**DIRECT VERSUS CALCULATED LDL CHOLESTEROL AND C REACTIVE PROTEIN IN CARDIOVASCULAR DISEASE RISK ASSESSMENT IN THE FRAMINGHAM OFFSPRING STUDY**

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**Objective:** Elevated serum LDL cholesterol (LDL-C) and high sensitivity C reactive protein (hsCRP) levels have been identified as major risk factors for cardiovascular disease (CVD). Our goal was to assess direct versus calculated LDL-C and hsCRP levels as compared to standard risk factors in the prospective Framingham Offspring Study.

**Method:** Stored frozen plasma samples (-80 degrees C) obtained after an overnight fast from male and female participants free of CVD at cycle 6 of the Framingham Offspring Study were used (n=3,147, mean age 58 years) and 677 or 21.5% developed a CVD endpoint over 16 years. Total cholesterol, triglycerides, HDL cholesterol (HDL-C), direct LDL-C, and hsCRP were measured by standardized automated analysis, and LDL-C was also calculated.

**Results:** For inclusive CVD risk on univariate analysis significant factors in order included the standard risk factors age, hypertension, HDL-C, hypertension treatment, gender, diabetes, smoking, and total cholesterol, as well as the non-standard risk factors non-HDL-C, direct LDL-C, calculated LDL-C, triglycerides (TG), and hsCRP. On multivariate analysis only direct LDL-C and hsCRP were still significant after inclusion of the standard model. Both parameters significantly improved the model C statistic and the net risk reclassification index. The same findings were noted for other CVD risk categories including hard CVD with procedures and hard CVD.

**Conclusion:**Our data indicate that direct LDL-C is superior to calculated LDL-C in CVD risk prediction, and that both direct LDL-C and hsCRP add significant information to CVD risk prediction versus the standard model.