

# Abstract

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## Cardiovascular events with increased lipoprotein-associated phospholipase A(2) and low high-density lipoprotein-cholesterol: the Veterans Affairs HDL Intervention Trial.

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**OBJECTIVE:** Lipoprotein-associated phospholipase A(2) (Lp-PLA(2)), a proinflammatory enzyme that predominantly circulates with low-density lipoprotein (LDL), has been shown in general populations to predict cardiovascular (CV) events. We sought to determine whether increased Lp-PLA(2) would also predict CV events in the absence of high LDL-cholesterol (LDL-C), in a population with low high-density lipoprotein-cholesterol (HDL-C).

**METHODS AND RESULTS:** Plasma Lp-PLA(2) activity was measured at baseline and after 6 months on-trial in 1451 men with low HDL-C (mean, 32 mg/dL) and low LDL-C (mean 110 mg/dL), randomized to either placebo or gemfibrozil therapy in the Veterans Affairs HDL Intervention Trial (VA-HIT). Over a quartile range of increasing Lp-PLA(2) there was a significant increase in LDL-C and decrease in HDL-C ( $P < 0.0001$ ), and an increased percentage of myocardial infarction (MI), stroke, or CHD death ( $P=0.03$  for trend). In Cox models, adjusted for major CV risk factors, a 1-SD increase in Lp-PLA(2) was associated with a significant increase in CV events (hazard ratio [HR] 1.17 95% CI 1.04 to 1.32). Although gemfibrozil reduced Lp-PLA(2) only modestly (6.6%), at higher levels of Lp-PLA(2) gemfibrozil produced a significant reduction in CV events.

**CONCLUSIONS:** In VA-HIT, a population with low HDL-C and LDL-C, high Lp-PLA(2) independently predicted CV events that were reduced by gemfibrozil.

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