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Original Research

Low prevalence of testing for apolipoprotein B and lipoprotein (a) in the real world

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ABSTRACT

Objective: Apolipoprotein B (ApoB) and lipoprotein (a) (Lp[a]) are predictors of cardiovascular disease (CVD) risk; therefore, current recommendations for CVD risk assessment and management advocate that patients receive testing for ApoB and Lp(a) in addition to the standard lipid panel. However, US guidelines around ApoB and Lp(a) testing have evolved over time and vary slightly by expert committee. The objective of this analysis was to estimate the number of insured individuals in the USA who received any component of a lipid test, or ApoB and/or Lp(a) testing, during 2019.

Methods: We conducted a cross-sectional analysis to estimate the prevalence of any component of a lipid test, ApoB, and/or Lp(a) in the USA using four different claim data sources (including Medicaid, Medicare, and commercially insured enrollees). Prevalence estimates were age-, sex-, payor-, and region-standardized to the 2019 US Annual Social and Economic Supplement of the Current Population Survey. We also described the clinical profile of patients who received lipid testing between 2019 and 2021 (cohort analysis) in Optum claims database. Enrollees were grouped into four non-mutually exclusive cohorts based on their completion of any component of the lipid panel, ApoB, Lp(a), or ApoB and Lp(a).

Results: In the prevalence cohort, over a third (38 %) of insured adults in the USA underwent testing for any component of a lipid panel in 2019. This proportion was higher for individuals aged ≥65 years compared to younger adults (62% vs 31 %). The proportion of ApoB and Lp(a) testing represented only <1 % of testing for any component of a lipid panel. In the cohort analysis, we found that lipid testing increased with age and comorbidities.

Conclusion: These data should be considered by guideline-issuing agencies and organizations to develop education campaigns encouraging more frequent use of tests beyond the standard lipid panel.

1. Background

Reducing low-density lipoprotein cholesterol (LDL-C) is often the goal for preventing the development and progression of atherosclerotic cardiovascular disease (ASCVD); however, other biomarkers, such as apolipoprotein B (ApoB) and lipoprotein (a) (Lp[a]), may better predict atherogenic risk. Thus, measuring both may offer improved ASCVD risk assessment over LDL-C alone. As such, recent global guidelines and consensus statements recommend testing for ApoB and Lp(a) in certain circumstances [1-4].

Recent US guidelines and consensus recommendations on the use of ApoB and Lp(a) testing vary slightly based on the professional organization issuing the guidance as well as on the strength of the recommendation [1,2]. The 2018 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines advocate the measurement of ApoB under certain circumstances, particularly when individuals have high triglyceride levels [2]. The 2018 American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE) consensus statement considers that measurement of ApoB may be useful among individuals with ASCVD, and to assess the success of lipid-lowering therapy [1].

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Regarding Lp(a), the 2018 guidelines from the ACC/AHA [2], and while not accounted for the current analysis, the 2019 consensus recommendations from the National Lipid Association (NLA) [3], and the 2020 guidelines from the AACE/ACE [4] recommend testing Lp(a) in patients with a premature family history of ASCVD, or in individuals with ASCVD not explained by conventional risk factors. The NLA also recommend Lp(a) testing for individuals at very high risk of ASCVD, or those with primary severe hypercholesterolemia, and state that it is reasonable to measure Lp(a) values in individuals with a family history of elevated Lp(a) [3]. The NLA has issued a focused update on these guidelines in 2024 that will likely increase the future rate of testing for Lp(a) [5].

While the frequency of ApoB and Lp(a) testing is thought to be low [6,7], the current use of ApoB and Lp(a) testing nationally in the USA is not well understood. Therefore, we performed a retrospective observational study using administrative healthcare claims to estimate the prevalence of testing beyond the standard lipid panel in the USA as well as to describe the clinical profile of the individuals who had these tests.

2. Methods

2.1. Study population

We conducted 2 separate analyses of data from US healthcare plan enrollees: 1) a cross-sectional prevalence study; and 2) a cohort study to describe the population enrolled in a large healthcare plan who received any component of a lipid panel, ApoB, or Lp(a) testing during 2019–2021. We restricted the cross-sectional analyses to 2019 in order to avoid reporting a prevalence that may have been driven lower due to a decrease in healthcare resources during the COVID-19 pandemic. Lipid panel components, ApoB, and Lp(a) tests were identified in the claims data based on the presence of Current Procedural Terminology (CPT) procedure codes of interest (listed in Supplemental Table 1). Because no specific procedure codes were available for ApoB testing, we used procedure codes for testing of any apolipoprotein (such as ApoA1 or ApoB) and ascribed them to ApoB in this study. A subanalysis of the Optum dataset was completed to evaluate the relative proportion of ApoA1 or ApoB testing among those with a procedure code for apolipoprotein, and found that 99 % of apolipoprotein testing was for ApoB (data not shown).

2.2. Cross-sectional prevalence study

For the prevalence estimation, we identified all individuals who were ≥18 years of age and enrolled in a health plan on July 15, 2019, in 4 healthcare claims databases (see Data Sources below). These include individuals enrolled in commercial, Medicaid, and Medicare health plans.

2.3. Descriptive cohort study

For the descriptive cohort study, we included health plan enrollees in the Optum CDM database who received any component of the lipid panel, ApoB, or Lp(a) during 2019–2021, were continuously enrolled for at least 6 months (baseline period) before the date of the first test of interest (index date), and were aged ≥18 years at the index date. Enrollees were grouped into 4 non-mutually exclusive cohorts based on their completion of any component of the lipid panel, ApoB, Lp(a), or both ApoB and Lp(a), identified using the same CPT codes as for the prevalence estimation. Within each cohort, for enrollees who had multiple tests of interest on different days during the study period, the date of the first test during the time period was used as the index date. We also examined the following comorbidities of interest: cardiovascular disease (CVD; defined as ASCVD, hypertension, atrial fibrillation, or heart failure); kidney disease; diabetes; dementia; and healthcare resource use (inpatient, outpatient, and emergency department visits). ASCVD subtypes examined included acute coronary syndrome, cerebrovascular disease, other coronary heart disease, and peripheral arterial disease.

2.4. Data sources

All databases used in this study contained fully adjudicated claims of de-identified health plan enrollees. Brief descriptions of each data source are provided below:

1) The IQVIA PharMetrics® Plus database is comprised of fully adjudicated medial and pharmacy claims. Data contributors to the database are mainly commercial health plans.
2) Optum's Clinformatics® Data Mart contains fully adjudicated medical and pharmacy claims from United HealthCare, a large, national payor. It comprises commercial and Medicare Advantage claims.
3) The Medicaid Analytic Files (TAF) claims files contain fully adjudicated medical and pharmacy claims from Medicaid and Children's Health Insurance Program service records. Only US states were included in this analysis. Based on the evaluation of the data quality report for TAF data in 2019 [8], data from Alabama, Minnesota, Rhode Island, Tennessee, Utah, North Dakota, New York, and Illinois were excluded due to suboptimal linkage between enrollment and service records, or the extent of incompleteness of the outpatient procedures (where most of the tests of interest are captured).
4) The Centers for Medicare & Medicaid Services Limited Data Set (LDS) included final action fee-for-service (FFS) claims. Because carrier claims are only available in the LDS for the 5 % sample, we subset the population to the 5 % sample by using the sample group variable in the Master Beneficiary Summary File Base.
5) The census 2019 household survey (Annual Social and Economic Supplement of the Current Population Survey [ASEC CPS]) was used to estimate the US national population size within each age, sex, insurance type, and census region (Supplemental Table 2). The ASEC CPS provides annual population estimates based on a survey of more than 75,000 households within the civilian, non-institutionalized population of the US.

2.5. Analyses

For the cross-sectional prevalence analyses, we report descriptive characteristics of the populations that were included for prevalence estimates from each respective database.

For the cohort study, descriptive characteristics and comorbidities of interest (eg, ASCVD, hypertension, and dyslipidemia) were reported for enrollees based on the completion of the following: 1) any component of a lipid panel, 2) ApoB tests; 3) Lp(a) tests; and 4) both ApoB and Lp(a) tests.

2.6. Estimation of prevalence

The crude prevalence within a given dataset was calculated as all who were ≥18 years of age, enrolled in healthcare insurance on July 15, 2019, and underwent: 1) any component of a lipid panel; 2) ApoB testing; 3) Lp(a) testing; or 4) both ApoB and Lp(a) testing, divided by all enrollees who were ≥18 years of age on July 15, 2019.

Sex-, age group- (18–44, 45–54, 55–64, 67–74, and ≥75 years), and insurance- (commercial, Medicare FFS, Medicare Advantage, Medicaid, and uninsured/others) specific strata were used to tabulate prevalence. Full details for crude prevalence estimates in each database are provided in Supplemental Methods. Crude prevalence estimates were calculated based on enrollees with available sex, age, and insurance type.

2.7. Standardization and extrapolation to US prevalence

Estimates were directly age-, sex-, and payor-standardized to the population estimates based on 2019 ASEC CPS. National prevalence estimates were then calculated by dividing the estimated national total number of patients receiving the tests by the overall population from the survey. US prevalence estimates were reported for all US adults, as well as stratified by sex and age (18–64 years and ≥65 years).

Ethical approval was not required for this retrospective observational study using administrative healthcare claims data.

3. Results

3.1. Prevalence estimation of lipid tests in the USA in 2019

Population characteristics for each database used in the prevalence calculations are presented in Table 1. Enrollees in commercial insurance plans were younger (mean age [standard deviation; SD]: IQVIA: 43.26 [14.91] years and Optum: 41.95 [14.12] years) than those in Medicare (Optum Medicare Advantage: 73.13 [9.11] years and FFS: 70.80 [11.70] years), but older than those in Medicaid (37.1 [13.85] years). The percentage of females varied across the databases from 45.33 % in Medicaid to 57.48 % in Medicare Advantage. Variations in the region and distribution of race were observed across databases (Table 1).

The adult prevalence of any lipid testing in 2019 was 38 % (approximately 98 million Americans; Table 2). Less than a third (31 %) of those aged 18–64 years and nearly two-thirds (62 %) of those aged ≥65 years completed any lipid test during 2019. Across age groups, ApoB testing was more common than Lp(a) testing in all age groups. The age groups with the highest proportion of the US population receiving ApoB tests were 65–74 years and 75–99 years (Central Illustration). The prevalence of lipid testing was similar for males and females (Table 2). The prevalence of ApoB testing was significantly lower than any lipid component testing, with only 0.21 % (approximately 516,000 individuals) receiving an ApoB test during 2019. Similar to overall lipid testing, we observed that testing for ApoB was higher for the older age group than the younger age group (0.13 % for those aged 18–64 years and 0.51 % for those aged ≥65 years). Males and females had a similar prevalence of ApoB testing (0.20 % of males and 0.21 % of females; Table 2). Likewise, the prevalence of Lp(a) testing was also very low at 0.14 % (approximately 350,000 Americans; Table 2). Similar to the findings for lipid and ApoB testing, testing for Lp(a) was higher for individuals aged ≥65 years than those aged 18–64 years and was slightly lower in males than in females (Table 2). Only 0.10 % ($n = 250,039$) of adults received both ApoB and Lp(a) tests during 2019. Following the same trend, the prevalence of receiving both tests was higher for individuals aged ≥65 years than those aged 18–64 years, and was similar for males and females (Table 2). Having a test for Lp(a) was strongly correlated with having a test for ApoB, with 71.4 % of people who completed an Lp(a) test also having completed an ApoB test, while 48 % of people who received an ApoB test also completed an Lp(a) test. Among people who completed any component of a lipid panel, only 0.55 % had an ApoB test and 0.37 % had an Lp(a) test. Having an ApoB test was also correlated with Lp(a), although to a lesser extent, with 48 % of people who received an ApoB test also completing an Lp(a) test.

3.2. Clinical profile of individuals in the USA who completed lipid testing during 2019–2021

Data from the descriptive cohort of patients identified in the Optum CDM commercial and Medicare Advantage databases were used to further describe the clinical characteristics of patients who received lipid testing during 2019–2021 (Table 3). While age increased across the lipid panel, ApoB, Lp(a), and both ApoB and Lp(a) testing groups, the ratio of males to females was similar across groups (Table 3). The distribution of race varied slightly across the groups, with the group receiving both ApoB and Lp(a) having a higher proportion of Black individuals and a lower proportion of Asian individuals when compared to the standard lipid panel group. On average, those who received ApoB testing had a higher Charlson Comorbidity Index compared with those who received the lipid panel alone (1.35 [SD: 1.72], and 0.67 [SD: 1.30], respectively). Aortic stenosis, ASCVD, hypertension, hyperlipidemia, diabetes, atrial fibrillation, heart failure, and dementia were more common among those who completed ApoB and Lp(a) testing. Healthcare utilization during the baseline period was similar across groups.

4. Discussion

Advocacy efforts in favor of testing beyond the standard lipid panel have been increasing in recent years. These include endorsement of

Table 1
Characteristics of the US database population for prevalence estimates in 2019.

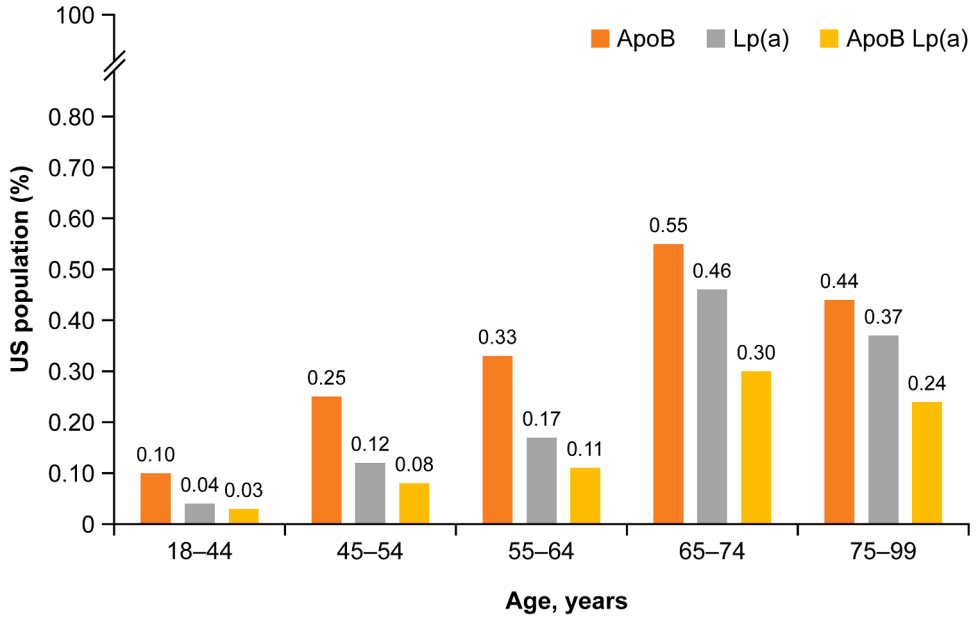
	Medicare FFS (n = 1642,126)	Optum-Commercial (n = 8925,239)	Optum-Medicare Advantage (n = 5651,663)	IQVIA Commercial (n = 39,234,360)	Medicaid (n = 26,594,358)
Mean age at index (SD), years	70.80 (11.70)	41.95 (14.12)	73.13 (9.11)	43.26 (14.91)	37.1 (13.85)
Female, No. (%)	895,436 (54.53)	4331,276 (48.53)	3248,828 (57.48)	19,816,202 (50.51)	10,554,345 (39.69)
Region, No. (%)					
Midwest	643,753 (39.20)	2218,813 (24.86)	1025,892 (18.15)	10,483,552 (26.72)	4259,498 (16.02)
Northeast	373,030 (22.72)	820,597 (9.19)	748,301 (13.24)	6026,778 (15.36)	3587,274 (13.49)
South	292,437 (17.81)	3725,604 (41.74)	2370,345 (41.94)	17,583,073 (44.82)	7156,313 (26.91)
West	325,613 (19.83)	1807,902 (20.26)	1505,337 (26.64)	5116,624 (13.04)	11,577,143 (43.53)
Unknown	7292 (0.44)	352,323 (3.95)	1788 (0.03)	24,333 (0.06)	14,130 (0.05)
Race, No. (%)					
Asian	33,664 (2.05)	500,479 (5.61)	191,720 (3.39)		1244,348 (4.68)
Black	149,396 (9.10)	828,765 (9.29)	648,939 (11.48)		4848,972 (18.23)
White	1351,157 (82.28)	5598,931 (62.73)	3834,979 (67.86)		10,753,466 (40.44)
Hispanic	36,613 (2.21)	1188,342 (13.31)	629,180 (11.13)		6078,058 (22.85)
Unknown	34,819 (2.12)	808,722 (9.06)	346,845 (6.14)		2991,740 (11.25)
Other	36,776 (2.24)				677,774 (2.55)
Received lipid tests, No. (%)					
Any component of a lipid panel	1000,993 (60.96)	2907,932 (32.58)	3363,414 (59.51)	13,365,045 (34.06)	5471,072 (20.57)
ApoB	10,416 (0.63)	2610 (0.03)	19,451 (0.34)	79,018 (0.20)	28,685 (0.11)
Lp(a)	7936 (0.48)	1611 (0.02)	17,599 (0.31)	36,943 (0.09)	13,942 (0.05)
ApoB and Lp(a)	5431 (0.33)	866 (0.01)	10,433 (0.18)	24,060 (0.06)	7176 (0.03)

Abbreviations: ApoB, apolipoprotein B; FFS, fee-for-service; Lp(a), lipoprotein (a); SD, standard deviation.

Table 2
Estimated Prevalence of Obtaining At Least 1 Lipid Test in the USA in 2019.

	Overall	By age, years		By sex	
		18–64	≥65	Male	Female
Lipid panel or component					
Estimated patients receiving tests, No.	94,259,406	61,316,481	32,942,925	43,454,698	50,804,708
Estimated prevalence,[a] %	38	31	62	36	39
ApoB test					
Estimated patients receiving tests, No.	516,443	249,192	267,251	243,877	272,566
Estimated prevalence,[a] %	0.21	0.13	0.51	0.20	0.21
Lp(a) test					
Estimated patients receiving tests, No.	350,228	124,005	226,223	162,020	188,208
Estimated prevalence,[a] %	0.14	0.06	0.43	0.13	0.15
ApoB and Lp(a) tests					
Estimated patients receiving tests, No.	250,039	104,269	145,770	115,568	134,471
Estimated prevalence,[a] %	0.10	0.05	0.28	0.10	0.10

Abbreviations: ApoB, apolipoprotein B; Lp(a), lipoprotein (a).
[a] 95 % confidence interval is not presented because the standard errors for prevalence estimates are <1E-5.



Central Illustration. Percentage of the US adult population who received ApoB, Lp(a), or both ApoB and Lp(a) testing during 2019
Abbreviations: ApoB, apolipoprotein B; Lp(a), lipoprotein (a).

ApoB testing for both CVD risk attribution and responses to ApoB-lowering therapies [9], and recommended Lp(a) testing for both CVD and aortic stenosis risk attribution as well as identification of individuals who may benefit from lipid-lowering therapies, since no specific Lp(a)-lowering therapy is currently available [10].

We examined several large US healthcare plan datasets to derive a prevalence estimate as well as to highlight gaps and opportunities for improvement in current clinical practice. The results of our retrospective cross-sectional analysis show a low prevalence of ApoB (0.21 %) and Lp (a) (0.14 %) testing in the USA in 2019, which contrasts with the prevalence of testing for any component of a lipid panel (38 %) during the same time frame. These observations suggest that a temporal gap may exist between dissemination of expert committee recommendations and implementation by healthcare professionals.

Our results confirm that testing of any component of a lipid panel was prevalent in the USA, and was most common (62 %) among individuals aged ≥65 years. In contrast, testing for ApoB and Lp(a) was rare (<0.5 %). Since 2018, evidence and recommendations about the value of ApoB and Lp(a) testing have been published [11-13], and so we anticipate a higher prevalence of the use of ApoB testing and Lp(a) in future analyses of the US population.

Previous work has emphasized the role of ApoB and Lp(a) as better predictors of CVD risk and response to therapy compared with LDL-C [14-17]. Subsequently, clinical guidelines have been updated to reflect the use of lipid testing, with an increasing emphasis on the importance of testing for ApoB and Lp(a) to increase detection of elevated CVD risk [16] and to identify patients in need of more aggressive or more specific therapies [3,18].

There are many benefits of expanding beyond the traditional cholesterol panel. Lp(a) levels have a strong genetic predisposition, and therefore testing will identify individuals who may warrant cascade screening in first-degree relatives and who may be eligible for future specific therapies. Similarly, ApoB testing provides a single measurement that includes information from all known risk contributors of the lipid panel, such as triglycerides, LDL-C, and remnant cholesterol.

The general assumption that the use and popularity of ApoB and Lp (a) tests have grown organically within medical practice has yet to be proven. Often there is a lag in time between the issuing of guidelines from expert committees and professional organizations, and their implementation in clinical practice. During this lag time, adherence to the guidelines may be low due to lack of awareness, lack of insurance coverage, potential cost to the patient, and perception of unnecessary

Table 3
Characteristics of Patients Receiving Lipid Screening, ApoB, Lp(a), or both ApoB and Lp(a) Testing in the USA from 2019 to 2021.

	Lipid panel (n = 9010,914)	ApoB (n = 43,173)	Lp(a) (n = 38,938)	ApoB and Lp(a) (n = 22,321)
Age, years				
Mean (SD)	59.21 (16.97)	68.56 (11.37)	69.94 (10.35)	70.14 (9.98)
Median (Q1–Q3)	62 (47–72)	70 (65–75)	71 (66–76)	71 (66–76)
Min:max	18:90	18:90	18:90	18:90
Age group, years, No. (%)				
18–24	269,912 (3.00)	178 (0.41)	130 (0.33)	69 (0.31)
25–34	678,030 (7.52)	529 (1.23)	339 (0.87)	155 (0.69)
35–44	1011,418 (11.22)	1286 (2.98)	794 (2.04)	379 (1.70)
45–54	1301,209 (14.44)	2659 (6.16)	1666 (4.28)	903 (4.05)
55–64	1542,351 (17.12)	5255 (12.17)	3870 (9.94)	2212 (9.91)
65–74	2485,215 (27.58)	20,952 (48.53)	19,928 (51.18)	11,639 (52.14)
≥75	1722,779 (19.12)	12,314 (28.52)	12,211 (31.36)	6964 (31.20)
Sex, No. (%)				
Male	4085,953 (45.34)	19,495 (45.16)	17,340 (44.53)	9900 (44.35)
Race/ethnicity, No. (%)				
White	6045,623 (67.09)	27,778 (64.34)	25,781 (66.21)	14,676 (65.75)
Black	955,633 (10.61)	5930 (13.74)	5162 (13.26)	3258 (14.60)
Hispanic	1042,054 (11.56)	5549 (12.85)	4590 (11.79)	2509 (11.24)
Asian	420,329 (4.66)	1343 (3.11)	1248 (3.21)	649 (2.91)
Missing	547,275 (6.07)	2573 (5.96)	2157 (5.54)	1229 (5.51)
Region, No. (%)				
Midwest	1987,100 (22.05)	4168 (9.65)	4337 (11.14)	1794 (8.04)
Northeast	1122,770 (12.46)	4835 (11.20)	5575 (14.32)	2002 (8.97)
South	4031,528 (44.74)	23,895 (55.35)	18,915 (48.58)	12,389 (55.50)
West	1859,514 (20.64)	10,215 (23.66)	10,007 (25.70)	6096 (27.31)
Missing	10,002 (0.11)	60 (0.14)	104 (0.27)	40 (0.18)
Comorbidities during the baseline period including the index date				
Charlson comorbidity index				
Mean (SD)	0.67 (1.30)	1.35 (1.72)	1.16 (1.61)	1.14 (1.57)
Median (IQR)	0 (0–1)	1 (0–2)	0 (0–2)	0 (0–2)
Comorbidities of interest, No. (%)				
Aortic stenosis	124,486 (1.38)	1191 (2.76)	1352 (3.47)	648 (2.90)
ASCVD	1451,241 (16.11)	16,138 (37.38)	16,847 (43.27)	8998 (40.31)
ASCVD subtype				
CeVD	330,597 (3.67)	3924 (9.09)	4483 (11.51)	2347 (10.51)
Other CHD	921,105 (10.22)	11,572 (26.80)	12,278 (31.53)	6524 (29.23)
PAD	561,589 (6.23)	5728 (13.27)	5653 (14.52)	3122 (13.99)
ACS	77,433 (0.86)	869 (2.01)	1113 (2.86)	505 (2.26)
Hypertension	4527,479 (50.24)	30,339 (70.27)	27,513 (70.66)	15,919 (71.32)
Hyperlipidemia	4715,674 (52.33)	35,595 (82.45)	33,383 (85.73)	19,457 (87.17)
Pure hypercholesterolemia, unspecified	1022,523 (11.35)	8655 (20.05)	8558 (21.98)	5079 (22.75)
Familial hypercholesterolemia	35,544 (0.39)	606 (1.40)	728 (1.87)	368 (1.65)
Pure hyperglyceridemia	119,077 (1.32)	1332 (3.09)	1099 (2.82)	612 (2.74)
Mixed hyperglyceridemia	1524,944 (16.92)	14,900 (34.51)	14,147 (36.33)	8559 (38.35)
Hyperchylomicronemia	3954 (0.04)	87 (0.20)	73 (0.19)	46 (0.21)
Other hyperlipidemia	206,244 (2.29)	2340 (5.42)	2241 (5.76)	1236 (5.54)
Elevated lipoprotein(a)	10,666 (0.12)	546 (1.26)	865 (2.22)	294 (1.32)
Hyperlipidemia, unspecified	2710,809 (30.08)	21,844 (50.60)	20,768 (53.34)	11,867 (53.17)
Kidney disease	493,696 (5.48)	3748 (8.68)	3305 (8.49)	2074 (9.29)
Diabetes	1962,205 (21.78)	15,789 (36.57)	13,540 (34.77)	8095 (36.27)
Atrial fibrillation	505,078 (5.61)	4275 (9.90)	4269 (10.96)	2343 (10.50)
Heart failure	392,451 (4.36)	4065 (9.42)	4023 (10.33)	2184 (9.78)
Dementia	237,551 (2.64)	1663 (3.85)	1474 (3.79)	806 (3.61)
Healthcare resource utilization during the baseline period, including the index date				
Outpatient visits (excluding ED visits)				
Mean (SD)	7.08 (8.28)	11.15 (10.10)	11.32 (10.44)	11.10 (10.23)
Median (Q1–Q3)	4 (2–9)	8 (5–14)	9 (5–15)	8 (5–14)
Any inpatient visit	370,478 (4.11)	2791 (6.46)	2641 (6.78)	1321 (5.92)
Any ED visit	1065,334 (11.82)	6979 (16.17)	6073 (15.60)	3327 (14.91)
Visits for preventative screening				
Mean (SD)	1.15 (1.37)	1.05 (1.67)	1.01 (1.62)	0.99 (1.48)
Median (IQR)	1 (0–2)	1 (0–2)	1 (0–1)	1 (0–1)
Completed a chest CT gated for CAC	133,515 (1.48)	1421 (3.29)	1422 (3.65)	728 (3.26)
Payer				
Commercial	4543,464 (50.42)	5656 (13.10)	3479 (8.93)	1638 (7.34)
Medicare	4467,450 (49.58)	37,517 (86.90)	35,459 (91.07)	20,683 (92.66)

Abbreviations: ACS, acute coronary syndrome; ApoB, apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; CAC, coronary calcium scan; CeVD, cerebrovascular disease; CHD, coronary heart disease; CT, computed tomography; ED, emergency department; IQR, inter-quartile range; Lp(a), lipoprotein (a); PAD, peripheral arterial disease; SD, standard deviation.

layering of complex testing. Within our study cohort database, approximately 0.5 % of patients with any component of a lipid panel test in 2019 had either an ApoB or an Lp(a) test. This low use of testing occurred despite publication of guidelines in 2018 that recommended the use of ApoB testing for CVD risk assessment and management, and the use of Lp(a) testing for CVD risk assessment. In addition, these tests help identify individuals who may benefit from targeted therapies, such as proprotein convertase subtilisin/kexin type 9 inhibitors [19] and drugs in development targeting Lp(a) [20]. Our results on the low prevalence of Lp(a) testing are in line with those recently reported on the 10-year experience of a network of academic hospitals in southern California [21], and expand their relevance by showing that this observation occurs nationwide and is equivalent to that of ApoB. In addition, we show that the prevalence of testing for either ApoB or Lp(a) is highly correlated with use of the other test, as approximately 50 % of individuals who were tested for ApoB were also tested for Lp(a) and approximately 75 % of individuals who were tested for Lp(a) were also tested for ApoB.

This study has strengths and limitations. The datasets analyzed in this paper represent a wide variety of the US population by age, sex, geography, socio-economic status, and healthcare coverage options, including Medicare, Medicaid, and commercial insurance. However, claim-based datasets are subject to data entry and coding error, and our approach only utilized data for a single year (2019), thus limiting efforts to generalize the lack of concordance between standard lipid testing which is performed repeatedly and additional testing which is performed sporadically. Due to clinical inertia, the use of 2019 data may not have allowed enough time for clinicians to fully endorse the use of, or payors to incorporate coverage for, these lipoprotein tests. However, it provides a baseline prevalence that will inform future studies and any potential progress the guidelines have made in impacting clinical practice. It is important to note that our prevalence estimates are not influenced by changes in clinical practice caused by the COVID-19 pandemic. Given the low use of ApoB and Lp(a) testing in 2019, future research is warranted to assess the uptake of US national guidelines and consensus recommendations regarding ApoB and Lp(a).

5. Conclusions

We show an extremely low rate of utilization of ApoB and Lp(a) testing in the USA, possibly indicating a temporal or behavioral gap between the issuing of expert recommendations and their implementation in clinical practice. At minimum, there is a strong need to improve education among healthcare providers and to increase awareness among patients regarding the development of inexpensive and accessible clinical tests that add value to CVD risk management. Expert committees should include primary care agencies, federal and state regulators, and insurers to increase support for pragmatic implementation of best-practice guidelines and consensus recommendations for lipid testing.

Data sharing

Qualified researchers may request access to study documents (including the clinical study report, study protocol with any amendments, blank case report form, and statistical analysis plan) that support the methods and findings reported in this manuscript. Individual anonymized participant data will be considered for sharing once the indication has been approved by a regulatory body, if there is legal authority to share the data and there is not a reasonable likelihood of participant re-identification. Submit requests to https://vivli.org/.

CRediT authorship contribution statement

Dana J Murdock: Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Keran Moll:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Robert J Sanchez:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Jing Gu:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Sergio Fazio:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Gregory P Geba:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Fatima Rodriguez:** Writing – review & editing, Methodology, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Robert Sanchez reports administrative support, article publishing charges, and writing assistance were provided by Regeneron Pharmaceuticals Inc. Dana Murdock reports a relationship with Regeneron Pharmaceuticals Inc that includes: employment and equity or stocks. Robert Sanchez reports a relationship with Regeneron Pharmaceuticals Inc that includes: employment and equity or stocks. Keran Moll reports a relationship with Regeneron Pharmaceuticals Inc that includes: employment and equity or stocks. Jing Gu reports a relationship with Regeneron Pharmaceuticals Inc that includes: employment and equity or stocks. Sergio Fazio reports a relationship with Regeneron Pharmaceuticals Inc that includes: employment and equity or stocks. Gregory P Geba reports a relationship with Regeneron Pharmaceuticals Inc that includes: employment and equity or stocks. Fatima Rodriquez reports a relationship with HealthPals, Inc. that includes: consulting or advisory. Fatima Rodriquez reports a relationship with Novartis that includes: consulting or advisory. Fatima Rodriquez reports a relationship with Amgen Inc that includes: consulting or advisory. Fatima Rodriquez reports a relationship with NovoNordisk that includes: consulting or advisory. Fatima Rodriquez reports a relationship with Movano Health that includes: consulting or advisory. Fatima Rodriquez reports a relationship with Edwards that includes: consulting or advisory. Fatima Rodriquez reports a relationship with Inclusive Health that includes: consulting or advisory. Fatima Rodriquez reports a relationship with HeartFlow that includes: consulting or advisory. Fatima Rodriquez reports a relationship with Kento Health that includes: consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

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