Discussant:
HDL Cholesterol efflux capacity and incident CV events in the Dallas Heart Study

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Raising plasma HDL-C levels will reduce CV events.
Time to retire the HDL-C hypothesis?

Raising plasma HDL-C levels will reduce CV events.
Anti-atherogenic HDL functions

HDL

- Anti-oxidant
- Anti-inflammatory
- NO-promoting
- Anti-thrombotic

Cholesterol efflux and reverse cholesterol transport
Measuring Steps of Reverse Cholesterol Transport in Humans

Liver: FC, CE, SR-BI

Bile: A-I

FC: LCAT, ABCG1, ABCA1

Macrophage:
Measuring HDL Cholesterol Efflux Capacity in Humans

After George Rothblat, et al
Cholesterol efflux capacity has been shown to be inversely associated with prevalent CHD.

Is cholesterol efflux capacity associated with first *incident* CV events?
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Yes, in the Dallas Heart Study, CEC was inversely associated with CV events even after adjusting for HDL-C.
Cholesterol efflux capacity and incident CV events in the Dallas Heart Study: Strengths

- Dallas Heart Study: population-based, multi-ethnic and mean follow-up nearly 10 years
Cholesterol efflux capacity and incident CV events in the Dallas Heart Study: Strengths

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• Bodipy-cholesterol efflux assay: adapted for high-throughput and rigorously quality-controlled, primarily assesses ABCA1-mediated efflux
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Cholesterol efflux capacity and incident CV events in the Dallas Heart Study: Strengths

- Dallas Heart Study: population-based, multi-ethnic and mean follow-up nearly 10 years
- Bodipy-cholesterol efflux assay: adapted for high-throughput and rigorously quality-controlled, primarily assesses ABCA1-mediated efflux
- Design: Entire cohort assayed for CEC
- Statistical analysis: CEC robustly inversely associated with incident CV events independent of HDL-C and other risk factors
Cholesterol efflux capacity and incident CV events in the Dallas Heart Study: Caveats

- Relatively small number of CV events (n=132)
Cholesterol efflux capacity and incident CV events in the Dallas Heart Study: Caveats

• Relatively small number of CV events (n=132)
• Limited previous experience with fluorescent bodipy-cholesterol efflux assay
HDL cholesterol efflux capacity and first incident coronary events

EPIC-Norfolk study: CEC inversely associated with first incident CHD events independent of HDL-C

Danish Saleheen
AOS.202.01 Wed AM S504
The HDL flux hypothesis

Promoting cholesterol efflux and RCT will reduce CV events.
Can efflux capacity and macrophage RCT be used to assess pharmalogical interventions?
# Effects of interventions on HDL-C, cholesterol efflux capacity, and CAD in humans

<table>
<thead>
<tr>
<th>Intervention</th>
<th>HDL-C</th>
<th>CEC</th>
<th>CAD</th>
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</thead>
<tbody>
<tr>
<td>ER-Niacin</td>
<td>↑</td>
<td>→</td>
<td>→</td>
</tr>
<tr>
<td>Dalcetrapib</td>
<td>↑</td>
<td>→</td>
<td>→</td>
</tr>
<tr>
<td>Evacetrapib*</td>
<td>↑</td>
<td>↑</td>
<td>?</td>
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<tr>
<td>CSL112 (rHDL)**</td>
<td></td>
<td>↑</td>
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APS.202.04 Poster Session  Tuesday Nov 18
*2062    **2064
Some Remaining Questions

- Could HDL cholesterol efflux capacity be developed as a clinical test for assessment of cardiovascular risk?
- Might HDL cholesterol efflux capacity be useful in assessing the potential of new HDL-targeted therapeutic interventions?