Estimating Prostate Cancer Overdiagnosis in Individuals

February 17, 2014

JM Kocarnik

Cancer screening programs have been highly successful at reducing morbidity and mortality due to screening-preventable or treatable cancers. Such programs, however, also carry the risk of detecting cancers that would never have become symptomatic or clinically apparent without screening. As they would not pose a risk to the patient, the identification and unnecessary treatment of such indolent or slow growing tumors can potentially lead to both individual and systemic harms. One type of cancer in which such overdiagnosis can be problematic is prostate cancer. Under the direction of Dr. Ruth Etzioni in the Public Health Sciences Division, Mr. Roman Gulati and colleagues developed a clinical tool to help inform patients with screen-detected prostate cancer of the chance their cancer was overdiagnosed, which may be helpful for guiding treatment decisions. This work was reported in a recent issue of the *Journal of the National Cancer Institute*.

Overdiagnosis is a serious issue, says senior author Etzioni, as "in the United States, about one in four to one in three men detected by prostate-specific antigen (PSA) screening is overdiagnosed." However, the chance than an individual case has been overdiagnosed can vary widely. Unfortunately, "men with screen-detected prostate cancers are making treatment decisions with only limited information about the chance that their cancer is overdiagnosed," says lead author Gulati, which makes it difficult to weigh the likely harms and benefits of different treatment options. In order to give patients this information, the authors first developed a novel mathematical simulation model of prostate cancer natural history (see other references below). This model provides "a reasonable reflection of what would have happened to screen-detected cases had they not been treated," says Etzioni, and "is what we need to know to calculate the chance of overdiagnosis."

The authors used this framework to predict the individualized risk of overdiagnosis among non-metastatic patients diagnosed by screening with a PSA less than 10 ng/mL, given the patient's age, Gleason score, and PSA at diagnosis. Each of these factors was important for determining the chances of overdiagnosis, which ranged from 2.9% to 88.1% (see figure). Age was the most important factor, since overdiagnosis is highly dependent on remaining life expectancy. Each

additional year of age at diagnosis was associated with a 12.9% increase in the odds of overdiagnosis. For the other factors, each additional 1 ng/mL of serum PSA (up to 10 ng/mL) was associated with a 16.6% decrease in the odds of overdiagnosis, while a Gleason score of 7 or more (compared to 6 or less) was associated with a 19.5% decrease in the odds of overdiagnosis. Together, the model predicts the risk of overdiagnosis among PSA-detected patients reasonably accurately, with an area under the curve of 0.75.

Says Gulati, "we present this information in the form of a nomogram so that patients can better understand their personalized risk of overdiagnosis." This nomogram allows an easy calculation of the overall chance of overdiagnosis given these individual patient characteristics. Such information could be useful for patients making treatment decisions following a screen-detected diagnosis. For patients with a very high chance of overdiagnosis, says Etzioni, "perhaps our results can help these cases feel more comfortable with an active surveillance approach."

While this tool is a valuable resource, the authors are working towards refining these predictions further. "We intend to improve the nomogram by incorporating patient comorbidities and additional tumor staging information," said Gulati. Furthermore, additional work in small patient groups may help identify how to most clearly communicate this information to patients. Given their success in prostate cancer, the authors are also working to develop a similar tool for breast cancer detected in women undergoing mammography screening. As with prostate cancer, the goal remains the same, says Etzioni: "to package these results into an educational aid for patients at risk of overdiagnosis, so that they can fully participate in shared and informed decision-making regarding their care."

Other PHS investigators contributing to this project were Drs. Lurdes Inoue, John Gore, and Jeffrey Katcher.

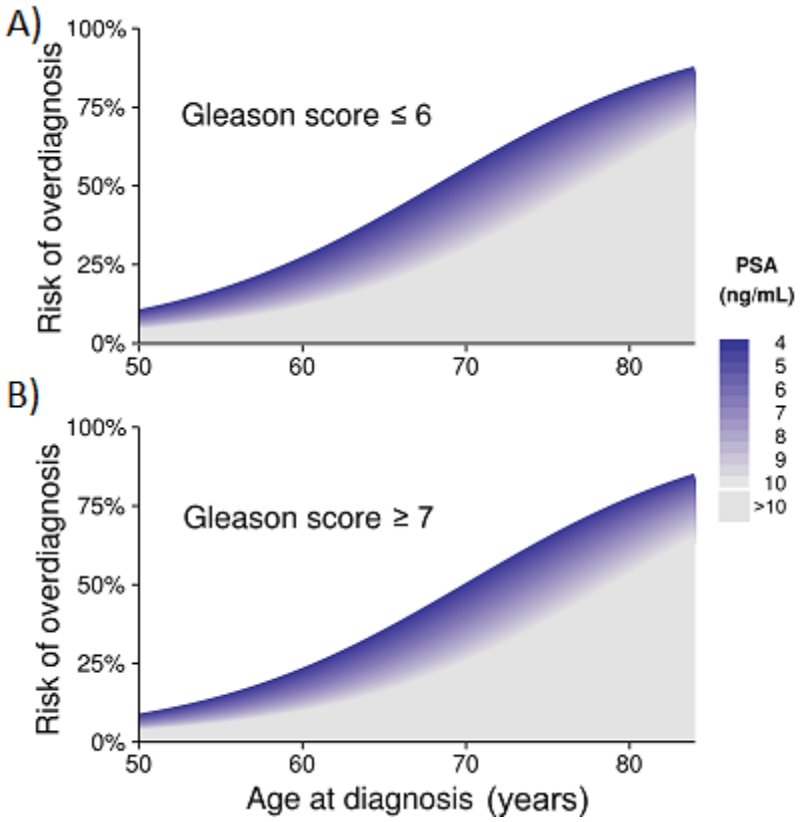
Gulati R, Inoue LYT, Gore JL, Katcher J, Etzioni R. 2014. Individualized estimates of overdiagnosis in screen-detected prostate cancer. *J Natl Cancer Inst*. 2014 Feb 1;106(2):djt367. Doi: 10.1093/jnci/djt367.

Additional resources:

Gulati R, Gore JL, Etzioni R. 2013. Comparative effectiveness of alternative prostate-specific antigen-based prostate cancer screening strategies: model estimates of potential benefits and harms. *Ann Intern Med*. 158(3):145-53.

Gulati R, Inoue L, Katcher J, Hazelton W, Etzioni R. 2010. Calibrating disease progression models using population data: a critical precursor to policy development in cancer control. *Biostatistics.* 11(4):707-19.

Gulati R, Wever EM, Tsodikov A, Penson DF, Inoue LY, Katcher J, Lee SY, Heijnsdijk EA, Draisma G, de Koning HJ, Etzioni R. 2011. What if I don't treat my PSA-detected prostate cancer? Answers from three natural history models. *Cancer Epidemiol Biomarkers Prev*. 20(5):740-50.



(Image provided by Mr. Roman Gulati)

Plot showing the chance that a prostate-specific antigen (PSA) screening-detected prostate cancer given a patient's age (x-axis), PSA (color gradient), and Gleason score (6 or less (A) versus 7 or more (B)), among non-metastatic men with PSA less than 10 ng/mL.