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ORIGINAL RESEARCH

# Lipoprotein(a) Levels in Disaggregated Racial and Ethnic Subgroups Across Atherosclerotic Cardiovascular Disease Risk Levels

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## ABSTRACT

**BACKGROUND** Lipoprotein(a) [Lp(a)] is a causal risk factor for atherosclerotic cardiovascular disease (ASCVD).

**OBJECTIVES** The authors assessed differences in Lp(a) testing and levels by disaggregated race, ethnicity, and ASCVD risk.

**METHODS** This was a retrospective cohort study of patients from a large California health care system from 2010 to 2021. Eligible individuals were ≥18 years old, with ≥2 primary care visits, and complete race and ethnicity data who underwent Lp(a) testing. Race and ethnicity were self-reported and categorized as follows: non-Hispanic (NH) White, NH-Black, Hispanic (Mexican, Puerto Rican, other), NH-Asian (Asian Indian, Chinese, Filipino, Japanese, Korean, Vietnamese, other). Logistic regression models tested associations between elevated Lp(a) (≥50 mg/dL) and race, ethnicity, and ASCVD risk.

**RESULTS** 13,689 (0.9%) individuals underwent Lp(a) testing with a mean age of 54.6 ± 13.8 years, 49% female, 28.8% NH Asian. Over one-third of those tested had Lp(a) levels ≥50 mg/dL, ranging from 30.7% of Mexican patients to 62.6% of NH-Black patients. The ASCVD risk of those tested varied by race: 73.6% of Asian Indian individuals had <5% 10-year risk, whereas 27.2% of NH-Black had established ASCVD. Lp(a) prevalence ≥50 mg/dL increased across the ASCVD risk spectrum. After adjustment, Hispanic (OR: 0.76 [95% CI: 0.66-0.88]) and Asian (OR: 0.88 [95% CI: 0.81-0.96]) had lower odds of Lp(a) ≥50 mg/dL, whereas Black individuals had higher odds (OR: 2.46 [95% CI: 1.97-3.07]).

**CONCLUSIONS** Lp(a) testing is performed infrequently. Of those tested, Lp(a) levels were frequently elevated and differed significantly across disaggregated race and ethnicity groups. The prevalence of elevated Lp(a) increased with increasing ASCVD risk, with significant variation by race and ethnicity. (JACC Adv 2024;3:100940) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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**ABBREVIATIONS AND ACRONYMS**

**ASCVD** = atherosclerotic cardiovascular disease

**Lp(a)** = lipoprotein(a)

**NH-Asian** = non-Hispanic Asian

**NH-Black** = non-Hispanic Black

**SD** = standard deviation

Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of death in men and women in the United States.[1] Traditional risk factors—sex, race, age, smoking, diabetes, non-high-density lipoprotein cholesterol, and blood pressure—are typically incorporated into a 10-year risk score that categorizes adults into low, borderline, intermediate, and high-risk groups.[2] Multi-society guidelines have incorporated blood- and imaging-based biomarkers to refine risk, including lipoprotein(a) [Lp(a)].[3,4]

Lp(a) is a genetically determined[5,6] atherogenic cholesterol molecule that is associated with ASCVD[7] and can further refine risk within 10-year ASCVD risk groups.[8] Clinical practice guidelines differ in both the indication and strength of recommendation for Lp(a) testing: the European Society of Cardiology recommends testing adults at least once in their lifetime,[9] whereas the National Lipid Association (United States) recommends testing adults at high ASCVD risk.[10] Other guidelines support incorporating Lp(a) levels, when available, into shared decision-making.[3,4]

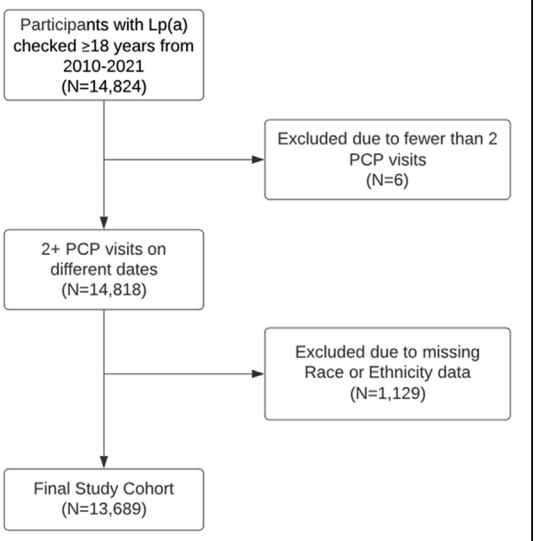
There are differences in Lp(a) levels by race and ethnicity; individuals of African ancestry tend to have the highest Lp(a) levels and those of East Asian descent tend to have the lowest,[5] though non-White groups remain understudied.[11] Race and ethnicity are not a monolith, however, and heterogeneity in Lp(a) levels exists within groups.[12] Despite these known differences in Lp(a) distribution, an elevated Lp(a) confers an increased risk of ASCVD independent of race and ethnicity[5] illustrating that certain race and ethnicity groups will have higher proportions of at-risk individuals.[5,13,14]

We investigated the differences in Lp(a) testing and levels by disaggregated race and ethnicity, and whether these rates differed by ASCVD risk levels.

## METHODS

**STUDY DESIGN AND SAMPLE.** This is a retrospective cohort study of individuals who received care through a large California health system. Eligible individuals were at least 18 years old, had ≥2 primary care appointments on different dates between the years 2010 to 2021, and underwent Lp(a) testing. If an individual underwent Lp(a) testing more than once during the study period, only the first test was included, and the date of the first Lp(a) test was defined as the index date. Individuals without complete race or ethnicity data were excluded.

**FIGURE 1 Participant Flow Diagram**




Lp(a) = lipoprotein (a).

Lp(a) levels were reported in mg/dL and the date of Lp(a) testing was considered as the index date for all other covariates. The following Lp(a) thresholds were used due to clinical significance: <30 mg/dL (upper limit of normal for the Lp(a) assay), 30 mg/dL to <50 mg/dL (abnormal level, but not a risk-enhancing factor), 50 mg/dL to <70 mg/dL (considered a risk-enhancing factor by clinical practice guidelines),[4] and ≥70 mg/dL (significantly elevated and currently studied as a threshold for targeted Lp(a) lowering trials).[15]

The study was approved by the Sutter Health and Stanford University Institutional Review Boards.

**COVARIATES.** Age and sex information was collected on or within 2 years of the index date. Race and ethnicity were self-reported and categorized: non-Hispanic White, Hispanic, non-Hispanic Black (NH-Black), non-Hispanic Asian (NH-Asian), and other. Individuals were analyzed as Hispanic irrespective of race when Hispanic ethnicity was noted. For non-Hispanic individuals, if multiple races (Black, Asian, or White) were reported, individuals were categorized as other. Then, Hispanic individuals were further disaggregated into Mexican, Puerto Rican, or other Hispanic. Asian individuals were then further disaggregated into Asian Indian, Chinese, Filipino, Japanese, Korean, Vietnamese, or other Asian. Of note, Asian Indian is a self-reported group and includes individuals commonly included in the South

**TABLE 1 Baseline Demographic Information and Clinical Characteristics**

| | | | Hispanic (N = 900) | | NH-Asian (N = 3,939) | | | |
|---|---|---|---|---|---|---|---|---|
| | NHW (N = 8,078) | NH-Black (N = 345) | Mexican (n = 322) | Other Hispanic (n = 578) | Asian Indian (n = 2,670) | Chinese (n = 471) | Other Asian (n = 798) | NH-Other (N = 427) |
| Age, y | 58.6 ± 13.2 | 55 ± 13.1 | 52.2 ± 14.6 | 53.4 ± 14.0 | 44.7 ± 9.6 | 52.0 ± 13.3 | 52.0 ± 13.2 | 52.3 ± 13.5 |
| Sex | | | | | | | | |
| Female | 4,307 (53.3%) | 180 (52.2%) | 179 (55.6%) | 321 (55.5%) | 824 (30.9%) | 250 (53.1%) | 395 (49.5%) | 194 (45.4%) |
| Male | 3,771 (46.7%) | 165 (47.8%) | 143 (44.4%) | 257 (44.5%) | 1,846 (69.1%) | 221 (46.9%) | 403 (50.5%) | 233 (54.6%) |
| Lp(a), mg/dL | 36 (17-85) | 65 (35-131) | 29 (15-69) | 32 (16-71) | 34 (18-66) | 28 (15-58) | 28 (15-63) | 34 (18-78) |
| Proportion with Lp(a) ≥50 mg/dL | 3,233 (40.0%) | 216 (62.6%) | 99 (30.7%) | 202 (34.9%) | 954 (35.7%) | 147 (31.2%) | 259 (32.5%) | 159 (37.2%) |
| Lipid panel, mg/dL | | | | | | | | |
| Total cholesterol | 203.4 ± 52.9 | 194.2 ± 51 | 200.3 ± 53.8 | 195.2 ± 53.3 | 199.8 ± 44.2 | 213.4 ± 53.4 | 206.3 ± 52.1 | 203.4 ± 50.6 |
| HDL | 59.1 ± 19.1 | 57.4 ± 20 | 52 ± 15.9 | 53.9 ± 17.0 | 47.4 ± 13.1 | 60 ± 17.2 | 54.5 ± 17.1 | 54.1 ± 17.1 |
| LDL | 118.7 ± 45.2 | 117.1 ± 46.8 | 116.9 ± 42.2 | 112.6 ± 43.9 | 123.4 ± 39.6 | 125.3 ± 46.7 | 120.4 ± 43.8 | 119.2 ± 44.1 |
| Triglycerides | 119.3 ± 91.5 | 101.2 ± 60.3 | 144.1 ± 86 | 134.7 ± 83.2 | 142.6 ± 92.7 | 119 ± 74.5 | 139.3 ± 152.1 | 140.4 ± 100.2 |
| ASCVD 10-y risk[a] | | | | | | | | |
| <5% | 3,076 (48.7%) | 100 (39.8%) | 143 (55.6%) | 265 (58.0%) | 1965 (78.2%) | 268 (65.4%) | 413 (60.6%) | 209 (61.1%) |
| 5% to <7.5% | 691 (10.9%) | 29 (11.6%) | 30 (11.7%) | 45 (9.8%) | 201 (8.0%) | 43 (10.5%) | 78 (11.5%) | 34 (9.9%) |
| 7.5% to <20% | 1,661 (26.3%) | 90 (35.9%) | 59 (23.0%) | 95 (20.8%) | 281 (11.2%) | 63 (15.4%) | 127 (18.6%) | 71 (20.8%) |
| >20% | 888 (14.1%) | 32 (12.7%) | 25 (9.7%) | 52 (11.4%) | 66 (2.6%) | 36 (8.8%) | 63 (9.3%) | 28 (8.2%) |
| History of ASCVD | 1,762 (21.8%) | 94 (27.2%) | 65 (20.2%) | 121 (20.9%) | 157 (5.9%) | 61 (13%) | 117 (14.7%) | 85 (19.9%) |
| Type 2 DM | 680 (8.4%) | 78 (22.6%) | 56 (17.4%) | 90 (15.6%) | 232 (8.7%) | 23 (4.8%) | 103 (12.9%) | 64 (15.0%) |
| Hypertension | 2,549 (31.6%) | 177 (51.3%) | 109 (33.9%) | 210 (36.3%) | 379 (14.2%) | 96 (20.4%) | 263 (33.0%) | 126 (29.5%) |
| Body mass index, kg/m$^2$ | 27.8 ± 5.7 | 31.6 ± 8.2 | 30.7 ± 7 | 29.5 ± 6.5 | 26.3 ± 4.2 | 24.1 ± 3.6 | 26.2 ± 4.9 | 27.9 ± 6 |
| Current smoker | 438 (3.2%) | 17 (4.9%) | 14 (4.3%) | 26 (4.5%) | 60 (2.2%) | 5 (1.1%) | 21 (2.6%) | 21 (4.9%) |
| Lipid-lowering therapy | | | | | | | | |
| Statin | 2,040 (25.3%) | 91 (26.4%) | 78 (24.2%) | 159 (27.5%) | 443 (16.6%) | 109 (23.1%) | 196 (24.6%) | 110 (25.8%) |
| Ezetimibe | 193 (2.4%) | 11 (3.2%) | 10 (3.1%) | 18 (3.1%) | 9 (0.3%) | 9 (1.9%) | 10 (1.3%) | 9 (2.1%) |
| PCSK9 inhibitor | 41 (0.5%) | 2 (0.6%) | 2 (0.6%) | 4 (0.7%) | 1 (0.0%) | 0 (0%) | 7 (0.9%) | 3 (0.7%) |
| Antihypertensive therapy | 2,549 (31.6%) | 171 (49.6%) | 98 (30.4%) | 196 (33.9%) | 447 (16.7%) | 106 (22.5%) | 258 (32.3%) | 133 (31.1%) |
| Primary insurance | | | | | | | | |
| HMO | 1,246 (15.4%) | 57 (16.5%) | 55 (17.1%) | 111 (19.2%) | 512 (19.2%) | 72 (15.3%) | 139 (17.4%) | 82 (19.2%) |
| Medicaid/Medi-Cal | 69 (0.9%) | 12 (3.5%) | 9 (2.8%) | 15 (2.6%) | 12 (0.4%) | 4 (0.8%) | 7 (0.9%) | 12 (2.8%) |
| Medicare FFS/HMO | 2,558 (31.7%) | 92 (26.7%) | 70 (21.7%) | 138 (23.9%) | 75 (2.8%) | 69 (14.6%) | 131 (16.4%) | 74 (17.3%) |
| PPO/FFS | 3,776 (46.7%) | 162 (47%) | 177 (55%) | 299 (51.7%) | 2,042 (76.5%) | 307 (65.2%) | 488 (61.2%) | 245 (57.4%) |
| Self/Other/Unknown | 429 (5.3%) | 22 (6.4%) | 11 (3.4%) | 15 (2.6%) | 29 (1.1%) | 19 (4.1%) | 33 (4.1%) | 14 (3.3%) |

Values are mean ± SD, n (%), or median (IQR). [a]Calculated for individuals without a baseline history of ASCVD. 2,332 individuals were missing covariates necessary for calculating ASCVD risk and required imputation.

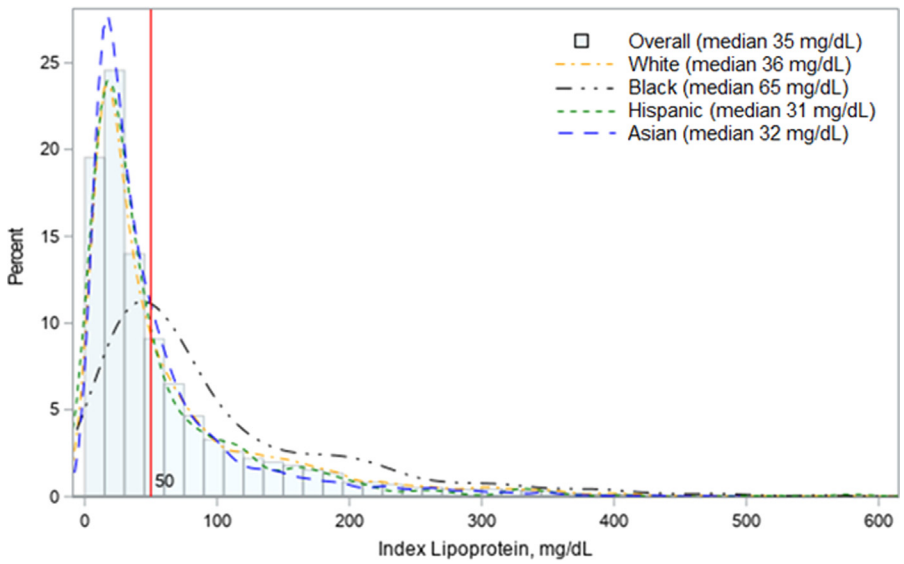
ASCVD = atherosclerotic cardiovascular disease; DM = diabetes mellitus; HDL = high-density lipoprotein; FFS = fee-for-service; HMO = Health Maintenance Organization; LDL = low-density lipoprotein; Lp(a) = lipoprotein (a); NH = non-Hispanic; NHW = non-Hispanic White; PCSK9 = proprotein convertase subtilisin/kexin type 9; PPO = Preferred Provider Organization.

Asian ethnic group. Race and ethnicity categories were defined with guidance from the Office of Management and Budget and the American Heart Association recent statements.[16,17]

To ensure sufficient statistical power at each disaggregated race and ethnicity level, when a disaggregated race and ethnicity group had fewer than 250 individuals, it was collapsed into an "other" group under corresponding larger race or ethnicity group, that is, Hispanic or NH-Asian. Puerto Rican individuals (n = 38) were included in the other Hispanic category and Filipino (n = 224), Japanese (n = 119), Korean (n = 54), and Vietnamese (n = 40) were included in the other Asian category.

Comorbidities, including type 2 diabetes mellitus, hypertension, and ASCVD history, were identified using International Classification of Diseases (ICD)-9 or ICD-10 codes and were present on at least two different encounters within 2 years preceding the index Lp(a) date for each condition (corresponding diagnosis codes for each condition can be found in Supplemental Table 1). Other comorbidities and laboratory data were extracted within 2 years closest to the index date and included body mass index, lipid results, and smoking history (never smoker, passive/quit, current smoker, or no smoking data available, ie, missing). Primary insurance was obtained in the same year as the index Lp(a) test and was categorized as

**FIGURE 2 Continuous Distribution of Lp(a) by Race**




Red line indicated ≥50 mg/dL. Lp(a) = lipoprotein (a).

Health Maintenance Organization, Medicaid/Medi-Cal, Medicare Fee-for-Service/Health Maintenance Organization, Preferred Provider Organization, self/other/unknown.

**STATISTICAL ANALYSIS.** We compared distribution of categorical variables across race and ethnicity groups using chi-square test, and compared continuous variables using *t*-test if normality was held; otherwise, Wilcoxon rank-sum test was applied. For patients without ASCVD, ASCVD risk score was estimated based on the Pooled Cohort Equations.[2] The risk scores were imputed for patients who had missing one or more variables in the risk score estimator, multiple imputation was conducted using Markov chain Monte Carlo approach,[18] and each missing ASCVD risk score was imputed 10 times and final imputed value was the average of the 10 imputed values. The 10-year ASCVD risk categories were characterized as low (<5% 10-year risk), borderline (5% to <7.5%), intermediate (7.5% to <20%), and high (≥20% 10-year risk).[4]

Logistic regression was used to determine the relationship of covariates and Lp(a) ≥50 mg/dL. The following models were used: model 1 = adjusted for race and ethnicity; model 2 = model 1 + sex + age + insurance status; model 3 = model 2 + diabetes mellitus, hypertension, hyperlipidemia; and model 4 = model 2 + ASCVD status. Odds ratio and associated 95% confidence interval were reported for each predictor from each model. Statistical analyses were performed using SAS version 9.5. A *P* value of <0.05 was considered statistically significant.

## RESULTS

**COHORT CHARACTERISTICS.** There were 1,484,410 individuals aged 18 years or older between 2010 and 2021. Of those, 13,689 (1%) underwent Lp(a) testing and had complete race or ethnicity data or regular care in the health system (**Figure 1**). The average age of the study cohort was 54.6 ± 13.8 years, with 48.6% female, 44.1% NH-White, 28.8% NH-Asian, and 18.0% with a history of ASCVD. Asian Indian individuals had the youngest average age (mean 44.7 ± 9.6 years) and NH-White had the oldest average age (mean 58.6 ± 13.2 years). Compared to the overall cohort of 1,484,410 individuals, there was a lower proportion of females, NH-Black, and Hispanic individuals in the Lp(a) tested cohort; conversely, though, there was a higher proportion of NH-Asian individuals tested (28.8% vs 18.8%) (Supplemental Table 2).

Among those without ASCVD at baseline, the average 10-year ASCVD risk was 8.5%. NH-Black individuals were more likely to have documented ASCVD (27.2% of NH-Black individuals), whereas Asian Indian individuals were more likely to have a low (<5%) 10-year ASCVD risk (78.2% of Asian Indian

**TABLE 2** Baseline Demographic Information and Clinical Characteristics by Lipoprotein(a) Levels

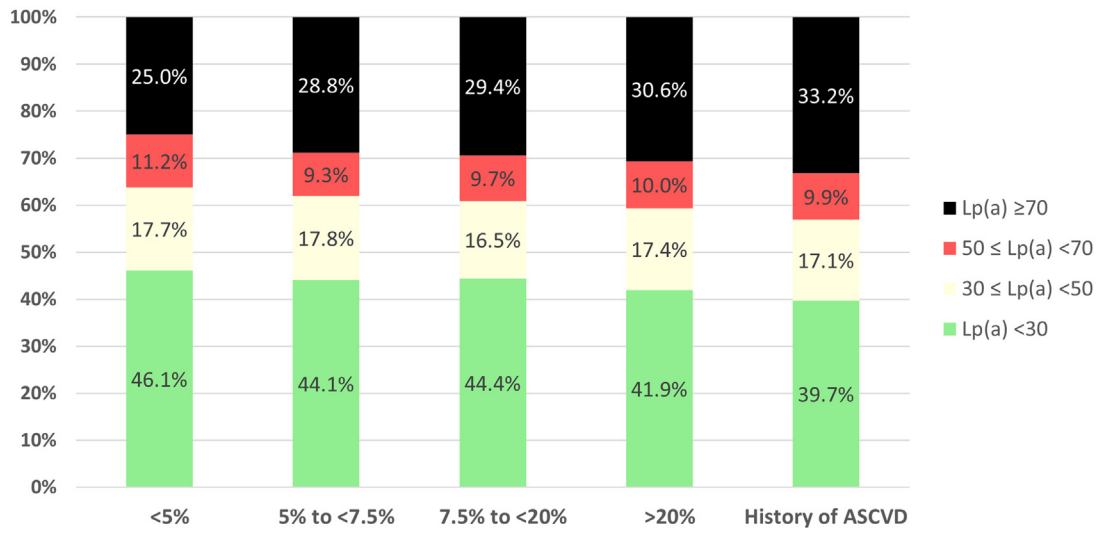
| | Overall (N = 13,689) | Lp(a) <30 mg/dL (n = 6,042) | Lp(a) ≤30 to <50 mg/dL (n = 2,378) | Lp(a) ≤50 to <70 mg/dL (n = 1,427) | Lp(a) ≥70 mg/dL (n = 3,842) |
|---|---|---|---|---|---|
| Age, y | 54.6 ± 13.8 | 53.7 ± 13.7 | 54.6 ± 13.8 | 55.7 ± 13.7 | 56.2 ± 13.8 |
| Sex | | | | | |
| Female | 6,650 (48.6%) | 2,808 (46.5%) | 1,117 (47%) | 691 (48.4%) | 2,034 (52.9%) |
| Male | 7,039 (51.4%) | 3,234 (53.5%) | 1,261 (53%) | 736 (51.6%) | 1,808 (47.1%) |
| Race and ethnicity | | | | | |
| NH White | 8,078 (59.0%) | 3,530 (58.4%) | 1,315 (55.3%) | 806 (56.5%) | 2,427 (63.2%) |
| NH Black | 345 (2.5%) | 69 (1.1%) | 60 (2.5%) | 49 (3.4%) | 167 (4.3%) |
| Hispanic | 900 (6.6%) | 434 (7.2%) | 165 (6.9%) | 75 (5.3%) | 226 (5.9%) |
| Mexican | 322 (2.4%) | 162 (2.7%) | 61 (2.6%) | 19 (1.3%) | 80 (2.1%) |
| Other Hispanic | 578 (4.2%) | 272 (4.5%) | 104 (4.4%) | 56 (3.9%) | 146 (3.8%) |
| NH Asian | 3,939 (28.8%) | 1,816 (30.1%) | 763 (32.1%) | 456 (32%) | 904 (23.5%) |
| NHA-Asian Indian | 2,670 (19.6%) | 1,162 (19.2%) | 554 (23.3%) | 323 (22.6%) | 631 (16.4%) |
| NHA-Chinese | 471 (3.4%) | 239 (4.0%) | 85 (3.6%) | 51 (3.6%) | 96 (2.5%) |
| NHA-other Asian | 798 (5.8%) | 415 (6.9%) | 124 (5.2%) | 82 (5.7%) | 177 (4.6%) |
| NH other | 427 (3.1%) | 193 (3.2%) | 75 (3.2%) | 41 (2.9%) | 118 (3.1%) |
| ASCVD 10-y risk[a] | | | | | |
| <5% | 6,438 (57.3%) | 2,970 (58.6%) | 1,141 (58.3%) | 719 (60.8%) | 1,608 (53.2%) |
| 5% to <7.5% | 1,153 (10.3%) | 509 (10.1%) | 205 (10.5%) | 107 (9.0%) | 332 (11.0%) |
| 7.5% to <20% | 2,448 (21.8%) | 1,087 (21.5%) | 403 (20.6%) | 238 (20.1%) | 720 (23.8%) |
| >20% | 1,188 (10.6%) | 498 (9.8%) | 207 (10.6%) | 119 (10.1%) | 364 (12.0%) |
| History of ASCVD | 2,462 (18.0%) | 978 (16.2%) | 422 (17.7%) | 244 (17.1%) | 818 (21.3%) |
| Type 2 DM | 1,326 (9.7%) | 591 (9.8%) | 246 (10.3%) | 134 (9.4%) | 355 (9.2%) |
| Hypertension | 3,909 (28.6%) | 1,674 (27.7%) | 658 (27.7%) | 369 (25.9%) | 1,208 (31.4%) |
| BMI, kg/m$^2$ | 27.5 ± 5.7 | 27.5 ± 5.7 | 27.5 ± 5.6 | 27.2 ± 5.4 | 27.6 ± 5.8 |
| Current smoker | 438 (3.2%) | 208 (3.4%) | 72 (3%) | 45 (3.2%) | 113 (2.9%) |
| Antihypertensives Rx | 3,958 (28.9%) | 1,697 (28.1%) | 680 (28.6%) | 388 (27.2%) | 1,193 (31.1%) |
| Lipid-lowering therapy | | | | | |
| Statin therapy | 3,226 (23.6%) | 1,271 (21%) | 548 (23%) | 339 (23.8%) | 1,068 (27.8%) |
| Ezetimibe | 269 (2.0%) | 93 (1.5%) | 46 (1.9%) | 20 (1.4%) | 110 (2.9%) |
| PCSK9 inhibitors | 60 (0.4%) | 27 (0.4%) | 10 (0.4%) | 2 (0.1%) | 21 (0.5%) |
| Lp(a), mg/dL | 35 (17-78) | 16 (11-21) | 38 (33-43) | 59 (54-64) | 131 (92-194) |
| Lipid panel mg/dL | | | | | |
| Total cholesterol | 202.6 ± 51.2, n = 11,325 | 199.3 ± 50.7, n = 5,079 | 203.1 ± 51.7, n = 1,991 | 202.4 ± 50.0, n = 1,196 | 207.8 ± 51.7, n = 3,059 |
| HDL | 56.1 ± 18.3, n = 13,455 | 55.3 ± 18.4, n = 5,908 | 55.5 ± 17.9, n = 2,347 | 56.5 ± 17.9, n = 1,407 | 57.6 ± 18.5, n = 3,793 |
| LDL | 119.6 ± 44.1, n = 13,434 | 116.9 ± 44.5, n = 5,892 | 120.1 ± 43.7, n = 2,344 | 120.0 ± 42.6, n = 1,405 | 123.6 ± 43.8, n = 3,793 |
| Triglycerides | 126.5 ± 95.7, n = 13,420 | 130.4 ± 104.6, n = 5,895 | 124.8 ± 102.5, n = 2,336 | 120.9 ± 75.9, n = 1,401 | 123.4 ± 82.3, n = 3,788 |
| Primary insurance | | | | | |
| HMO | 2,274 (16.6%) | 1,022 (16.9%) | 398 (16.7%) | 217 (15.2%) | 637 (16.6%) |
| Medicaid/Medi-Cal | 140 (1.0%) | 68 (1.1%) | 17 (0.7%) | 21 (1.5%) | 34 (0.9%) |
| Medicare FFS/HMO | 3,207 (23.4%) | 1,296 (21.4%) | 523 (22%) | 313 (21.9%) | 1,075 (28%) |
| PPO/FFS | 7,496 (54.8%) | 3,344 (55.3%) | 1,339 (56.3%) | 803 (56.3%) | 2,010 (52.3%) |
| Self/Other/Unknown | 572 (4.1%) | 312 (5.1%) | 101 (4.3%) | 73 (5.1%) | 86 (2.2%) |

Values are mean ± SD, n (%), or median (IQR). [a]Calculated for individuals without a baseline history of ASCVD. 2,332 individuals were missing covariates necessary for calculating ASCVD risk and required imputation.

ASCVD = atherosclerotic cardiovascular disease; BMI = body mass index; DM = diabetes mellitus; FFS = fee-for-service; HDL = high-density lipoprotein; HMO = Health Maintenance Organization; LDL = low-density lipoprotein; Lp(a) = lipoprotein (a); NH = non-Hispanic; NHW = non-Hispanic White; PCSK9 = proprotein convertase subtilisin/kexin type 9; PPO = Preferred Provider Organization.

individuals (Table 1). There were differences in cardiovascular risk factors and treatment between and within race and ethnicity groups. NH-White individuals had lower prevalence of diabetes mellitus (8.4% vs 22.6%) and hypertension (31.6% vs 51.3%) compared to NH-Black individuals. Among Asian individuals, Asian Indian individuals had a lower prevalence of hypertension (14.2% vs 20.4%) and lower proportion of statin use (16.6% vs 23.1%) compared with Chinese individuals. The use of these therapies did not clearly correlate with prior ASCVD history or high 10-year ASCVD risk (Table 1).

**FIGURE 3** Lp(a) Distribution by ASCVD Risk Status




ASCVD = atherosclerotic cardiovascular disease; Lp(a) = lipoprotein (a).

Additional differences in baseline demographic and clinical characteristics are highlighted in Table 1. Full demographic and clinical characteristics by disaggregated race and ethnicity are available in Supplemental Table 3.

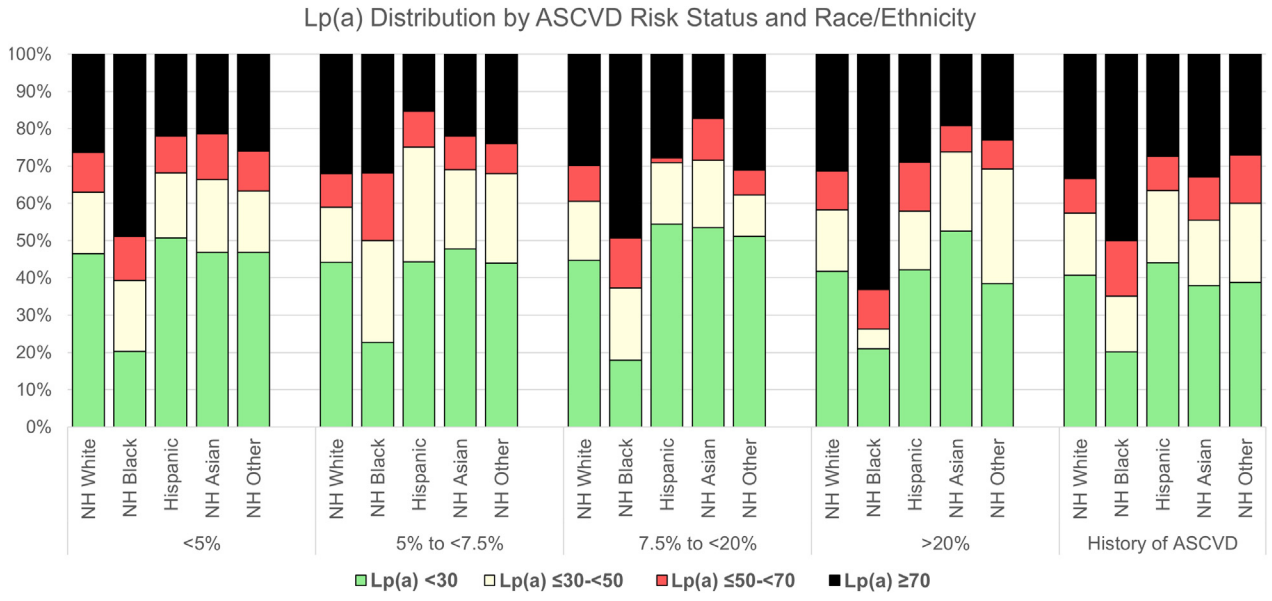
**Lp(a) levels by race and ethnicity.** The median Lp(a) level among those tested was 35 mg/dL with significant variation by race and ethnicity—ranging from 31 mg/dL for Hispanic individuals to 65 mg/dL for NH-Black individuals (Figure 2). The proportion of individuals with Lp(a) ≥50 mg/dL differed by race and ethnicity ranging from 30.7% for Mexican individuals to 62.6% for NH-Black individuals. Additionally, there was significant heterogeneity among disaggregated Asian subgroups with Chinese individuals having the lowest proportion of Lp(a) ≥50 mg/dL at 31.2% and Asian Indian individuals having the highest proportion at 35.7%. Additional demographic and clinical information by Lp(a) level are available in Table 2 and demonstrate differences in traditional risk factors for ASCVD and use of preventive therapies.

**LP(A) LEVELS BY ASCVD RISK LEVEL.** Across the spectrum of ASCVD risk—low, borderline, intermediate, high, and established ASCVD—there were significant but small differences in Lp(a) levels (Figure 3). The proportion of individuals with Lp(a) ≥50 mg/dL increased across ASCVD risk categories ranging from 36.2% of individuals at low risk to 43.1% of individuals with a history of ASCVD. When stratified by disaggregated race groups, the trend of an increasing proportion of individuals having Lp(a) ≥50 mg/dL as ASCVD risk increased was no longer apparent (Figure 4).

**LP(A), RACE, ETHNICITY, AND ASCVD RISK.** Within ASCVD risk groups, there were significant differences in median Lp(a) level by race: NH-White individuals tended to have similar median Lp(a) levels regardless of 10-year ASCVD risk, whereas Hispanic, NH-Black, and Asian individuals tended to have different median Lp(a) levels by 10-year ASCVD risk (Figure 5). NH-Black individuals were noted to have higher median Lp(a) levels at all ASCVD risk groups (Figure 4).

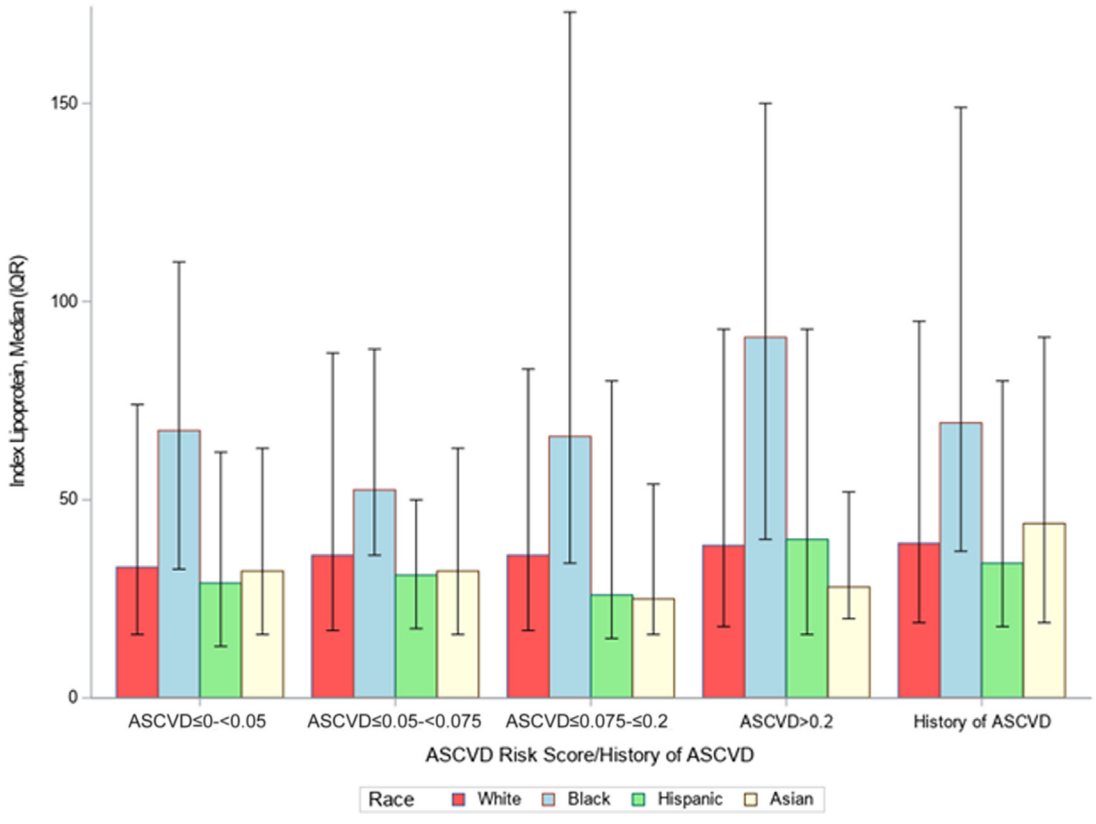
**PREDICTORS OF LP(A) ≥50 mg/dL.** Stepwise adjustment for additional covariates did not modify the association between race and ethnicity and elevated Lp(a). Compared to NH-White individuals, Hispanic individuals had the lowest odds of having an elevated Lp(a) (OR: 0.75 [95% CI: 0.64-0.86]), followed by Asian individuals (OR: 0.78 [95% CI: 0.72-0.85]). NH-Black individuals were more likely to have elevated Lp(a) (OR: 2.44 [95% CI: 1.95-3.04]). Compared to patients with established ASCVD, those at low ASCVD risk (ASCVD risk <5%), borderline (5%-<7.5%), and intermediate risk (7.5%-20%) were all less likely to have an elevated Lp(a) (Table 3). Those with self/other/unknown insurance types had a decreased odds of having an elevated Lp(a) (OR: 0.57 [95% CI: 0.46-0.70]).

**FIGURE 4** Lp(a) Level by Race, Ethnicity, and ASCVD Risk Level




ASCVD = atherosclerotic cardiovascular disease; Lp(a) = lipoprotein (a).

**FIGURE 5** Median Lp(a) Level by Race and ASCVD Risk Level




ASCVD = atherosclerotic cardiovascular disease; Lp(a) = lipoprotein (a).

**TABLE 3 Adjusted OR of Having an Lp(a) ≥50 mg/dL**

| | Model 1[a] | Model 2[b] | Model 3[c] | Model 4[d] |
|---|---|---|---|---|
| Race | | | | |
| White | Reference | Reference | Reference | Reference |
| Black | 2.44 (1.95-3.04) | 2.54 (2.03-3.17) | 2.70 (2.15-3.38) | 2.49 (1.99-3.11) |
| Hispanic | 0.75 (0.64-0.86) | 0.76 (0.66-0.88) | 0.78 (0.67-0.90) | 0.75 (0.65-0.87) |
| Asian | 0.78 (0.72-0.85) | 0.86 (0.79-0.93) | 0.85 (0.78-0.93) | 0.86 (0.79-0.94) |
| Other | 0.88 (0.72-1.08) | 0.92 (0.75-1.13) | 0.93 (0.76-1.14) | 0.92 (0.75-1.12) |
| Sex | | | | |
| Male | - | Reference | Reference | Reference |
| Female | - | 1.18 (1.10-1.27) | 1.19 (1.11-1.28) | 1.22 (1.13-1.31) |
| Age in years | - | 1.006 (1.002-1.009) | 1.004 (1.001-1.008) | 1.004 (0.999-1.008) |
| Primary insurance | | | | |
| HMO | Reference | Reference | Reference | Reference |
| Medicaid/Medi-Cal | - | 0.94 (0.66-1.35) | 0.94 (0.66-1.35) | 0.92 (0.64-1.31) |
| Medicare FFS/HMO | - | 1.06 (0.93-1.21) | 1.07 (0.93-1.22) | 1.03 (0.89-1.18) |
| PPO/FFS | - | 1.01 (0.91-1.11) | 1.01 (0.92-1.12) | 1.01 (0.92-1.11) |
| Self/other/unknown | - | 0.57 (0.47-0.71) | 0.61 (0.49-0.75) | 0.57 (0.46-0.7) |
| History of HTN (yes vs no) | - | - | 0.96 (0.88-1.05) | - |
| Type 2 DM (yes vs no) | - | - | 0.81 (0.71-0.92) | - |
| Hyperlipidemia (yes vs no) | - | - | 1.37 (1.27-1.48) | - |
| ASCVD status | | | | |
| 10-y risk 0% to <5% | - | - | - | 0.80 (0.71-0.90) |
| 10-y risk 5% to <7.5% | - | - | - | 0.85 (0.73-0.99) |
| 10-y risk 7.5% to <20% | - | - | - | 0.83 (0.74-0.94) |
| 10-y risk 20%+ | - | - | - | 0.86 (0.74-1.01) |
| ASCVD diagnosed | - | - | - | Reference |

Values are OR (95% CI). [a]Model 1 = adjusted for race. [b]Model 2 = model 1 + sex + age + insurance status. [c]Model 3 = model 2 + diabetes mellitus, hypertension, hyperlipidemia. [d]Model 4 = model 2 + ASCVD status (imputation for ASCVD risk score, if missing).

ASCVD = atherosclerotic cardiovascular disease; DM = diabetes mellitus; FFS = fee-for-service; HTN= hypertension; HMO = Health Maintenance Organization; PPO = Preferred Provider Organization.

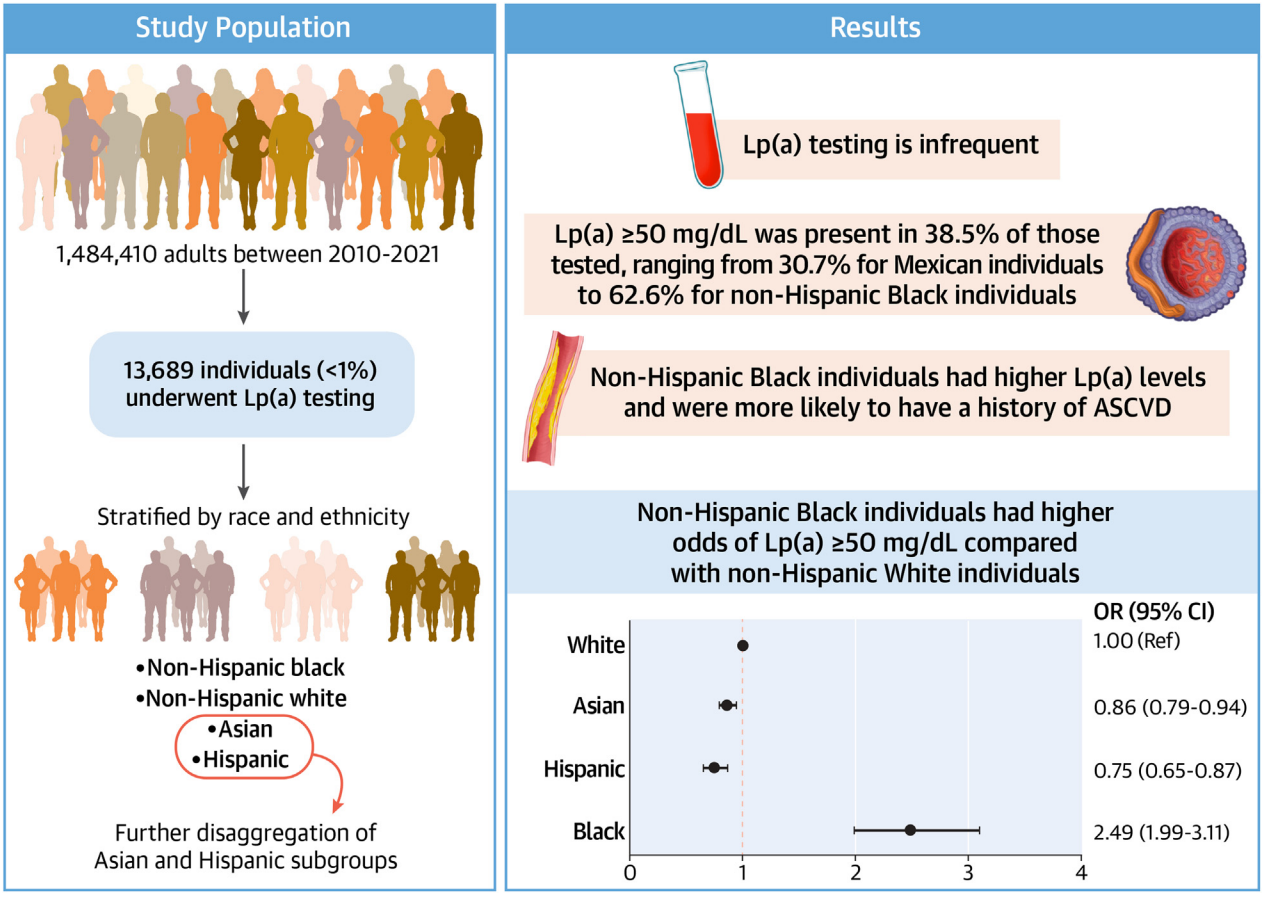
## DISCUSSION

Leveraging a decade of data from a large, multiethnic patient cohort, we found that Lp(a) testing occurred infrequently (<1% of individuals), more than half of tested individuals had elevated Lp(a) levels, and that the risk profile of individuals tested differed significantly by race and ethnicity (**Central Illustration**). For instance, NH-Black individuals tested had the highest burden of prevalent ASCVD, whereas Asian Indian individuals tested had the highest proportion of low ASCVD risk (<5% 10-year risk). Additionally, Lp(a) levels were highest among NH-Black individuals and there was significant heterogeneity within disaggregated Hispanic and Asian subgroups.

It is noteworthy that median Lp(a) levels were elevated across all race and ethnicity groups. The majority of individuals had abnormal Lp(a) values, with one in four having high enough levels to potentially qualify for Lp(a) lowering trials.[15] Although Lp(a)-specific therapies are not currently available, knowledge of elevated Lp(a) can lead to intensification of other preventive therapies.[3,10,19] These findings are in contrast to recent findings from a global cohort of individuals with ASCVD that found the median Lp(a) to be 18.0 mg/dL (IQR 7.9-57.1 mg/dL).[20] The difference in these findings is likely related to both international variation and sampling bias due to the clinical nature of our data.

Contrary to prior population-wide epidemiologic and genetic studies,[13,14] our study did not find a consistent dose-dependent relationship between Lp(a) and ASCVD risk. This is likely due to sampling differences in the relatively small proportion of patients who had Lp(a) testing. Whereas data from the UK Biobank[13] and Copenhagen[14] reflect general populations, our data on Lp(a) levels are obtained as part of clinical practice in a large patient sample. Although the proportion of individuals with Lp(a) ≥50 mg/dL increased across the spectrum of ASCVD risk, more than half of individuals at each ASCVD risk level had abnormal values. While prevalent 10-year ASCVD risk <20% was associated with a decreased odds of Lp(a) ≥50 mg/dL, clinical risk factors such as

**CENTRAL ILLUSTRATION** Racial and Ethnic Disparities in Lp(a) Testing




**Dudum R, et al. JACC Adv. 2024;3(6):100940.**

ASCVD = atherosclerotic cardiovascular disease; Lp(a) = lipoprotein (a).

hypertension, diabetes mellitus, and hyperlipidemia were not consistently associated.

The prevalence of elevated Lp(a) across ASCVD and clinical risk status provides credence for more recent guidelines that recommend expanding Lp(a) to all individuals,[9,21] rather than only those at high risk. Routine testing across all race and ethnicities at different levels of ASCVD risk can be used by clinicians and patients as part of shared decision-making focused on comprehensive prevention across the life course. This may inform the initiation and intensification of preventive efforts for those with higher Lp(a) levels. Particular focus should be on expanding testing in racial and ethnic groups where current ASCVD risk assessment models are limited and may systematically underestimate risk, such as Asian Indians.[22]

Racial and ethnic differences in Lp(a) testing by ASCVD risk level highlight opportunities for earlier ASCVD prevention efforts. We found that among those tested, Black individuals were more likely to carry a diagnosis of ASCVD (27.2%) at the time of testing compared to Asian Indian individuals (5.9%). These findings suggest that clinician-initiated Lp(a) testing thresholds are not uniform across race and ethnic groups—that is, NH-Black individuals may be tested more likely in the context of secondary prevention, whereas Asian Indian (and all NH-Asian) individuals may be tested more likely for primary prevention.

These findings are consistent with other studies that have found differences in the Lp(a) testing by race and ethnicity. Bhatia et al demonstrated in a cohort of over 5.5 million individuals that the

prevalence of Lp(a) testing was only 0.3% and differed significantly by race—65.9% were White, 8.6% were Asian, 3.2% were Black.[23] Gao and Shah et al found significant differences in cholesterol screening trends using a nationally representative sample—NH-White individuals were the most likely to have levels checked, followed by NH-Asian, NH-Black, and then Hispanic individuals ($P < 0.001$).[24]

Although many studies do not include Lp(a) testing of Asian Indian individuals, the high proportion of individuals of this race and ethnicity are likely due to the introduction of an Asian Indian specific clinic focused on cardiovascular health during the course of the study and growing awareness of Lp(a) as a risk-enhancing risk factor. These specialized clinics, which are becoming more common across the nation, may play an important role in helping identify Lp(a) as a particularly strong ASCVD risk factor in South Asian individuals.[25]

**STUDY LIMITATIONS.** This study should be interpreted in the context of several limitations. First, the study included patients from a single health system of predominantly insured individuals and may not be generalizable to other states and health systems. Second, sampling bias exists as those tested were done so as part of real-world clinical practice, and as such, tested individuals and the distribution of Lp(a) levels are not representative of the health system at large or the general population as has been seen in other epidemiologic cohorts. Third, despite the presence of detailed race and ethnicity data, certain groups had insufficient numbers to present individually and were thus grouped. Lastly, although the Lp(a) groupings used (<30 mg/dL, ≤30 to <50 mg/dL, ≤50 to <70 mg/dL, ≥70 mg/dL) correspond to regularly accepted cutoffs in both clinical practice[4] and trials,[15] it is not known if different race specific cutoffs should be used.[11,26]

Notably, our study is strengthened by the number of included patients as well as the granularity of race and ethnicity data. As California is known to have a plurality of diverse racial and ethnic groups, we are able to present disaggregated race and ethnicity data from many understudied populations in cardiovascular research. We also present a comprehensive assessment of Lp(a) levels and race across the spectrum of ASCVD risk, which, to our knowledge, has not been examined at this scale.

## CONCLUSIONS

In summary, we present findings of a diverse, real-world clinical practice that demonstrates marked undertesting of Lp(a), significant Lp(a) elevations, and differences in the risk profile of those tested by race and ethnicity. This work supports the need for more expansive Lp(a) testing as abnormalities are found at all spectrums of ASCVD risk and would warrant a comprehensive risk assessment and treatment, when indicated, to prevent ASCVD events.

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## PERSPECTIVES

**COMPETENCY IN PATIENT CARE:** Lp(a) is undertested across diverse populations and ASCVD risk levels. Clinicians should consider incorporating Lp(a) testing into routine ASCVD assessments for a more accurate assessment of cardiovascular risk.

**TRANSLATIONAL OUTLOOK:** Future research should evaluate the impact routine Lp(a) testing and emerging targeted Lp(a) lowering therapies on cardiovascular risk reduction and health equity across diverse populations.

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**KEY WORDS** lipoprotein(a), testing, race, ethnicity

**APPENDIX** For supplemental tables, please see the online version of this paper.