



Small Dense LDL (sd-LDL)

CPT Code **83722***

Order Code **1341**

Specimen Type **Serum**

Tube Type **Tiger-Top (with Gel Barrier)**

Elevated sd-LDL levels are associated with an increased relative risk for:

- Coronary heart disease (CHD)
- Cardiovascular events
- Metabolic syndrome

sd-LDL levels may be decreased by:

- Achieving/improving a healthy weight/diet
- Cholesterol-lowering medications (MetS)

Description

Small dense low-density lipoprotein particles demonstrate an increased risk of atherosclerosis.¹ These smaller particles are associated with an increased atherogenicity through various mechanisms, including decreased affinity to the LDL receptor, extended plasma half-life, increased permeation into the arterial wall, greater arterial retention, and higher susceptibility to oxidation.¹⁻² Measuring the cholesterol content of these small dense LDL (sd-LDL) particles provides an improved assessment of cardiovascular risk, independent of conventional risk factors.¹⁻³

Clinical Use

The sd-LDL test is used in conjunction with other lipid measurements and clinical evaluations to aid in the risk management of lipoprotein disorders associated with cardiovascular disease.

Clinical Significance

- Elevated sd-LDL levels are associated with increased risk of coronary heart disease (CHD) in apparently healthy individuals.¹⁻³
- sd-LDL-associated risk is independent of LDL-C levels.^{1,4} Those with LDL-C levels below 100 mg/dL and with elevated sd-LDL levels demonstrate a 1.6x increased relative risk of incident CHD compared to those with lower levels of sd-LDL.¹

- Levels of sd-LDL can increase with the severity of coronary artery disease (CAD).⁴
- In individuals with stable CAD, elevated sd-LDL levels are associated with an increased relative risk of a recurrent cardiovascular event.⁵
- Higher levels of sd-LDL are associated with a 4.3x increased relative risk of acute ischemic stroke.⁶
- Patients with MetS demonstrate higher levels of sd-LDL and concentration increases as more MetS diagnostic traits (defined by the National Cholesterol Education Program/Adult Treatment Panel III⁷) are present.⁸

Testing Frequency

sd-LDL testing is determined by an individual's medical history, but it may be performed semi-annually or annually as necessary. If the initial test result is abnormal, then follow-up testing may be performed within 3-6 months following treatment.

Specimen Type

The sd-LDL test should be performed on a serum specimen. Fasting may be required for this test. Please ask your doctor if you should fast prior to testing.

Commercial Insurance or Medicare Coverage

Coverage guidelines, also known as NCD (National Coverage Determination) or LCD (Local Coverage Determination) have been established or posted by CMS (Medicare & Medicaid). Guidelines should be reviewed for coverage and limitations. Limited information has been provided by the majority of the larger carriers (Aetna, United HealthCare, Cigna, Blues).

RELATIVE RISK

sd-LDL
(mg/dL)

<50.0
Low

≥50.0
High

Treatment Considerations[†]

These treatment considerations are for educational purposes only. Specific treatment plans should be provided and reviewed by the treating practitioner.

- ✓ **Assess lifestyle habits.**
 - Consider diet/exercise/weight reduction efforts if appropriate.⁹
- ✓ **Assess LDL levels.**
 - If LDL levels are not optimal,^{3,10} consider lipid-lowering therapies described in the National Cholesterol Education Program/Adult Treatment Panel III (NCEP ATP III) Guidelines.⁷
- ✓ **Assess insulin sensitivity.**
 - If not at an optimal level,^{11,12} consider insulin-sensitizing therapies described in the American Diabetes Association guidelines for the management of pre-diabetes/diabetes.¹³
- ✓ **Assess Omega-3 fatty acid levels.**
 - If not at an optimal level consider fish oil supplements, other dietary supplements, and dietary recommendations for increasing omega-3 fatty acid levels.^{14,15}
- ✓ **Assess the presence of coronary artery disease (CAD)⁶ with imaging techniques such as carotid intima media thickness testing (CIMT) or coronary artery calcium (CAC) scoring.**

* The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

† The treatment considerations are provided for informational purposes only and are not intended as medical advice. A physician's test selection and interpretation, diagnosis, and patient management decisions should be based on his/her education, clinical expertise, and assessment of the patient.

References

1. Hoogeveen RC, Gaubatz JW, Sun W, et al. Small dense low-density lipoprotein-cholesterol concentrations predict risk for coronary heart disease: the Atherosclerosis Risk In Communities (ARIC) study. *Arterioscler Thromb Vasc Biol.* 2014;34(5):1069-77. 2. Tsai MY, Steffen BT, Guan W, et al. New automated assay of small dense low-density lipoprotein cholesterol identifies risk of coronary heart disease: the Multi-ethnic Study of Atherosclerosis. *Arterioscler Thromb Vasc Biol.* 2014;34(1):196-201. 3. Ai M, Otokozawa S, Asztalos BF, et al. Small dense LDL cholesterol and coronary heart disease: results from the Framingham Offspring Study. *Clin Chem.* 2010;56(6):967-76. 4. Koba S, Hirano T, Ito Y, et al. Significance of small dense low-density lipoprotein-cholesterol concentrations in relation to the severity of coronary heart diseases. *Atherosclerosis.* 2006;189(1):206-14. 5. Nishikura T, Koba S, Yokota Y, et al. Elevated small dense low-density lipoprotein cholesterol as a predictor for future cardiovascular events in patients with stable coronary artery disease. *J Atheroscler Thromb.* 2014;21(8):755-67. 6. Zeljkovic A, Vekic J, Spasojevic-Kalimanovska V, et al. LDL and HDL subclasses in acute ischemic stroke: prediction of risk and short-term mortality. *Atherosclerosis.* 2010;210(2):548-54. 7. Third report of the National Cholesterol Education Program (NCEP). Expert panel on detection, evaluation and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *National Institutes of Health.* September 2002. NIH Publication No. 02-5215. 8. Gazi I, Tsimihodimos V, Filippatos T, Bairaktari E, Tselepis AD, Elisaf M. Concentration and relative distribution of low-density lipoprotein subfractions in patients with metabolic syndrome defined according to the National Cholesterol Education Program criteria. *Metab Clin Exp.* 2006;55(7):885-91. 9. López-Domènech S, Martínez-Herrera M, Abad-Jiménez Z, et al. Dietary weight loss intervention improves subclinical atherosclerosis and oxidative stress markers in leukocytes of obese humans. *Int J Obes (Lond).* 2019. doi:10.1038/s41366-018-0309-5. 10. Tokuno A, Hirano T, Hayashi T, et al. The effects of statin and fibrate on lowering small dense LDL-cholesterol in hyperlipidemic patients with type 2 diabetes. *J Atheroscler Thromb.* 2007;14(3):128-32. 11. Hayashi T, Hirano T, Yamamoto T, Ito Y, Adachi M. Intensive insulin therapy reduces small dense low-density lipoprotein particles in patients with type 2 diabetes mellitus: relationship to triglyceride-rich lipoprotein subspecies. *Metab Clin Exp.* 2006;55(7):879-84. 12. Hayashi T, Fukui T, Nakanishi N, et al. Dapagliflozin decreases small dense low-density lipoprotein-cholesterol and increases high-density lipoprotein 2-cholesterol in patients with type 2 diabetes: comparison with sitagliptin. *Cardiovasc Diabetol.* 2017;16(1):8. 13. American Diabetes Association: Standards of Medical Care in Diabetes-2018. *Diabetes Care.* 2018;41(Supplement 1). 14. Satoh N, Shimatsu A, Kotani K, et al. Purified eicosapentaenoic acid reduces small dense LDL, remnant lipoprotein particles, and C-reactive protein in metabolic syndrome. *Diabetes Care.* 2007;30(1):144-6. 15. Wilkinson P, Leach C, Ah-sing EE, et al. Influence of alpha-linolenic acid and fish-oil on markers of cardiovascular risk in subjects with an atherogenic lipoprotein phenotype. *Atherosclerosis.* 2005;181(1):115-24.

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