

# Abstract

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## Lipoprotein(a), Hormone Replacement Therapy, and Risk of Future Cardiovascular Events

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**OBJECTIVES:** This study assesses whether the relationship of lipoprotein(a) [Lp(a)] with cardiovascular risk may be modified by concurrent hormone replacement therapy (HT).

**BACKGROUND:** Prior studies indicate that HT decreases plasma levels of Lp(a), but few have been powered to assess whether it modifies the relationship of Lp(a) with cardiovascular disease.

**METHODS:** Lipoprotein(a) at baseline was measured among 27,736 initially healthy women, of whom 12,075 indicated active HT use at the time of blood draw at study initiation and 15,661 did not. The risk of first-ever major cardiovascular event (nonfatal myocardial infarction, nonfatal cerebrovascular event, coronary revascularization, or cardiovascular death) over a 10-year period was assessed with Cox proportional hazard models according to Lp(a) levels and HT status and adjusted for potential confounding variables.

**RESULTS:** As anticipated, Lp(a) values were lower among women taking HT (median 9.4 mg/dl vs. 11.6 mg/dl,  $p < 0.0001$ ). In women not taking HT, the hazard ratio of future CVD for the highest Lp(a) quintile compared with the lowest was 1.8 ( $p$  trend  $< 0.0001$ ), after adjusting for age, smoking, blood pressure, diabetes, body mass index, total cholesterol, high-density lipoprotein, C-reactive protein, and treatment arms of aspirin and vitamin E. In contrast, among women taking HT, there was little evidence of association with CVD (hazard ratio: 1.1,  $p$  trend = 0.18; interaction  $p$  value = 0.0009 between Lp(a) quintiles and HT on incident CVD).

**CONCLUSIONS:** The relationship of high Lp(a) levels with increased CVD is modified by HT. These data suggest that the predictive utility of Lp(a) is markedly attenuated among women taking HT and may inform clinicians' interpretation of Lp(a) values in such patients.

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