RE: A Model Too Far

Freidlin and Korn's editorial (1) concerning our article on prostate cancer overdiagnosis questioned the utility of our personalized overdiagnosis estimates for informing treatment decision making. Their comments suggest that knowing the risk of overdiagnosis does not help to inform about the outcomes of various treatment options after diagnosis. However, overdiagnosis informs about the outcome of a key treatment option—that of no treatment. Consider the dilemma faced by a patient who has just been diagnosed with prostate cancer after a screening test. Knowing that treatment can reduce the risk of dying from cancer but the treatment could leave him impotent or incontinent, should he be treated or not? The value of our results is that they inform the patient about what might happen if his cancer were to be left untreated. Thus, for a 50-year-old man with a biopsy Gleason score of 7 and a prostate-specific antigen of 4.5 ng/mL, there is a high risk (risk of 9 of 10) that he will have to deal with a symptomatic tumor at some point in his life if he does not treat his cancer, whereas for an 80-year-old man with a Gleason score 6 and a prostate-specific antigen of 5 ng/mL, this risk is much lower, approximately one in five. For this older patient, if he does absolutely nothing at this point, there is an 80% chance that his cancer will never cause symptoms or problems. This kind of information could be very helpful in persuading many older, low-risk patients to consider active surveillance, which is likely to be the single most important change in clinical practice to reduce the problem of overtreatment.

Freidlin and Korn also critique our modeling approach, stating that "the most reliable and transparent approach to estimating overdiagnosis … is with an appropriate analysis of data from a randomized screening trial" (1). However they do not tell us what an "appropriate analysis" might be. Conventional statistical analysis runs into problems when attempting to infer overdiagnosis frequencies from trials because whether a case has been overdiagnosed is not observable. There have been attempts to use observed excess incidence in the screened arm as a proxy for overdiagnosis, but this approach, because it typically produces inflated estimates (2), particularly under insufficient follow-up, which is a limitation of all published prostate screening trials. A modeling approach goes beneath the surface of empirical data and can be applied to trials as well as to population incidence data. This approach has a long history in the biostatistics literature [eg, (3,4)]. In general, we support a healthy and constructive skepticism of models. Yet, in this this situation, only a model can provide personalized estimates of the chance that a screen-detected prostate cancer has been overdiagnosed, and the resulting nomogram adds materially to the information currently available for patients considering the option of no treatment.

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References

1. Freidlin B, Korn EL. A model too far. *J Natl Cancer Inst*. 2014;106(4):dju059 doi:10.1093/jnci/dju059.
2. Etzioni R, Gulati R, Mallinger L, et al. Influence of study features and methods on overdiagnosis estimates in breast and prostate cancer screening. *Ann Intern Med*. 2013;158(11):831–838.
3. Zelen M, Feinleib M. On the theory of screening for chronic diseases. *Biometrika*. 1969;56(3):601–614.
4. Pinsky PF. Estimation and prediction for cancer screening models using deconvolution and smoothing. *Biometrics*. 2001;57(2):389–395.

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