, but very few men actually benefit from early detection and treatment, and more will be harmed. A man who places a higher value on the possibility of avoiding a prostate cancer death than on the harms of overdiagnosis and overtreatment may make the autonomous decision to be screened. But we should not make it for him. It is fair to advise patients that different thresholds exist for further evaluation, but incremental benefit from the lower threshold remains to be demonstrated, and an increase in harms is almost certain.

References

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