Relationship Between High-Density Lipoprotein Cholesterol and Cardiovascular and Non-Cardiovascular Mortality: A Population-Based Study of More than 630,000 Individuals Without Prior Cardiovascular Conditions in Ontario, Canada

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Background
The prognostic importance of high-density lipoprotein cholesterol (HDL-C) as a modifiable risk factor of cardiovascular (CV) disease has been challenged. Our study was to explore the extent to which HDL-C levels are associated with non-cardiovascular risk factors and CV and non-CV mortality.

Methods
Our cohort was created by linking together m large population-based databases. Residents aged 40 to 105 years in 2008, who had no prior cardiac conditions or severe comorbidities were eligible for inclusion. The primary outcome was cause-specific mortality (CV, cancer, and others). Cox proportional hazard models were constructed to estimate the hazard ratios of death associated with pre-specified HDL-C strata. Analyses were adjusted for age, income, non HDL-C levels, cardiac risk factors, and comorbidities, and stratified by sex.

Results
Among the 631,762 individuals, their mean age was 57.2 years, 55.4% were women, and mean HDL-C level was 55.2 mg/dL. There were 17,952 deaths from any causes during a mean follow-up of 4.9 ± 0.4 years. Individuals with lower HDL-C levels were more likely to be at lower income, have unhealthy lifestyle, suboptimal cholesterol profile, more cardiac risk factors, and medical comorbidities. Low HDL-C levels were associated with higher hazards of CV, cancer, and other mortality (Figure). The dose-response associations between HDL-C levels and outcomes was non-linear, whereby patients whose HDL-C levels were very low and very high experienced a greater hazards of death than those whose HDL-C levels fell within intermediate HDL-C levels (41 - 80 mg/dL in men; 51 - 90 mg/dL in women).

Conclusions
Individuals with low HDL-C levels were independently associated higher risk of CV and non-CV mortality. Complex associations between HDL-C levels and non-cardiac factors, and cause-specific mortality suggest it is a heavily confounded measure, which undermines the validity of making causal-inferences with cardiovascular disease.
Disclosure: