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Cardiovascular Risk Assessment: A Synthesis of Guidelines on Lipoprotein(a)

KEY TAKEAWAYS

- Results from prospective, genetic, and observational studies suggest a causal relationship between elevated plasma levels of lipoprotein(a) (Lp(a)) and a heightened risk of atherosclerotic cardiovascular disease (ASCVD) and aortic stenosis.¹⁻⁵
- US medical society guidelines and consensus statements have supported Lp(a) measurement for certain patient populations, including individuals with a personal or family history of premature ASCVD and those with moderate to high ASCVD risk.⁶⁻¹⁰
- Measuring Lp(a) levels is recommended, even before Lp(a)-lowering treatments become available, to improve ASCVD risk classification and to aid in clinical decision-making.^{1,2,6-9,11-13}
- Current international medical society guidelines recommend measurement of Lp(a) at least once in a patient's lifetime.^{1,13,14} In April 2024, the National Lipid Association became the first US medical society to recommend Lp(a) measurement for all adults.²

INTRODUCTION

Lipoprotein(a) (Lp(a)) is 1 of 6 primary types of lipoproteins, which transport lipids to tissues for storage, energy use, and the synthesis of bile acids and steroid hormones.¹ Lp(a) has proatherogenic, proinflammatory, and prothrombotic properties.¹⁵

An individual's serum Lp(a) level is largely influenced by genetics—80% to 90% of its determination follows an autosomal codominant inheritance pattern.¹⁰ Lp(a) concentration has been reported to reach adult levels by 5 years of age, and more recent research results suggest that levels may increase into early adulthood.² Apart from the presence of select states (eg, pregnancy, acute inflammation), development of diseases (eg, liver disease, kidney disease), and use hormone treatments (eg, growth hormone therapy, menopausal hormone replacement), the fully expressed Lp(a) level remains relatively stable throughout an individual's lifetime and varies little in response to lifestyle factors.^{10,16} Results from prospective, genetic, and observational studies suggest that there is a causal relationship between elevated plasma levels of Lp(a) and a heightened risk of ASCVD and aortic stenosis.¹⁻⁵

This article reviews the impact of elevated Lp(a) levels, highlighting its role as an independent causal risk enhancer for cardiovascular disease (CVD), and summarizes professional guidelines and managed care considerations to enhance awareness and understanding of this risk.

CLINICAL IMPACT

The relationship between Lp(a) levels and ASCVD risk is now understood to be continuous, with a 50 nmol/L increase in Lp(a) concentration associated with an 11% rise in ASCVD risk (95% CI, 10%-12%).^{2,3} Lp(a) levels exceeding 30 mg/dL or 75 nmol/L have been deemed to be in the atherothrombotic range, with levels of at least 125 nmol/L (or 50 mg/dL) considered elevated, and those in between (30-50 mg/dL or 75-125 nmol/L) deemed intermediate.^{2,7-9,13,14,17,18}

Globally, an estimated 1.5 billion people are believed to have elevated Lp(a) levels, with a prevalence of 20%.¹⁸ The incidence of elevated Lp(a) levels in patients with established ASCVD, calcific aortic valve disease, or chronic kidney disease may be even higher.¹⁷ In the US, a considerable proportion

of the population exhibits elevated Lp(a) levels. The results of a study involving 531,144 patients (median age, 57.0 years; sex, 51.9% female) conducted at a referral diagnostic laboratory revealed that 35.0% of patients had Lp(a) concentrations greater than 30 mg/dL, and 24.0% had levels surpassing 50 mg/dL.¹⁹ Lp(a) levels can vary across ethnicities, with the lowest mean concentrations seen in East Asian (15 nmol/L), Latino (20 nmol/L), and White (25 nmol/L) populations and higher mean Lp(a) levels noted in South Asian (30 nmol/L) and Black (75 nmol/L) populations.¹⁸ However, race has not been shown to impact Lp(a)-attributable ASCVD risk, and no evidence exists to support race-based definitions of elevated Lp(a).² This has led the National Lipid Association (NLA) to call for the elimination of race-based definitions of elevated Lp(a) levels.²

Several studies have shown a correlation between increasing Lp(a) levels and a heightened risk of cardiovascular (CV) events.^{14,20-23} Statistical analyses of data from the UK Biobank, an observational study that enrolled 500,000 ethnically diverse individuals 40 to 69 years between 2006 and 2010, have been influential in demonstrating that Lp(a) levels below the “elevated” threshold can increase ASCVD risk.^{2,3,24,25} The results of 1 study showed that the risk of incident ASCVD and Lp(a) levels was estimated to be largely linear in 460,506 individuals in whom Lp(a) levels were measured. A hazard ratio (HR) of 1.11 (95% CI, 1.10-1.12) ASCVD events per 50 nmol/L increase in Lp(a) concentration was observed (median follow-up, 11.2 years; IQR, 10.5-11.9 years).³ In a second investigation using UK Biobank data for 413,734 people, an HR of 1.12 (95% CI, 1.10-1.15) ASCVD events per 18 nmol/L increase in Lp(a) concentration was seen.²⁵

ECONOMIC IMPACT

ASCVD accounted for approximately \$251.4 billion in annual direct costs in the United States from 2018 to 2019, with direct costs of coronary heart disease and stroke being \$117.0 billion and \$36.5 billion, respectively.²⁶ Research on the economic impact of elevated Lp(a) concentrations is limited, although available evidence suggests that elevated Lp(a) levels may be associated with increased use of health care resources.

Lp(a)-Associated Health Care Resource Utilization

Results of a 2007-2020 Optum claims-based study of 8372 adults with ASCVD demonstrated that rates for ASCVD-related inpatient hospitalizations at 1-year follow-up were higher among patients with elevated Lp(a) levels than for those having normal Lp(a) levels (13.33 vs 9.46 hospitalizations/100 person-years, respectively; $P < .0001$).^{27,*}

Elevated Lp(a) levels also were associated with subsequent composite cardiovascular (CV) hospitalization. The results of an observational

cohort study of electronic health record data of laboratory tests administered in the United States and recorded between January 1, 2015, and December 31, 2019, showed that among 20,551 adult patients, those with elevated Lp(a) levels (50-100 mg/dL) were 25% more likely to be hospitalized than were individuals with lower Lp(a) levels (< 50 mg/dL) (adjusted odds ratio [aOR], 1.25; 95% CI, 1.02-1.53; $P < .03$). Those with very elevated Lp(a) levels (> 100 mg/dL) were 23% more likely to be hospitalized (aOR, 1.23; 95% CI, 1.08-1.40; $P < .01$).^{28,†}

MEDICAL SOCIETY GUIDANCE FOR TESTING OF LP(A)

Current international medical society guidelines recommend measurement of Lp(a) at least once in a patient's lifetime.^{1,13,14} US medical society guidelines and consensus statements support Lp(a) measurement for certain patient populations, including those with a personal or family history of premature ASCVD and those with moderate to high ASCVD risk.^{6,7,9,10} Guidelines and consensus statements from US medical society guidelines and consensus statements are summarized in the [Table](#).^{2,6-9,11,13,14} In April 2024, the NLA became the first US medical society to recommend Lp(a) measurement for all adults.²

2024 Focused Update to 2019 National Lipid Association Statement

Noting the rapid evolution of the Lp(a) field, the NLA issued a focused update to its 2019 position statement regarding Lp(a) levels. Authors cite results of 2 large studies involving more than 400,000 patients to advise that the relationship between increased Lp(a) levels and heightened ASCVD risk be understood as a continuous gradient. Moreover, the authors conclude that the degree of Lp(a) elevation rather than the simple presence of elevated Lp(a) should be used to guide clinical decision-making.²

The NLA now recommends that Lp(a) be measured in all adults and that providers incorporate an intermediate risk category (75-125 nmol/L [30-50 mg/dL]) when Lp(a) levels are used to assess ASCVD risk. Repeat measurement of Lp(a) may be reasonable for a large percentage of individuals at intermediate risk who may enter into the high-risk range if they are postmenopausal, if they have hypothyroidism, if they develop proteinuria and chronic kidney disease, or for other reasons.²

The NLA also notes that Lp(a) testing is reasonable for assessing ASCVD risk in children and adolescents younger than 18 years with²:

- clinically suspected or genetically confirmed familial hypercholesterolemia (FH);
- idiopathic ischemic stroke;

*Study limitations include the possibility of coding errors in diagnoses and recorded data, that the Optum database represents only a subset of patients with an Lp(a) measurement in the real world, and the potential for selection bias since Lp(a) levels are not commonly measured.²⁷

†Study limitations include the inability to capture information on hospitalizations outside of the observed health system and unmeasured variables that may have confounded study results.²⁸

- first-degree relatives with premature ASCVD characterized by the onset of ASCVD in men younger than 55 years or women younger than 65 years; or
- first-degree relatives with elevated Lp(a) levels.

If elevated Lp(a) levels are found in a child, cascade screening (also called cascade testing) of immediate family members is recommended.² This may involve informing family members that the patient has an elevated Lp(a) level, testing those family members most likely to have an elevated Lp(a) level, and cascading this testing through the family based upon members' genetic connection with diagnosed patients.^{29,30} Although the NLA favors measurement of Lp(a) in nmol/L, authors of the 2024 update note that measurement in mg/dL is substantially better than no measurement.²

Absolute decreases in Lp(a) concentration of 50 mg/dL or more, especially in individuals with very high baseline concentrations, may be required to achieve a substantial clinical benefit.^{10,31-33}

2022 EAS Consensus Statement

In a 2022 consensus statement about Lp(a) in ASCVD and aortic stenosis, authors of the European Atherosclerosis Society (EAS) recommend that Lp(a) be measured in adults at least once and in youth when there is a history of hemorrhagic or ischemic stroke or when a parent has premature ASCVD without other known risk factors. The EAS also recommends cascade screening in the presence of FH, a family history of markedly high Lp(a) levels, or a personal or family history of ASCVD.^{11,14} The recommendation that Lp(a) be measured once in a lifetime is also made in 2019 guidelines for the

Table. Supported Settings for Lp(a) Measurement by North American and European Medical Societies Publications^{2,6-11,13,14}

Supported setting for Lp(a) measurement	NLA (2024 [2019]) ^a	AHA/ACC (2018)	AACE/ACE (2020)	CCS (2021)	AHA (2021)	EAS (2022, 2023)	ACC (2022)
At least once in all patients' lifetimes	Y ^b			Y		Y ^b	
Family history of premature ASCVD ^c	Y ^d	Y	Y	Y		Y ^d	Y
Personal history of premature ASCVD ^c	Y ^{b,e}	Y ^f	Y	Y ^g		Y	
Moderate to high ASCVD risk	Y ^{b,e}		Y	Y	Y	Y ^{b,e}	
Refractory elevation of LDL-C level despite LLT	Y ^{b,e}		Y	Y ^g		Y ^{b,e}	
Family history of elevated Lp(a) levels	Y ^d			Y ^g	Y	Y	
Personal history of primary severe hypercholesterolemia	Y ^{b,e}			Y ^g		Y ^{b,e}	
Suspected familial hypercholesterolemia	Y ^d			Y ^g		Y	
Personal history of aortic stenosis	Y ^{b,e}		Y	Y ^g		Y ^{b,e}	
Family history of aortic stenosis	Y ^{b,e}		Y	Y ^g		Y ^{b,e}	
South Asian or African ancestry	Y ^{b,e}		Y	Y ^g		Y ^{b,e}	
Personal history of stroke (in youth)	Y			Y ^g		Y	

AACE, American Association of Clinical Endocrinologists; ACC, American College of Cardiology; ACE, American College of Endocrinology; AHA, American Heart Association; ASCVD, atherosclerotic cardiovascular disease; CCS, Canadian Cardiovascular Society; EAS, European Atherosclerosis Society; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; Lp(a), lipoprotein(a); NLA, National Lipid Association; Y, yes.

^aIn its 2024 publication, the NLA updated its 2019 scientific statement and summarized all current NLA recommendations regarding Lp(a).²

^bRefers to adults.^{2,14}

^cPremature is defined as ASCVD occurring in males younger than 55 years and females younger than 65 years.^{9-10,13}

^dFor patients younger than 18 years.^{2,14}

^eEncompassed in recommendation to test all adults.^{2,14}

^fASCVD is not explained by major risk factors.⁹

^gEncompassed in recommendation to test all patients.¹³

management of dyslipidemias issued by the EAS and the European Society of Cardiology.¹

2022 ACC Expert Consensus Decision Pathway

In 2022, the ACC issued an expert consensus decision pathway regarding the role of nonstatin therapies for reducing LDL cholesterol (LDL-C) levels when managing ASCVD risk. Its authors recommend that Lp(a) be measured in patients with a family history of premature ASCVD and highlight that patients with Lp(a) levels of at least 50 mg/dL or 125 nmol/L are at enhanced risk.⁸

2021 AHA Scientific Statement

According to a 2021 Scientific Statement from the AHA, Lp(a) level can be used to individualize 10-year risk of ASCVD in patients for whom the pooled cohort equations initially estimate a 5% to 19.9% risk. The statement highlights the importance of cascade screening for family members of patients with elevated Lp(a) levels.⁶

2021 CCS Dyslipidemia Guideline

In a 2021 guideline for the management of dyslipidemia, authors for the Canadian Cardiovascular Society (CCS) recommend measuring Lp(a) level once in a patient's lifetime as part of the patient's initial lipid screening. Guideline authors note the utility of identifying elevated Lp(a) levels for patients with any level of ASCVD risk and particularly for young patients with a very strong family history of premature ASCVD.¹³

2020 AACE/ACE Consensus Statement

The 2020 American Association of Clinical Endocrinologists (AACE)/American College of Endocrinology (ACE) consensus statement on the management of dyslipidemia and prevention of CVD advises consideration of Lp(a) testing in patients with⁷:

- clinical ASCVD or a family history of ASCVD and/or increased Lp(a) level;
- South Asian or African ancestry;
- a 10-year ASCVD risk of at least 10%;
- a personal or family history of aortic valve stenosis; or
- refractory LDL-C levels despite use of LDL-C-lowering therapy.

In the absence of an FDA-approved medication targeted to reduce Lp(a) levels, the recommended treatment for individuals with elevated Lp(a) involves aggressively lowering LDL-C concentrations to help mitigate the associated risk linked to Lp(a) elevation. The authors recommend use of lifestyle therapy, a statin, a PCSK9 inhibitor, ezetimibe, colesvelam, and/or bempedoic acid to lower LDL-C levels depending upon patient ASCVD risk.⁷

This remains the only major North American guideline to recommend that South Asian ancestry be considered in Lp(a) treatment decisions.

2018 ACC/AHA Task Force Guideline

The 2018 *Guideline on the Management of Blood Cholesterol* by authors from the ACC, AHA, and other organizations recommends Lp(a)

testing when a patient has a family history of premature ASCVD or a personal history of ASCVD not explained by major risk factors.⁹

MANAGED CARE CONSIDERATIONS

Measuring Lp(a) levels can improve overall CV risk assessments. In a study of 826 adults in their fifth to eighth decade of age at enrollment, Lp(a) measurement improved 15-year CVD risk classification by a net 39.6% among patients initially thought to be at intermediate risk (95% CI, 17.5% to 61.6%; $P < .001$).³⁴ Study participants were selected randomly from their community and followed for 15 years. Extensive clinical and laboratory examinations and a review of medical records were performed to determine whether patients experienced a CV event. Baseline risk of 15-year CVD was assessed using the Reynolds Risk Score (RRS). Lp(a) values were then added to the RRS model, patients were reclassified, and the accuracy of these reclassifications was measured against observed CV events. Among those initially estimated to be at intermediate risk (15%–30%), measurement of Lp(a) levels enabled accurate reclassification: 66.5% of those who demonstrated CVD in the ensuing 15 years and 90.2% of those with demonstrated ASCVD during that time were correctly placed into lower- and higher-risk groups (at $< 15\%$ and $\geq 30\%$ risk, respectively) (Figure).³⁴

The EAS highlights that measurement of Lp(a) levels influences management of other risk factors and provides important epidemiological data on risk associated with elevated Lp(a) concentrations.¹¹ In an advisory board discussion, clinical, policy, and bioethics experts and patient organization representatives believed that widespread Lp(a) testing could provide benefit to patients, health care systems, and society even before Lp(a)-lowering pharmaceuticals are available.¹²

Low Testing Rates

Lp(a) testing rates are low, especially in patients with established ASCVD. In a global prevalence study of 48,135 patients with established ASCVD (Lp[a]HERITAGE), 27.9% of participants had Lp(a) levels above established thresholds for increased ASCVD risk, but only 13.9% had received Lp(a) testing before enrollment.^{35,36}

In a subanalysis, investigators explored the prevalence of high Lp(a) levels in patients with established ASCVD in the United States. Of 7679 participants enrolled from 192 sites, approximately 1 in 3 had an Lp(a) level exceeding the established threshold for increased ASCVD risk (≥ 50 mg/dL). Compared with the overall group, greater percentages of Black participants and female participants exceeded the threshold. Further, approximately 1 of 2 Black participants and about 2 of 5 female participants had an Lp(a) level exceeding the threshold.³⁶

Findings presented at the American Heart Association Scientific Sessions in November 2023 indicated that Lp(a) testing for adults in the United States remains low. Results of a real-world analysis using the Family Heart Database indicated that from 2012 to 2021, only 500,899 (1.1%) of 44,857,734 patients in the United States underwent Lp(a) testing.³⁷ Among 10,658,820 participants with ASCVD, the screening marginally increased 2.0% over the same period ($\approx 218,331$ people). A separate analysis of data from Sutter Health, a Northern

California health system servicing over 3 million patients, revealed similar findings.³⁸ Among 1,484,410 adults who had at least 2 primary care visits between 2010 and 2021, only 14,818 people (1%) underwent Lp(a) testing during the study period.

Lipoprotein Apheresis

Lipoprotein apheresis is the only FDA-approved nonpharmacological therapy for high Lp(a) levels.³⁹ It is indicated only for patients with FH who have established ASCVD (coronary or another artery disease), LDL levels of at least 100 mg/dL, and Lp(a) levels of at least 60 mg/dL despite use of maximally tolerated lipid-lowering therapy.^{2,39,40} The procedure can be time-consuming and expensive, and it is not offered at all health care centers. Moreover, LDL-C and Lp(a) concentrations return to pretreatment levels between procedures. The NLA guidelines highlight that additional treatment options are needed.²

Strategies Under Investigation

Various strategies are currently under investigation for reducing Lp(a) levels. These approaches include use of lipid-lowering therapies, antisense oligonucleotides and small-interfering RNAs. In clinical trials to date, use of these agents resulted in reduced serum Lp(a) levels. These agents currently are at different stages of research and development, including phase 2 and 3 trials.^{2,16,41}

Overcoming Barriers to Lp(a) Testing

A lack of awareness of Lp(a), a perceived lack of clinical value of testing, and limited reimbursement constitute principal barriers to Lp(a) testing.⁴² Educational opportunities for and collaborative decision-making between health care providers and patients may help overcome these challenges. In 2018, two *International Statistical Classification of Diseases, Tenth Revision (ICD-10)* codes were added for

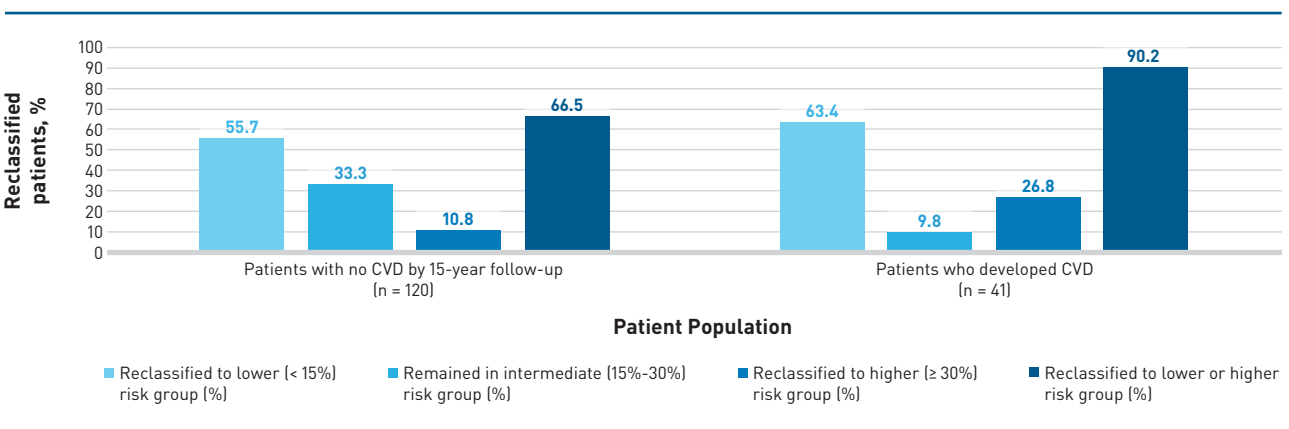
Lp(a) testing: E78.41, Elevated Lp(a); and Z83.430, Family history of elevated Lp(a).^{10,43} The current procedural terminology (CPT) code for elevated Lp(a) is 83695; use of this code requires advance beneficiary notice and use of a supportive *ICD-10* code.⁴⁴ Use of appropriate *ICD-10* codes may help make billing for Lp(a) testing more standardized; further analyses of the costs and benefits of testing may reveal associated savings. Finally, collaboration between policymakers and test manufacturers may foster access to low-cost testing.⁴²

Incorporating Lp(a) Measurement Into ASCVD Risk Assessment and Prevention Strategy

Lp(a) measurement may help improve ASCVD risk assessment, allow targeted management of risk factors, and influence patient adherence to risk mitigation strategies. Moreover, economic costs of once-in-a-lifetime Lp(a) testing may be outweighed by reduced health care utilization among patients with elevated Lp(a) levels who are able to manage their ASCVD risk factors.⁴² In April 2024, Reyes-Soffer et al offered actionable strategies for primary and secondary prevention of Lp(a)-associated ASCVD.⁴⁵ The authors first suggested incorporating into 10-year risk assessment the aforementioned 11% increase in ASCVD events associated with each 50 nmol/L increase in Lp(a). The authors proposed a formula that incorporates the impact of Lp(a) and additional risk factors, including the patient's coronary artery calcium score.

Lifestyle modifications were also recommended for all patients with high Lp(a) levels. These included following a balanced diet, exercising regularly, abstaining from nicotine, promoting quality sleep, maintaining a healthy weight, and achieving optimal levels of blood lipids, blood glucose, and blood pressure. For primary prevention in patients at intermediate or high risk and for secondary prevention, the authors advised consideration of pharmacological

Figure Reclassification of Individuals Predicted to Be at Intermediate 15-Year CVD Risk by Additional Assessment of Lp(a)^{34,a}



CVD, cardiovascular disease; Lp(a), lipoprotein(a); RRS, Reynolds Risk Score.

^aIn a study of 826 adults selected randomly from the community and who were in their fifth to eighth decade of age at enrollment, Lp(a) measurement used in the classification of 15-year CVD risk was assessed. Study participants were followed for 15 years, extensive clinical and laboratory examinations and a review of medical records were performed to determine if a CVD event occurred, and baseline risk of 15-year CVD was assessed using the RRS. Lp(a) values were then added to the RRS model, patients were reclassified, and the accuracy of these reclassifications was measured against observed CV events.³⁴

treatment of modifiable risk factors and referral to a lipidologist or preventative cardiologist.⁴⁵

CONCLUSIONS

Results of research published over the last 3 years demonstrated a log-linear relationship between Lp(a) levels and ASCVD event risk. This fostered the recommendation that the degree of Lp(a) elevation be used to guide clinical decision-making rather than just the presence of elevated levels. The NLA and other medical societies support Lp(a) measurement for patients with a personal or family history of premature ASCVD, those with moderate to high ASCVD risk, and other eligible individuals. Measuring Lp(a) levels is recommended to improve ASCVD risk classification and aid in clinical decision-making. •

REFERENCES

- Mach F, Baigent C, Catapano AL, et al; ESC Scientific Document Group. 2019 ESC/EAS guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk. *Eur Heart J*. 2020;41(11):111-188. doi:10.1093/eurheartj/ehz455
- Koschinsky ML, Bajaj A, Boffa MB, et al. A focused update to the 2019 NLA scientific statement on use of lipoprotein(a) in clinical practice. *J Clin Lipidol*. 2024;18(3):e308-e319. doi:10.1016/j.jacl.2024.03.001
- Patel AP, Wang [汪敏先] M, Pirruccello JP, et al. Lp(a) [Lipoprotein(a)] concentrations and incident atherosclerotic cardiovascular disease: new insights from a large national biobank. *Arterioscler Thromb Vasc Biol*. 2021;41(11):465-474. doi:10.1161/ATVBAHA.120.315291
- Clarke R, Peden JF, Hopewell JC, et al; PROCARDIS Consortium. Genetic variants associated with Lp(a) lipoprotein level and coronary disease. *N Engl J Med*. 2009;361(26):2518-2528. doi:10.1056/NEJMoa0902604
- Guddeti RR, Patil S, Ahmed A, et al. Lipoprotein(a) and calcific aortic valve stenosis: A systematic review. *Prog Cardiovasc Dis*. 2020;63(4):496-502. doi:10.1016/j.pcad.2020.06.002
- Reyes-Soffer G, Ginsberg HN, Berglund L, et al. Lipoprotein(a): A genetically determined, causal, and prevalent risk factor for atherosclerotic cardiovascular disease: A scientific statement from the American Heart Association. *Arterioscler Thromb Vasc Biol*. 2022;42(11):e48-e60. doi:10.1161/ATV.000000000000147
- Handelsman Y, Jellinger PS, Guerin CK, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the management of dyslipidemia and prevention of cardiovascular disease algorithm – 2020 executive summary. *Endocr Pract*. 2020;26(10):1196-1224. doi:10.4158/CS-2020-0490
- Writing Committee, Lloyd-Jones DM, Morris PB, et al. 2022 ACC expert consensus decision pathway on the role of nonstatin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: A report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2022;80(14):1366-1418. doi:10.1016/j.jacc.2022.07.006
- Grundey SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/AphA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;139(25):e1082-e1143. doi:10.1161/CIR.0000000000000625
- Wilson DP, Jacobson TA, Jones PH, et al. Use of lipoprotein(a) in clinical practice: A biomarker whose time has come. A scientific statement from the National Lipid Association. *J Clin Lipidol*. 2019;13(3):374-392. doi:10.1016/j.jacl.2019.04.010
- Kronenberg F, Mora S, Stroes ESG, et al. Frequent questions and responses on the 2022 lipoprotein(a) consensus statement of the European Atherosclerosis Society. *Atherosclerosis*. 2023;374:107-120. doi:10.1016/j.atherosclerosis.2023.04.012
- Catapano AL, Daccor M, Damato E, et al. How should public health recommendations address Lp(a) measurement, a causative risk factor for cardiovascular disease (CVD)? *Atherosclerosis*. 2022;349:136-143. doi:10.1016/j.atherosclerosis.2022.02.013
- Pearson GJ, Thanassoulis G, Anderson TJ, et al. 2021 Canadian Cardiovascular Society guidelines for the management of dyslipidemia for the prevention of cardiovascular disease in adults. *Can J Cardiol*. 2021;37(8):1129-1150. doi:10.1016/j.cjca.2021.03.016
- Kronenberg F, Mora S, Stroes ESG, et al. Lipoprotein(a) in atherosclerotic cardiovascular disease and aortic stenosis: A European Atherosclerosis Society consensus statement. *Eur Heart J*. 2022;43(39):3925-3946. doi:10.1093/eurheartj/ehac361
- Tsimikas S. A test in context: lipoprotein(a): diagnosis, prognosis, controversies, and emerging therapies. *J Am Coll Cardiol*. 2017;69(6):692-711. doi:10.1016/j.jacc.2016.11.042
- Alemba PL, Mehta A. An update on lipoprotein(a): The latest on testing, treatment, and guideline recommendations. American College of Cardiology, September 19, 2023. Accessed August 7, 2024. <https://www.acc.org/Latest-in-Cardiology/Articles/2023/09/19/10/54/An-Update-on-Lipoprotein-a>
- Tsimikas S, Fazio S, Ferdinand K, et al. NHLBI working group recommendations to reduce lipoprotein(a)-mediated risk of cardiovascular disease and aortic stenosis. *J Am Coll Cardiol*. 2018;71(2):177-192. doi:10.1016/j.jacc.2017.11.014
- Tsimikas S, Marcovina SM. Ancestry, lipoprotein(a), and cardiovascular risk thresholds: JACC review topic of the week. *J Am Coll Cardiol*. 2022;80(9):934-946. doi:10.1016/j.jacc.2022.06.019
- Varvel S, McConnell JP, Tsimikas S. Prevalence of elevated Lp(a) mass levels and patient thresholds in 532 359 patients in the United States. *Arterioscler Thromb Vasc Biol*. 2016;36(11):2239-2245. doi:10.1161/ATVBAHA.116.308011
- Emerging Risk Factors Collaboration, Erqou S, Kaptoge S, et al. Lipoprotein(a) concentration and the risk of coronary heart disease, stroke, and nonvascular mortality. *JAMA*. 2009;302(4):412-423. doi:10.1001/jama.2009.1063
- Nestel PJ, Barnes EH, Tonkin AM, et al. Plasma lipoprotein(a) concentration predicts future coronary and cardiovascular events in patients with stable coronary heart disease. *Arterioscler Thromb Vasc Biol*. 2013;33(12):2902-2908. doi:10.1161/ATVBAHA.113.302479
- Kaiser Y, Daghem M, Tzolos E, et al. Association of Lipoprotein(a) with atherosclerotic plaque progression. *J Am Coll Cardiol*. 2022;79(3):223-233. doi:10.1016/j.jacc.2021.10.044
- Kamstrup PR, Tybjaerg-Hansen A, Steffensen R, Nordestgaard BG. Genetically elevated lipoprotein(a) and increased risk of myocardial infarction. *JAMA*. 2009;301(22):2331-2339. doi:10.1001/jama.2009.801
- Sudlow C, Gallacher J, Allen N, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med*. 2015;12(3):e1001779. doi:10.1371/journal.pmed.1001779
- Welsh P, Welsh C, Celis-Morales CA, et al. Lipoprotein(a) and cardiovascular disease: Prediction, attributable risk fraction, and estimating benefits from novel interventions. *Eur J Prev Cardiol*. 2022;28(18):1991-2000. doi:10.1093/eurjpc/zwaa063
- Tsao CW, Aday AW, Almarazooq ZI, et al; on behalf of the American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2023 update: A report from the American Heart Association. *Circulation*. 2023;147(8):e93-e621. doi:10.1161/CIR.0000000000001123
- Fonseca AF, Byrne H, Laguna A, et al. Burden of lipoprotein(a) for patients with atherosclerotic cardiovascular disease: A retrospective analysis from the United States. *J Manag Care Spec Pharm*. 2023;29(5):519-529. doi:10.18553/jmcp.2023.29.5.519
- Kelsey MD, Mulder H, Chiswell K, et al. Contemporary patterns of lipoprotein(a) testing and associated clinical care and outcomes. *Am J Prev Cardiol*. 2023;14:100478. doi:10.1016/j.ajpc.2023.100478
- Cascade screening. American Heart Association. August 2023. Accessed August 7, 2024. <https://www.heart.org/-/media/Files/Health-Topics/Cholesterol/Cascade-Screening.pdf>
- About cascade testing. Centers for Disease Control and Prevention. May 15, 2024. Accessed August 7, 2024. <https://www.cdc.gov/cascade-testing/about/index.html>
- Madsen CM, Kamstrup PR, Langsted A, Varbo A, Nordestgaard BG. Lipoprotein(a)-lowering by 50 mg/dL [105 nmol/L] may be needed to reduce cardiovascular disease 20% in secondary prevention: A population-based study. *Arterioscler Thromb Vasc Biol*. 2020;40(11):2556-2566. doi:10.1161/ATVBAHA.119.312951
- Burgess S, Ference BA, Staley JR, et al; European Prospective Investigation Into Cancer and Nutrition-Cardiovascular Disease (EPIC-CVD) Consortium. Association of LPA variants with risk of coronary disease and the implications for lipoprotein(a)-lowering therapies: A Mendelian randomization analysis. *JAMA Cardiol*. 2018;3(7):619-627. doi:10.1001/jamacardio.2018.1470
- Parish S, Hopewell JC, Hill MR, et al; HPS2-THRIVE Collaborative Group. Impact of apolipoprotein(a) isoform size on lipoprotein(a) lowering in the HPS2-THRIVE Study. *Circ Genom Precis Med*. 2018;11(2):e001696. doi:10.1161/CIRCGEN.117.001696
- Willleit P, Kiechl S, Kronenberg F, et al. Discrimination and net reclassification of cardiovascular risk with lipoprotein(a): Prospective 15-year outcomes in the Bruneck Study. *J Am Coll Cardiol*. 2014;64(9):851-860. doi:10.1016/j.jacc.2014.03.061
- Nissen SE, Wolski K, Cho L, et al; Lp(a)HERITAGE Investigators. Lipoprotein(a) levels in a global population with established atherosclerotic cardiovascular disease. *Open Heart*. 2022;9(2):e002060. doi:10.1136/openhrt-2022-002060
- Shapiro MD, Haddad TM, Weintraub HS, et al. Lipoprotein(a) levels in a population with established atherosclerotic cardiovascular disease in the United States: A subanalysis from the Lp(a)HERITAGE study. Presented at ACC.23 Annual Scientific Session & Expo Together With World Congress of Cardiology; March 4-6, 2023; New Orleans, Louisiana. Presentation 1008-09.
- McGowan MP, MacDougall DE, Hu X, Boatwright W, Wilemon KA. Lipoprotein(a) screening practices in a large US healthcare dataset. Poster presented at: American Heart Association Scientific Sessions 2023; November 10-13, 2023; Philadelphia, PA.
- Brar S, Huang Q, Yan S, et al. Predictors of Lp(a) testing among multiethnic individuals. Poster presented at: AHA Scientific Sessions 2023; November 10-13, 2023; Philadelphia, PA. Session GR.APS.P5.
- About lipoprotein (a). Centers for Disease Control and Prevention. May 15, 2024. Accessed August 7, 2024. <https://www.cdc.gov/heart-disease-family-history/about/about-lipoprotein-a.html>
- Premarket approval (PMA): LIPOSORBER LA-15 system (PMA supplement). US Food and Drug Administration. Updated August 5, 2024. Accessed August 7, 2024. <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P910018S027>
- Schwartz GG, Steg PG, Szarek M, et al; ODYSSEY OUTCOMES Committees and Investigators. Alirocumab and cardiovascular outcomes after acute coronary syndrome. *N Engl J Med*. 2018;379(22):2097-2107. doi:10.1056/NEJMoa1801174
- Cifone N, McNeal CJ, McGowan MP, Ferdinand KC. Lipoprotein(a): An important piece of the ASCVD risk factor puzzle across diverse populations. *Am Heart J Plus*. 2023;38:100350. doi:10.1016/j.ahj.2023.100350
- Engler RJM, Brede E, Villines T, Vernalis MN. Lipoprotein(a) elevation: A new diagnostic code with relevance to service members and veterans. *Fed Pract*. 2019;36(suppl 7):S19-S31.
- Lipoprotein (a). Quest Diagnostics. Accessed August 7, 2024. <https://testdirectory.questdiagnostics.com/test/test-detail/34604/lipoprotein-a?cc=MASTER>
- Reyes-Soffer G, Yeang C, Michos ED, Boatwright W, Ballantyne CM. High lipoprotein(a): Actionable strategies for risk assessment and mitigation. *Am J Prev Cardiol*. 2024;18:100651. doi:10.1016/j.ajpc.2024.100651

