Prognosis in the era of comparative effectiveness research

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To the Editor:

We read with great interest the review article by Shaw et al,¹ aimed at providing an update on contemporary concepts in risk stratification with stress myocardial perfusion imaging (MPI). We agree that the recently introduced concept of risk reclassification as an improved statistical calculation of incremental value has enhanced the clinical value of risk stratification.²⁻⁴ However, we have some concern about the interpretation of the results obtained with the net reclassification improvement (NRI) analysis. Shaw et al¹ stated that the NRI examines the delta improvement in a model (model #2) which includes clinical variables plus an imaging marker (e.g., left ventricular function or stress MPI abnormalities) vs another model (model #1) which includes only clinical variables, in so far as the percentage of patients calculated as being newly identified as low or high risk. As an example, they quoted a recent study reporting on the NRI with stress MPI.⁵ The results of that study revealed that the NRI for percent ischemic myocardium was ~36%, or that one in three patients had improved risk reclassification of CAD or myocardial infarction after stress MPI when compared with a Cox model that included the Duke treadmill score and pretest clinical risk.⁵ It must be considered that 1,656/4,575 patients (~36%) were correctly reclassified and the NRI also was ~0.36.⁵ However, the NRI value is not merely the ratio between the number of patients correctly reclassified and the total study population. The NRI is based on event-specific reclassification tables and only for the particular distribution of reclassification between “event” and “no event,” the two values (NRI and percent of correct reclassification) may coincide. As an example, consider a study of 1,000 subjects with 300 events (30%) and a new marker that correctly reclassified 30% of the total study population. If all the 300 subjects reclassified are “event” subjects, then the NRI is 1 (300/300), while if the 300 subjects reclassified are “no event” subjects, then the NRI is 0.43 (300/700). In fact, if all “event” and “no event” subjects are

correctly reclassified, the NRI is 2 (the maximum possible value), and thus NRI is perhaps better expressed in absolute units than in percentage, to avoid misleading interpretation. As an ancillary question, the authors of that study stated that only 40% of patients underwent an exercise stress test and the remaining underwent a pharmacologic stress test, with monitoring procedures similar to an exercise test.⁵ It is unclear how the Duke treadmill score was calculated in patients undergoing pharmacologic stress test and whether this score has been validated for pharmacologic stress test for diagnostic and/or prognostic purposes.

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