Response

We thank Etzioni and Gulati, who argue that their modeling of overdiagnosis (developed for assessing screening strategies) can be expanded to guide treatment of screen-diagnosed cancer patients, for their letter. The key issue is not whether estimates of prostate-cancer overdiagnosis are useful in the absence of other information. The issue we raised is different: for a patient with screen-diagnosed prostate cancer who is given the distribution of outcomes and side-effects for all available treatment options (including no treatment), does the estimate of overdiagnosis provide additional help in guiding treatment decisions?

Consider the two patients Etzioni and Gulati discussed. For the first, an 80-year-old patient with Gleason score of 6 and prostate-specific antigen of 5 ng/mL, empirical clinical data are available to demonstrate that under conservative management this patient would have a relatively low chance of dying from prostate cancer (<20%) (1). Given this information, of what additional value to the patient is it to know that there is a 20% chance that his cancer is overdiagnosed? For the second, a 50-year-old patient with Gleason score of 7 and prostate-specific antigen of 4.5 ng/mL, the probability of dying from prostate cancer is as high as 80% (2). This patient needs to know, for the available treatment strategies (including active surveillance), the probabilities of various side effects and the time-to-event distributions for symptoms, metastatic disease, death from prostate cancer, and death from any cause. Younger prostate cancer patients need personalized biomarkers that accurately predict their disease aggressiveness based on the individual's tumor characteristics (3). Etzioni and Gulati say that their nomogram provides "personalized overdiagnosis estimates." However, their nomogram is almost completely driven by age (eg, Gleason score has a negligible role), reflecting age-adjusted life expectancy rather than tumor behavior on an individual level.

We further suggest that overdiagnosis is less-useful information for patients than treatment-outcome distributions. First, the probability of overdiagnosis may or may not be equivalent to the probability that this particular patient "will have to deal with a symptomatic tumor at some point in his life" because of the uncertainties in his health status and future medical follow-up (4,5). Second, except for elderly patients who need no therapy, overdiagnosis lacks any information on the competing treatments (including active surveillance), which is needed for informed decision making. Third, overdiagnosis may be misleading; for example, for a 50-year-old man, overdiagnosis equates the effect of prostate cancer diagnosis at his current 50 years with diagnosis at a later age (eg, when he is aged 80 years). However, given the morbidity of prostate cancer treatments, the effect on the patient's lifetime quality-of-life of being diagnosed and treated at 50 years is quite different than that at 80 years. Fourth, overdiagnosis does not directly estimate its potential primary harm, overtreatment (4), but is an upper bound for it.

We recognize that it may not be straightforward to get the outcome distributions for the treatments (including active surveillance) based on prognostic variables. An appropriate analysis using data from randomized trials, observational studies, and registries may involve modeling to interpolate and extrapolate to various treatment options [with the appropriate caveats (6)].

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