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Summary:
Chronic lower respiratory disease (CLRD) is the 3rd leading cause of death in the United States (US). The most prevalent components of CLRD are chronic obstructive pulmonary disease (COPD), emphysema, chronic bronchitis and asthma. The primary cause of CLRD mortality and morbidity is exacerbations, yet risk factors for exacerbations are inadequately understood, especially among the elderly, never-smokers and minorities. High density lipoprotein cholesterol (HDL-c) and HDL subfractions may contribute to CLRD pathogenesis due to their roles in sphingolipid regulation and transport, which have been implicated in both asthma and emphysema. Preliminary results from one cohort suggest that higher levels of HDL-c and large HDL subfractions are associated with higher rates of CLRD events and more rapid decline in lung function. We propose to perform analyses across five NHLBI population-based cohorts of predominantly older adults to test if higher baseline HDL-c levels and large HDL subfractions will be associated with increased rates of CLRD events and a more rapid longitudinal decline in lung function independent of standard socio- demographic and clinical risk factors, whereas small HDL subfractions will demonstrate the inverse associations. We will further examine if these associations are similar across strata defined by race/ethnicity, smoking status and age group; consistent across components of CLRD; and comparable for genetically- estimated HDL-c based on genotype at LIPG rs61755018. Confirmation of these hypotheses would impact future lipid management for patients at risk for CLRD events and suggest targets for drug development on the HDL-sphinoglipid pathway to prevent CLRD events.