Cleveland Clinic Innovations

**PRODUCT**
ApoA1 exchange rate assay as a diagnostic tool for CVD risk

**INDICATION**
CVD, MACE

**VALUE PROPOSITION**
Novel assay to measure ApoA1 exchange rate as a marker for MACE

**DEVELOPMENT STAGE**
Validated in prospective samples

**INTELLECTUAL PROPERTY**
Patent Application Submitted

**RELATED PUBLICATIONS**
Lorkowski, Shuhui Wang et al. "A Novel Cell-Free Fluorescent Assay for HDL Function: Low Apolipoprotein A1 Exchange Rate Associated with Increased Incident Cardiovascular Events." *The journal of applied laboratory medicine* vol. 5,3 (2020): 544-557.

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# Cardiovascular Functional Risk Assessment via ApoA1 Exchange Rate Assay

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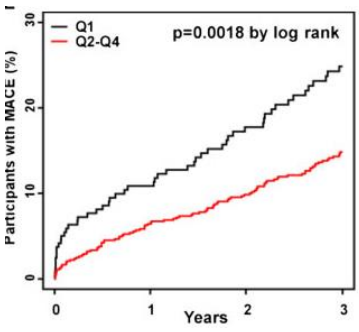
## UNMET NEED

Low levels of HDL-cholesterol (HDL-C) levels are associated with prevalent and incident risk for coronary heart disease, thus HDL-C has been called the "good cholesterol". However, drug trials targeting HDL-C as well as a genetic instrument called mendelian randomization have called into question whether low HDL is causal for MACE. As HDL is a major player in reverse cholesterol transport (RCT), the process of removing peripheral cholesterol to the liver for excretion into the bowel, the concept has emerged that it is low HDL function, rather than HDL-cholesterol, that is causal for MACE. Indeed, there is a growing literature that one HDL functional assay, the cholesterol efflux capacity (CEC) of apoB-depleted serum, is associated with both prevalent and incident MACE. However, the cholesterol efflux capacity assay requires cell culture and radioactivity, and it cannot be performed as a routine, relativity inexpensive, diagnostic assay. The deficiency in practical and scalable HDL function assays presents a significant challenge to seamlessly integrating effective risk assessment strategies into routine clinical practice, leaving a critical gap in preventive cardiology that urgently requires innovative solutions to reduce the global burden of cardiovascular diseases.

## SOLUTION

Researchers at Cleveland Clinic have developed a novel method for performing an apoA1 exchange assay to determine the risk of MACE. ApoA1 is freely exchangeable between lipid-free and lipid-bound state, and lipid-free apoA1 is the major ABCA1-dependent acceptor to initiate the RCT pathway and mobilize cholesterol from peripheral tissues.




ApoA1 exchange into HDL is an indication of HDL remodeling, which might be an indicator of HDL's cholesterol efflux capacity via ABCA1-dependent or ABCA1-independent pathways, or its altered protein or lipid composition that may influence HDL's antiatherogenic properties. ApoA1 exchange rate (AER) was assayed in a large prospective cohort where low AER was associated with an increased incident risk of MACE (Fig. 1).

**Fig 1**. Low apoA1 exchange rate is associated with increased incident MACE. A Kaplan-Meier curve for incident MACE over 3 years for AER Q1 (black line) and Q2–4 (red line) yielded a significant log rank order for time to MACE. Patients were stratified in Q1-Q4 based on ApoA1 exchange rate levels.