

**Appendix 7:** Computation of net reclassification improvement statistics characterizing the difference in predictive ability when inflammation was assessed using 2 measures (model 2) versus one measure (model 1)

	Successful aging, <i>n</i> = 721	Fatal or nonfatal CVD events, <i>n</i> = 321	Non-CVD death, <i>n</i> = 147						
	OR (95% CI)	OR (95% CI)	OR (95% CI)						
<b>Model 1: Interleukin-6 assessed at baseline</b>									
Low	1.00 (ref)	1.00 (ref)	1.00 (ref)						
Intermediate	0.70 (0.58–0.86)	1.41 (1.00–1.99)	1.33 (0.78–2.28)						
High	0.45 (0.35–0.59)	1.76 (1.21–2.55)	2.64 (1.53–4.55)						
<b>Model 2: Interleukin-6 assessed 5-yr before baseline and at baseline</b>									
Interleukin-6 assessed 5-yr before baseline									
Low	1.00 (ref)	1.00 (ref)	1.00 (ref)						
Intermediate	0.67 (0.55–0.83)	1.39 (0.98–1.97)	1.62 (0.91–3.06)						
High	0.65 (0.49–0.85)	1.73 (1.16–2.58)	1.67 (0.95–2.79)						
Interleukin-6 assessed at baseline									
Low	1.00 (ref)	1.00 (ref)	1.00 (ref)						
Intermediate	0.79 (0.64–0.97)	1.28 (0.90–1.81)	1.18 (0.67–2.05)						
High	0.53 (0.41–0.71)	1.46 (0.98–2.17)	2.24 (1.26–3.98)						
<b>Net reclassification improvement (NRI) between model 1 and model 2*</b>	NRI	Standard error	<i>p</i> value	NRI†	Standard error	<i>p</i> value	NRI†	Standard error	<i>p</i> value
	0.236	0.040	< 0.001	0.154	0.058	0.009	0.221	0.062	0.009

Note: CI = confidence interval, CVD = cardiovascular, OR = odds ratio.

Analyses assessed the associations of inflammation with: (1) successful aging (v. non-cases: normal aging phenotype, CVD events and non-CVD death phenotypes combined), total *n* = 3044; (2) CVD events (non-cases: successful and normal aging phenotypes combined), total *n* = 2897 (the 147 participants with non-CVD death were excluded); (3) non-CVD death (non-cases: successful and normal aging phenotypes combined), total *n* = 2723 (the 321 participants with a CVD event were excluded). Models were adjusted for sex, age, socioeconomic status, smoking status, physical activity, acute inflammation and use of anti-inflammatory drugs.

\*Calculation of the NRI statistics<sup>1,2</sup> provides the difference in predictive ability when inflammation was assessed using 2 Interleukin-6 measurements (both 5-yr before baseline and at baseline) versus one Interleukin-6 measurement (at baseline) by comparing the predicted risk levels among participants who developed a specific aging phenotype and those who did not.

**References**

1. Pencina MJ, D'Agostino RB Sr, D'Agostino RB Jr, et al. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. *Stat Med* 2008;27:157-72.
2. Pencina MJ, D'Agostino RB Sr, Steyerberg EW. Extensions of net reclassification improvement calculations to measure usefulness of new biomarkers. *Stat Med* 2011;30:11-21.