

Table E5. Net reclassification results when comparing the clinical model to models with biomarkers of increasing strength (OR ranging from 1.5 to 6.0), and alternative parameterization of risk thresholds (<10%, 10-50%, >50%) and sample size of 10,000 subjects.

Odds ratio (OR) of biomarker	Overall NRI (95%CI)	NRI for cases (95% CI)	NRI for controls (95% CI)
1.5	0.007 (-0.024, 0.050)	0.007 (-0.025, 0.044)	0.003 (-0.006, 0.003)
2.0	0.072 (0.030, 0.126)	0.070 (0.026, 0.122)	-0.002 (-0.014, 0.002)
2.5	0.072 (0.025, 0.135)	0.068 (0.017, 0.126)	-0.004 (-0.015, -0.001)
3.0	0.131 (0.070, 0.184)	0.136 (0.079, 0.194)	-0.005 (-0.017, -0.004)
4.5	0.178 (0.125, 0.235)	0.187 (0.138, 0.250)	-0.009 (-0.025, -0.003)
6.0	0.300 (0.257, 0.374)	0.308 (0.269, 0.380)	-0.008 (-0.022, -0.002)

^ The 95% confidence intervals for all NRI data derive from the bootstrap (1000 replications).

Interpretive example: At higher risk thresholds, significant reclassification of critical illness risk was observed when including even a weak biomarker in a clinical risk model (OR 2.0, NRI=0.072 (95%CI: 0.030, 0.126)). However, reclassification of controls was not improved using a biomarker at these risk thresholds.