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Circulating cystatin-C is associated with dementia in a racial and ethnically diverse cohort: An interaction decomposition analysis

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Abstract

Background: Cystatin-C has an important role in the pathogenesis of dementia, as evidenced by expression in the brain and co-localization with beta-amyloid deposits. Circulating Cystatin-C may be directly implicated in neurodegeneration, or the result of a compensatory mechanism of neuroprotection. Our study aims to understand the relationship between circulating Cystatin-C and dementia, and to test the interaction between Cystatin-C and race/ethnicity.

Methods: We performed a cross-sectional analysis of serum Cystatin-C levels with dementia and cognitive impairment non-dementia (CIND) in two waves (2006 and 2008) of the Health and Retirement Study (n=9,984). We used Poisson regression with robust variance to estimate the interactive effect of race/ethnicity and Cystatin-C $>75^{th}$ on dementia. We calculated three measures of interaction in the additive scale: the excess risk due to interaction (RERI), the attributable proportion, and the synergy index (SI). We decomposed the interaction to calculate the percentage of the excess risk attributable to the effects of race/ethnicity and Cystatin-C alone.

Results: African Americans and Hispanics had higher levels of Cystatin-C at every decade of life except for the 80s with respect to Whites (see Figure 1). The prevalence ratio for dementia among African Americans with levels of Cystatin-C $>75^{th}$ was 7.33 (95%CI: 5.43, 9.89) times of White Americans with Cystatin-C $<75^{th}$. A RERI of 1.89 (95%CI: -0.17, 3.95) indicates more than an additive interaction; and attributable proportion of 0.26 (95%CI: 0.02, 0.50) suggests than roughly a quarter of the excess risk was due to the interaction of both race and Cystatin-C; and a synergy index of 1.43 (95%CI: 0.97, 2.10) provided evidence of synergism between the two exposures. We found 26% (95%CI: 2%, 50%) of the excess risk among the doubly exposed group (i.e., African Americans with levels of Cystatin-C $>75^{th}$) was attributable to the interaction between Cystatin-C and race. Similar patterns were observed for Hispanics in relation to Whites.

Conclusion: Elevated levels of circulating Cystatin-C are implicated in impaired cognition, and the association between Cystatin-C and cognition varies dramatically by race/ethnicity.

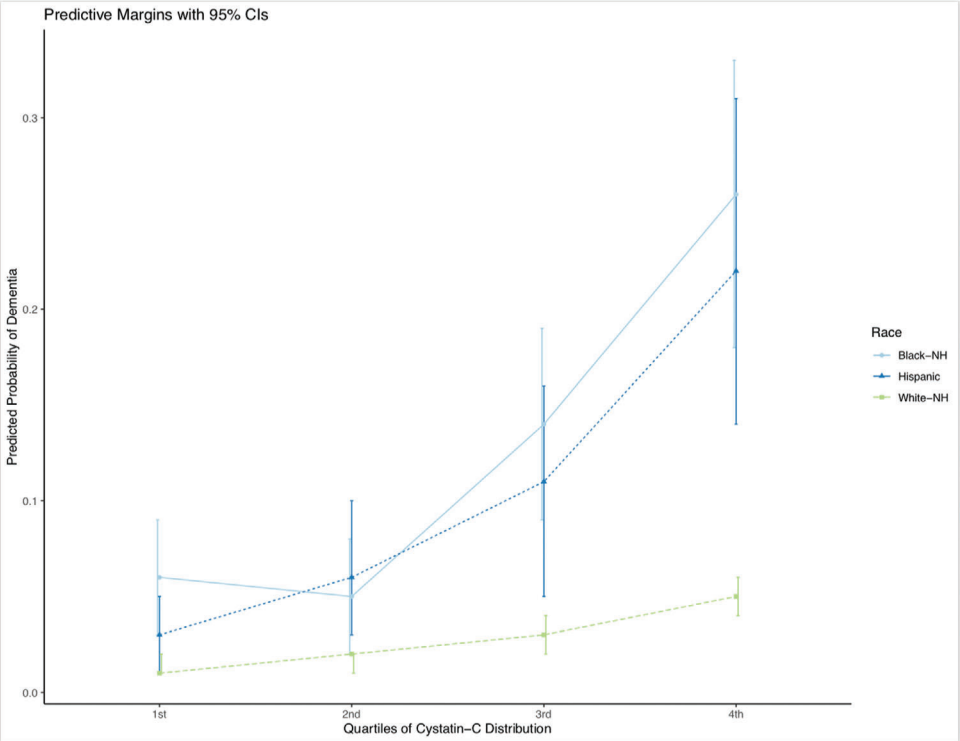
Predictive Margins with 95% CIs
Predicted Probability of Dementia
0.0
0.1
0.2
0.3
1st
2nd
3rd
4th
Quartiles of Cystatin–C Distribution
Race
Black–NH
Hispanic
White–NH

FIGURE 1