Misinterpretation of Prostate Cancer Data

In a recent issue of the *Journal*, Lauer (1) suggested that the lack of effect of prostate-specific antigen (PSA) screening for prostate cancer is an important reason to be cautious about screening for subclinical coronary artery disease. Unfortunately, his argument might be fallacious. First, he states that prostate cancer death rates have not declined, despite widespread screening. Quite the contrary is true. Death rates due to prostate cancer have substantially declined in the U.S. from 39.2 to 23.6/100,000 from 1992 to 2006 (2–4). This is an age-adjusted decline of approximately 4%/year. From 1991 to 2004, prostate cancer mortality has declined much more rapidly in the U.S. with the frequent use of PSA testing than in the United Kingdom, where there is less screening (4.2%/year in the United Kingdom, where there is less screening (4.2%/year in the United Kingdom; 5).

Second, he points to the recent report of the PLCO (Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial) that failed to document benefit of prostate cancer screening with PSA (6). Unfortunately, the PLCO trial was contaminated by high screening rates in the comparison group and a lack of control for therapies for prostate cancer. It is estimated that probably 50% of men 50 years of age and older in the U.S. have a PSA test. Most recently, PSA testing was evaluated in a population that was previously unexposed to PSA testing. A randomized trial of 20,000 men in Göteborg, Sweden, 50 to 64 years of age at entry were followed an average of 14 years (7). The reduction of prostate cancer deaths was 40% (range 0.17 to 64) in the PSA screening versus control group, p = 0.002. Approximately 293 men needed to be screened and 12 needed to be diagnosed to prevent 1 prostate cancer death—44 deaths in the intervention versus 78 in the control group. The effect of PSA testing on reducing mortality in this study was of similar magnitude as mammography screening for breast cancer.

A trial to evaluate screening of asymptomatic individuals for the prevention of subsequent clinical coronary artery disease events (i.e., screening asymptomatic individuals with coronary calcium detection) is impractical. The technology is widely available; its prognostic implications are well-published; and preventive therapies such as lipid lowering, antihypertensive therapy, and lifestyle modifications are now accessible and affordable. Such a trial, like the PLCO trial, will be contaminated by crossovers, use or lack of use of statins and other effective therapies, and poor compliance with dietary and pharmacological therapies. The trial of hard endpoints (i.e., coronary heart disease [CHD] deaths or myocardial infarction), will require long follow-up because of the early stage of incubation of atherosclerosis in which these individuals will be detected. Do we really need to prove that lipid lowering is effective in individuals with atherosclerosis for reducing CHD mortality? Do we need to waste another 7 to 10 years and millions of dollars of valuable research funds? The key is maximizing the use of proven effective preventive pharmacological and nonpharmacological therapies by targeting the population most likely to benefit from them and thereby substantially reducing CHD incidence, mortality, and costs of health care.

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REFERENCES


**Reply**

In their thoughtful letter, Drs. Kuller and Edmundowicz challenge my call for randomized trials of coronary artery screening (1). They cite U.S./United Kingdom ecological data demonstrating public health benefits from prostate–specific antigen (PSA) screening (2) and then cite a just-published randomized trial that found reduced mortality (3). They argue that, in our current environment, it is impractical to execute trials, and even so, they are unnecessary: we already know lipid-lowering therapy works.

Numerous authorities have cited the limitations of observational analyses of screening; these include lead- and length-time bias, misattribution bias, and overdiagnosis. Even Collin et al. (2), who wrote the positive ecological study that Kuller and Edmundowicz cite, conclude their report stating, “We can only continue to speculate about the relative contributions of differences in detection and treatment or the relative balance of benefits and harms, until the publication of findings from trials provides the robust evidence that is so eagerly awaited.” I agree!

Prostate cancer kills far less often than coronary artery disease, yet academic leaders have completed large-scale trials. Two trials that enrolled approximately 250,000 patients showed little or no benefit and much overdiagnosis, whereas 1 trial an order of magnitude smaller suggests benefit in some patients (3). Academic leaders have performed screening trials for other less common diseases, including breast cancer, lung cancer, and aortic aneurysm. Surely we can execute a screening trial for coronary disease, the nation’s leading cause of death.