

Letter to the Editor

Re: Determinants of participation in prostate cancer screening: A simple analytical framework to account for healthy-user bias

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Dear Editor,
Recently, Tabuchi *et al.* (*Cancer Sci* 2015; 106: 108–14)⁽¹⁾ investigated “determinants of prostate-specific antigen (PSA)-based screening participation while simultaneously taking into account factors associated with fecal occult blood test (FOBT).” They found “three factors related to healthy-user bias: i.e., older age, a technical or junior college education, and adherence to doctors’ suggestions,” and concluded that “it may be necessary to increase participation in the former (FOBT) and decrease it in the latter (PSA testing).” However, their observations appeared to be associated with the characteristics of screenees, but do not seem to be a solid reason for reducing participation in PSA-based screening. It appears that no problem exists in the statement for FOBT, but seems at least premature for PSA testing.

Prostate cancer (PCa) was very rare 30–40 years ago in Japan. The incidence has been rapidly growing,⁽²⁾ and PCa is now one of the major cancers. It is predicted to become the second most common cancer by 2020, following lung cancer, according to Globocan 2012.⁽³⁾ Not only primary prevention but also secondary prevention is crucial. However, because no definite preventive or risk factors for PCa are known,⁽⁴⁾ convincing primary prevention is unavailable at present. Thus, there is nothing else to adopt for early detection and treatments, including digital rectal examination, transrectal ultrasound examination, and PSA testing. Of these, PSA-based screening seems the most useful.

Randomized controlled trials (RCTs) were conducted to evaluate a PCa mortality-lowering effect of PSA testing; the findings were controversial in two major RCTs carried out in European countries (European Randomized Study of Screening for Prostate Cancer [ERSPC]),⁽⁵⁾ and the USA (US Prostate, Lung, Colorectal, and Ovarian [PLCO] Cancer Screening Trial).⁽⁶⁾ Both RCTs should be criticized in view of their limitations, statistical power, observation period, or biases. The higher contamination (or self-selection) of participation in PSA testing in the control arm in the US PLCO Cancer Screening Trial, in particular, poses a serious problem.⁽⁷⁾ Formerly, the Japanese Urologi-

cal Association recommended PSA testing⁽⁸⁾ in line with the results of the ERSPC study, which were confirmed by the inclusion of follow-up data up to 13 years.⁽⁹⁾ On the other hand, as also discussed by the authors, the US Preventive Services Task Force (USPSTF) declared an opposite statement,⁽¹⁰⁾ mostly based on the findings of the US PLCO Cancer Screening Trial. According to the guideline, which depended on a systematic literature review by a research group⁽¹¹⁾ under the auspices of the Ministry of Health, Labour and Welfare, Japan, the Ministry decided not to include PSA testing as a population-based screening program for PCa.⁽¹²⁾

For the PSA test performance with a cut-off figure of 4.0 ng/mL, the sensitivity was reported to be approximately 20%, specificity ~90%, and a positive predictive value of ~30%.⁽¹³⁾ The values appear rather low, but are acceptably robust. Problems include the fact that it detects certain latent/low-risk PCa along with prostate hypertrophy and inflammation as well as PCa to be treated; that is, there are some over-diagnoses and over-treatments. However, the USPSTF acknowledged: “This recommendation does not include the use of the PSA test for surveillance after diagnosis or treatment of PCa,”⁽¹⁰⁾ suggesting that the test is useful. Accordingly, PSA testing appears to be a double-edged sword, so we must handle it properly.

At least two proposals could be made regarding PSA-based screening. Provided that RCT is actually impractical, a case-control study should be conducted to assess the effectiveness of PSA screening in Japanese men having specific genetic backgrounds and lifestyle factors, while the prevalence of PCa and PSA testing remain low/lower. In order to reduce PCa mortality, prolong patients’ healthy life, and improve quality of life, while lessening undue medical expenditure, risk communication (informed decision-making) on the screening should be undertaken among physicians, patients, and responsible parties, including work-site, municipal, and governmental health sectors.

Disclosure Statement

The author has no conflict of interest.

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