Appendix 3: Details of the sensitivity analyses

To examine potential competing risk bias, we assessed the association between inflammation and aging phenotypes using multinomial regression. We estimated odds of successful aging and the 2 unhealthy aging outcomes within a single analysis with normal aging as the common reference point for all 3 outcomes, thus avoiding the substantial overlap in the different health components of aging (Appendix 5).

Three sets of sensitivity analyses were also carried out to assess the extent to which the association between inflammation and aging phenotypes were driven by obesity, use of anti-inflammatory drugs and acute inflammation, by excluding successively (a) obese participants (defined by a body mass index ≥ 30 kg/m^2); (b) users of anti-inflammatory medications and (c) participants with acute inflammation (C-reactive protein > 10 mg/L) (Appendix 6).

To assess whether the sample selection may affect the associations, we performed 2 supplementary analyses. First we compared the odds ratios of noncardiovascular mortality for all 5353 participants with complete data on inflammation and cause of death with the corresponding odds ratios for the 3044 participants included in the main analysis. Second, from the sample of 4165 participants with complete data on aging phenotypes, we applied a multiple imputation method to deal with missing data on inflammation and covariates.

Finally, we used net reclassification improvement statistics[1,2] to examine the extent by which assessing the level of inflammation by using 2 repeated measurements, as compared with using a single measurement, provides a stronger predictor for future aging phenotypes (Appendix 7).

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.

Appendix to: Akbaraly TN, Hamer M, Ferrie JE, et al. Chronic inflammation as a determinant of future aging phenotypes. *CMAJ* 2013. DOI:10.1503/cmaj.122072.