American Journal of Preventive Cardiology 18 (2024) 100673

Contents lists available at ScienceDirect

American Journal of Preventive Cardiology

journal homepage: www.journals.elsevier.com/american-journal-of-preventive-cardiology

Short Report

Temporal trends and racial/ethnic- and sex-differences in LDL cholesterol control among US adults with self-reported atherosclerotic cardiovascular disease

Danh Q. Nguyen [a], Neil Keshvani [a], Alvin Chandra [a], Pamela L. Alebna [b], Dave L. Dixon [b,c], Michael D. Shapiro [d], Erin D. Michos [e], Laurence S. Sperling [f], Ambarish Pandey [a], Anurag Mehta [b,*]

[a] Division of Cardiology, Department of Internal Medicine, UT Southwestern Medical Center, Dallas, TX, USA
[b] VCU Health Pauley Heart Center, Richmond, VA, USA
[c] Department of Pharmacotherapy & Outcomes Science, VCU School of Pharmacy, Richmond, VA, USA
[d] Section on Cardiovascular Medicine, Department of Medicine, Wake Forest University School of Medicine, Winston-Salem, NC, USA
[e] Division of Cardiology, Johns Hopkins University School of Medicine, Baltimore, MD, USA
[f] Emory Clinical Cardiovascular Research Institute, Emory University School of Medicine, Atlanta, GA, USA

ARTICLE INFO

Keywords:
Secondary prevention
LDL cholesterol
ASCVD

ABSTRACT

Objective: Current guidelines for secondary prevention of atherosclerotic cardiovascular disease (ASCVD) recommend targeting a low-density lipoprotein cholesterol (LDL-C) of < 70 mg/dL. However, temporal trends and racial/ethnic- and sex-differences in achievement of LDL-C targets are not well described. We assessed trends and racial/ethnic- and sex-differences in achievement of LDL-C < 70 mg/dL using data from the National Health and Nutrition Examination Survey (NHANES) from 2005 to 2008 to 2017-March 2020.

Methods: We combined NHANES cycles into 4 periods: 2005–2008, 2009–2012, 2013–2016, and 2017-March 2020 and included participants ≥ 40 years with self-reported ASCVD. We estimated LDL-C < 70 mg/dL prevalence over time and further stratified by sex and race/ethnicity. We used multivariable logistic regression adjusted for social determinants of health and clinical covariates to model LDL-C target attainment.

Results: Among 1,826 NHANES participants representing 7,161,221 US adults with self-reported ASCVD (59.6% ≥ 65 years, 56.4% male, 74.8% White), LDL-C target attainment increased from 19.0% (95% CI, 15.3%-23.3%) in 2005–2008 to 26.3% (95% CI, 20.4%-33.1%) in 2017-March 2020 ($P = 0.012$ for trend). Achievement of LDL-C < 70 mg/dL significantly rose among men from19.5% (95% CI, 15.1%-24.8%) to 29.4% (95% CI, 20.7%-29.9%) without significant change in women (from 18.3% [95% CI, 13.6%-24.2%] to 22.5% [95% CI, 13.0%-35.9%]; $P = 0.241$ for trend). Improvement in LDL-C target attainment was similar among White, Black, and Hispanic individuals (~5–7% increase) and was greatest among individuals of other (non-White, Hispanic, or Black) race/ethnicity (23.1% increase). In our multivariable analysis, comorbid diabetes and ages 65–75 and > 75 years were associated with LDL-C target attainment.

Conclusion: LDL-C control modestly improved between 2005 and 2008 and 2017-March 2020; however, only ~1/4 of individuals met guideline-directed LDL-C treatment targets by 2017-March 2020. Women had lower LDL-C control and lesser magnitude of improvement in LDL-C control than men, highlighting a need for targeted interventions to improve lipid-lowering therapy utilization in this population.

1. Introduction

The 2018 American Heart Association (AHA)/American College of Cardiology (ACC) multisociety cholesterol guideline recommends high-intensity or maximally tolerated statin therapy for all patients aged ≤ 75 years with atherosclerotic cardiovascular disease (ASCVD) [1]. For

* Corresponding author at: Preventive Cardiology, VCU Health Pauley Heart Center, Assistant Professor, Internal Medicine, Virginia Commonwealth University School of Medicine, 1200 East Broad Street, PO Box 980036, Richmond, Virginia 23298, USA.
E-mail address: anurag.mehta@vcuhealth.org (A. Mehta).

https://doi.org/10.1016/j.ajpc.2024.100673
Received 25 October 2023; Received in revised form 31 March 2024; Accepted 15 April 2024
Available online 15 April 2024

those whose low-density lipoprotein cholesterol (LDL-C) levels remain ≥ 70 mg/dL despite maximally tolerated statin, the guideline recommends adding ezetimibe (class IIa and class IIb recommendations for patients with and without very high future ASCVD risk, respectively), followed by a proprotein convertase subtilisin/kexin type 9 inhibitor (PCSK9i) if needed (class IIa recommendation for those with very high future ASCVD risk). The 2022 ACC Expert Consensus Decision Pathway (ECDP) on nonstatin therapies recommends using a lower threshold of LDL-C ≥ 55 mg/dL to consider adding ezetimibe and/or PCSK9i for individuals with very high ASCVD risk [2].

Aggarwal et al. recently reported that less than 1/4 US adults with coronary artery disease (CAD) met the guideline target LDL-C (< 70 mg/dL) between 2015 and 2020 [3]. While prior studies have shown increased statin utilization over time for primary prevention of ASCVD [4] and decreased LDL-C levels over time among adults with established ASCVD [5], longitudinal trends and racial/ethnic- and sex-differences in LDL-C target attainment in relation to the 2018 AHA/ACC multisociety cholesterol guideline are not well described. Accordingly, we sought to define contemporary trends and predictors of LDL-C control for secondary prevention of ASCVD in a large, nationwide cohort.

2. Methods

2.1. Study population

The National Health and Nutrition Examination Survey (NHANES) is a cross-sectional survey that uses stratified and multistage probability-cluster sampling to assess the health and nutritional status of the US noninstitutionalized civilian population [6]. We pooled data across eight 2-year survey cycles spanning January 2005 to March 2020 (the 2019–2020 cycle was halted prematurely due to the coronavirus pandemic and was thus combined with the 2017–2018 cycle) [7]. From a randomly selected and nationally representative subsample of individuals with fasting laboratory measurements, we included adults aged ≥ 40 years with a self-reported diagnosis of CAD (coronary heart disease, angina, or heart attack) or stroke.

The NHANES study protocols were approved by the National Center for Health Statistics Research Ethics Review Board. All study participants provided written informed consent.

2.2. Outcome

The primary outcome was the prevalence of LDL-C target attainment (< 70 mg/dL). For a subset of participants with very high risk for future ASCVD events, we explored a secondary outcome of LDL-C target attainment (< 55 mg/dL) as recommended by the 2022 ACC ECDP on nonstatin therapies. The 2018 ACC/AHA multisociety cholesterol guideline defines very high future ASCVD risk as having a history of ≥ 2 major ASCVD events or having 1 major ASCVD event and ≥ 2 high-risk conditions. We adapted these criteria to data available in NHANES to identify participants with very high ASCVD risk (**Supplementary Table S1**).

2.3. Covariates

We pre-specified social determinants of health (SDOH) and clinical predictors based on prior literature [8–10]. These included survey cycle, age, sex, race/ethnicity, education, marital status, employment, income, insurance status, having a routine place to go for healthcare, any food insecurity, smoking, physical activity level, comorbidities (depression, obesity, diabetes, hypertension, kidney disease), ASCVD phenotype (CAD, stroke), and use of statins, ezetimibe, and PCSK9i. Obesity, diabetes, hypertension, and kidney disease were either self-reported or determined by physical exam or laboratory measurements (see Footnote of Table 1). Medication use was ascertained by pill bottle review. All other covariates were self-reported.

Table 1
Baseline characteristics of US adults with self-reported ASCVD, 2005–2008 to 2017-March 2020.

	% (95% CI)			
	Overall cohort (n = 1826)	LDL-C ≥ 70 mg/dL (n = 1433)	LDL-C < 70 mg/dL (n = 393)	P value[a]
Weighted population estimate, no.	7161,221	5597,725	1563,496	
Sociodemographics				
Age in years				
40–64	40.4 (37.4–43.4)	40.8 (37.3–44.5)	25.6 (19.6–32.6)	<0.001
65–75	32.8 (30.1–35.6)	33.9 (30.8–37.1)	42.1 (35.0–49.5)	0.010
> 75	26.8 (24.1–29.7)	25.3 (22.3–28.5)	32.3 (26.9–38.3)	0.031
Male	56.4 (53.2–59.5)	54.5 (50.4–58.5)	63.2 (57.0–68.9)	0.030
Race/ethnicity				
White	74.8 (71.4–78.0)	73.7 (70.0–77.2)	78.6 (73.4–83.1)	0.055
Hispanic	7.9 (6.5–9.5)	8.3 (6.8–10.2)	6.2 (4.6–8.2)	0.049
Black	10.2 (8.5–12.1)	10.6 (8.7–12.8)	8.8 (6.6–11.8)	0.243
Other	7.1 (5.4–9.3)	7.3 (5.4–9.9)	6.3 (3.6–10.9)	0.616
Education level				
< High school	24.8 (22.1–27.7)	25.5 (22.6–28.7)	22.3 (17.9–27.3)	0.187
High school graduate	27.4 (24.5–30.5)	28.2 (25.1–31.6)	24.4 (19.3–30.4)	0.215
> High school	47.8 (44.1–51.5)	46.2 (42.3–50.2)	53.3 (46.7–59.8)	0.041
Married/living with partner	62.5 (59.3–65.7)	60.9 (57.4–64.4)	68.3 (61.9–74.1)	0.032
Employed	28.6 (25.8–31.6)	30.1 (26.7–33.7)	23.1 (17.6–29.8)	0.062
Poverty to income ratio > 1.30[a]	75.7 (72.9–78.3)	74.2 (71.2–77.0)	80.9 (75.5–85.4)	0.011
Household food insecurity	25.3 (22.7–28.1)	26.5 (23.3–30.0)	21.0 (15.5–27.8)	0.149
Access to care				
Insured	93.1 (91.3–94.5)	92.4 (90.3–94.2)	95.3 (92.1–97.2)	0.073
Routine place to go for healthcare	96.4 (95.2–97.3)	95.8 (94.4–96.9)	98.3 (95.2–99.4)	0.020
Lifestyle habits				
Current smoking	21.4 (18.5–24.6)	22.9 (19.6–26.5)	16.1 (12.0–21.2)	0.013
Physical activity ≥ 150 min/week[b]	44.0 (40.4–47.6)	44.7 (40.8–48.7)	41.2 (34.3–48.6)	0.379
Comorbidities				
Depression	11.6 (9.8–13.5)	12.1 (10.2–14.3)	9.7 (6.3–14.7)	0.312
Obesity[c]	44.8 (41.6–48.1)	44.5 (40.7–48.5)	45.8 (39.5–52.2)	0.757
Diabetes[d]	29.6 (26.6–32.8)	26.4 (23.4–29.6)	41.1 (34.5–48.1)	<0.001
Hypertension[e]	71.2 (67.8–74.3)	69.8 (65.3–73.9)	76.1 (70.0–81.4)	0.117
Kidney disease[f]	9.2 (7.8–10.9)	8.9 (7.4–10.7)	10.3 (7.5–14.1)	0.417
ASCVD phenotype				
Coronary artery disease	74.7 (72.1–77.2)	73.1 (69.7–762)	80.6 (74.6–85.4)	0.035
Stroke	37.1 (34.2–40.0)	38.1 (34.7–41.7)	33.3 (27.3–40.0)	0.214
Lipid-lowering therapy				
Statin	64.2 (60.8–67.3)	57.5 (53.5–61.5)	87.8 (83.6–91.0)	<0.001
Ezetimibe	7.2 (5.4–9.4)	6.1 (4.3–8.6)	10.9 (7.3–16.0)	0.043
PCSK9i	0.16 (0.05 - 0.51)	0.07 (0.01–0.50)	0.50 (0.12–1.99)	0.230

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor.

[a] Generated from weighted proportion test comparing LDL-C ≥ 70 mg/dL and LDL-C < 70 mg/dL groups.

[b] The 2018 Physical Activity Guidelines for Americans recommends ≥ 150 min/week of moderate-intensity exercise [20].

[c] Defined as body mass index ≥ 30 kg/m^2 based on weight and height measured by physical examination.

[d] Either self-reported or defined as a hemoglobin A1c ≥ 6.5% or fasting plasma glucose ≥ 126 mg/dL.

[e] Either self-reported or defined as a mean systolic blood pressure ≥ 130 mmHg or mean diastolic blood pressure ≥ 90 mmHg.

[f] Either self-reported or defined by an estimated glomerular filtration rate of 15–59 mL/min/1.73 m^2 estimated by the 2021 CKD-EPI equations [21].

2.4. Statistical analysis

To increase the precision of our estimates, we combined survey cycles into 4 periods: 2005–2008, 2009–2012, 2013–2016, and 2017-March 2020. The prevalence of LDL-C target attainment was estimated across each period and stratified by race/ethnicity and sex. We used univariate logistic regression to evaluate temporal trends, with the midpoint of each survey cycle modeled as a continuous independent variable. To identify factors associated with LDL-C control, we used multivariable logistic regression to model LDL-C target attainment with stepwise adjustment: Model 1: adjusted for demographics, ASCVD phenotype, and medical comorbidities; Model 2: Model 1+ SDOH parameters. We repeated analyses for the subset of participants at very high risk of future ASCVD events.

All analyses were performed with a significance threshold of $P < 0.05$ using Stata/SE 15.0 (StataCorp, College Station, TX) and incorporated sample weights to account for nonresponse and oversampling of certain populations [6].

3. Results

We identified 1,826 NHANES participants weighted to represent 7,161,221 US adults with self-reported ASCVD (59.6% age ≥ 65 years, 56.4% male, 74.8% White, Table 1). 60.6% of the cohort (1,180 participants representing 4341,615 US adults) had very high risk for future ASCVD events (**Supplementary Table S2**). The prevalence of statin, ezetimibe, and PCSK9i utilization were 64.2%, 7.2%, and 0.2%, respectively (Table 1).

Compared to participants who did not meet the LDL-C target of < 70 mg/dL, those who met the LDL-C target were more commonly 65–75 years old (42.1% vs 33.9%; $P = 0.031$) and > 75 years old (32.3% vs 25.3%; $P = 0.031$), male (63.2% vs 54.5%; $P = 0.030$), educated beyond high school (53.3% vs 46.2%; $P = 0.041$), married (68.3% vs 60.9%; $P = 0.032$), and more likely to have a routine place to go for healthcare (98.3% vs 95.8%; $P = 0.020$; Table 1). Individuals with LDL-C < 70 mg/dL were also more likely to have diabetes (41.1% vs 26.4%; $P < 0.001$), CAD (80.6% vs 73.1%; $P = 0.035$), and had greater utilization of statins (87.8% vs 57.5%; $P < 0.001$) and ezetimibe (10.9% vs 6.1%; $P = 0.043$; Table 1).

Baseline characteristics stratified by statin use and by LDL-C target attainment < 70 mg/dL among participants taking statins are shown in **Supplementary Table S2**.

3.1. Temporal trends by race/ethnicity and sex in LDL-C target attainment

Between 2005–2008 and 2017-March 2020, the prevalence of LDL-C target attainment significantly increased from 19.0% (95% CI, 15.3%-23.3%) to 26.3% (95% CI, 20.4%-33.1%) (P= 0.012 for trend; **Supplementary Table S3**, Fig. 1**A**). Achievement of LDL-C < 70 mg/dL significantly rose among men from 19.5% (95% CI, 15.1%-24.8%) to 29.4% (95% CI, 20.7%-39.9%) (P= 0.031 for trend) without significant differences in women (18.3% [95% CI, 13.6%-24.2%] to 22.5% [95% CI, 13.0%-35.9%]; $P = 0.241$ for trend; **Supplementary Table S3,** Fig. 1**A**). The magnitude of improvement in LDL-C target attainment < 70 mg/dL was similar but not significant across participants of White, Hispanic, and Black race/ethnicity and significantly increased among those of other (non-White, Hispanic, or Black) race/ethnicity from 7.4% (95% CI, 3.6%-14.6%) to 30.5% (95% CI, 13.7%-54.7%; $P = 0.048$ for trend; **Supplementary Table S3**, Fig. 1**B**).

Among the subset of participants with very high ASCVD risk, the prevalence of LDL-C < 55 mg/dL did not significantly change overall but did significantly improve among Black (1.6% [95% CI, 0.4%-6.6%] to 14.7% [95% CI, 8.0%-25.7%]; $P = 0.001$ for trend) and other race/ethnicity (0.0% to 35.1 [11.3–69.7]; $P = 0.031$ for trend; **Supplementary Table S4**).

3.2. Factors associated with LDL-C target attainment

In adjusted multivariable analysis, survey year (aOR, 1.05; 95% CI, 1.01–1.10), age 65–75 (aOR 2.40; 95% CI, 1.39–4.15) ≥ 75 years (aOR 2.06; 95% CI, 1.13–3.77), and diabetes (aOR, 1.97; 95% CI, 1.41–2.77) were associated with LDL-C target attainment < 70 mg/dL (**Supplementary Table S5**). Sex, race/ethnicity, and individual SDOH parameters did not show significant associations. Our findings were similar for the secondary analysis of LDL-C target attainment <55 mg/dL among the subset of participants with very high ASCVD risk, though point estimates were less precise with wider confidence intervals owing to the smaller sample size (**Supplementary Table S6**).

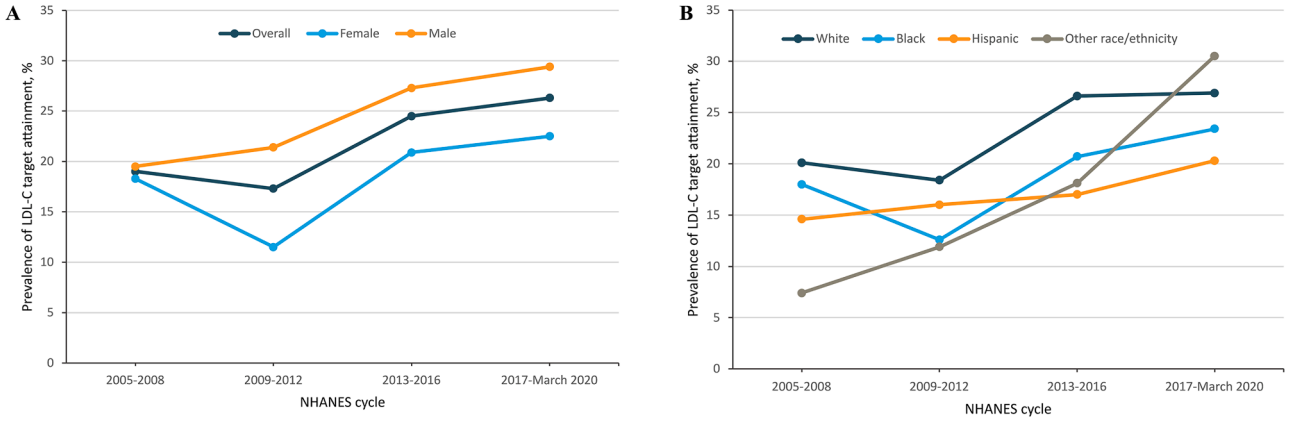

Fig. 1. Temporal trends in LDL-C target attainment (< 70 mg/dL) among US adults with ASCVD stratified by sex (Panel A) and stratified by race/ethnicity (Panel B). Abbreviations: LDL-C, low-density lipoprotein cholesterol; ASCVD, atherosclerotic cardiovascular disease.

4. Discussion

In this nationally representative sample of US adults with prevalent ASCVD, LDL-C control (< 70 mg/dL) modestly improved by 7.3% between 2005 and 2008 and 2017-March 2020; however, only ~1/4 of all participants achieved LDL-C < 70 mg/dL by 2017-March 2020. There were no racial/ethnic-differences in achievement of target LDL-C. Men (vs. women) had greater overall prevalence of LDL-C target attainment and only men (vs. women) had significant temporal increase in LDL-C target attainment over the study period. After multivariable adjustment, comorbid diabetes and older age were independently associated with LDL-C < 70 mg/dL.

While there was a modest improvement in LDL-C control, most patients with ASCVD do not meet guideline-recommended LDL-C levels. Only 64.2% of participants were taking a statin and much fewer were taking ezetimibe (7.2%) or PCSK9i (0.2%). Of the individuals on statin therapy, we found that 70.2% did not achieve LDL-C < 70 mg/dL, which may be reflective of known clinical inertia in escalating lipid-lowering therapy among patients with ASCVD already on statin therapy [11]. The low prevalence of ezetimibe use is also noteworthy and may represent an opportunity for improvement, as the RACING trial demonstrated that combination therapy with ezetimibe and moderate-intensity statin was non-inferior to high-intensity statin monotherapy [12]. Our findings highlight substantial gaps in care for patients in whom initiation and/or intensification of lipid-lowering therapy for secondary ASCVD prevention is indicated.

We report notable sex differences in LDL-C target achievement. Known disparities in treatment have been observed, with women (vs. men) less likely to be prescribed statin therapy (or at appropriate intensity) for both primary and secondary prevention of ASCVD [8,13-15]. However, despite numerous reports highlighting these sex differences, it is concerning that women had no difference in LDL-C control over the study period, while men had observed temporal improvements. Interventions to narrow this gap in LDL-C treatment are important to improve sex differences in ASCVD outcomes.

In our multivariable adjusted analysis, older age and comorbid diabetes were associated with greater LDL-C target attainment, whereas sex was not. Because patients > 75 years have been poorly represented in large secondary ASCVD prevention statin trials, the 2018 ACC/AHA multisociety cholesterol guideline recommends high-intensity statins only for those ≤ 75 years, whereas moderate-intensity statins are considered acceptable for those > 75 years [1]. Despite this, we found that participants aged > 75 years were more likely than those aged 40–64 years to achieve LDL-C < 70 mg/dL. While prior observational studies have demonstrated significant survival advantage with high-intensity statin use among adults > 75 years with ASCVD, clinical trials are needed to evaluate the safety and efficacy of statin therapy, including high-intensity therapy, in this population [16]. The association between diabetes and achievement of LDL-C < 70 mg/dL aligns with recommendations by the American Diabetes Association from 2005 to 2020 for LDL-C goal of < 70 mg/dL for people with diabetes and overt ASCVD [17]. The prevalence of type 2 diabetes is greater in men than women and may explain the lack of association between sex and LDL-C < 70 mg/dL [18].

Previous studies have reported a lower rate of prescriptions of lipid-lowering therapy for Black or Hispanic patients [19]. In the present study, there were no substantial differences in LDL-C target achievement across racial/ethnic groups, and all racial/ethnic groups observed numeric increases in LDL-C control over the study period. These improvements in LDL-C target achievement across all race/ethnicities are an important first step in rectifying longstanding racial/ethnic-differences in ASCVD care [19].

Study limitations include possible unmeasured confounders, reliance on self-reported ASCVD which is subject to recall bias, and inability to account for peripheral arterial disease or statin treatment intensity.

5. Conclusion

Among US adults with ASCVD, LDL-C control modestly improved between 2005 and March 2020, however, ~3/4 of individuals still fall short of the recommended LDL-C target. Women had worse LDL-C control and lesser improvement in LDL-C control than men. There were no observed racial/ethnic-differences in achievement of LDL-C < 70 mg/dL.

Source of funding/disclosures

Dr. Keshvani reported grants from the National Heart, Lung, and Blood Institute (5T32HL125247–08) and consultant fees from Heart Test Laboratories and Tricog Health. Dr. Dixon reported a grant from Boehringer Ingelheim. Dr. Pandey reported grants from the National Institute on Aging (1R03AG067960–01), the National Institute on Minority Health and Disparities (R01MD017529), Applied Therapeutics, Gilead Sciences Research, and Myovista Research, consultant fees from Roche Diagnostics, Tricog Health, Pieces Technologies, Rivus, Palomarin Inc, Emmi Solutions, nonfinancial support from Pfizer and Merck, advisory board fees from Lilly Inc, Cytokinetics, Alleviant Medical, Axon Therapies, and Bayer. Dr. Shapiro reports consultant fees with Ionis, Novartis, Regeneron, Aidoc and advisory boards Agepha, Amgen, Ionis, Novartis, and Precision BioScience. Dr. Michos reports consultant fees from Amgen, Amarin, Boehringer Ingelheim, Esperion, Edwards Lifescience, Medtronic, Novartis, Novo Nordisk, and Pfizer. No other authors have reported any disclosures.

CRediT authorship contribution statement

Danh Q. Nguyen: Conceptualization, Data curation, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Neil Keshvani:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing. **Alvin Chandra:** Conceptualization, Methodology, Writing – review & editing. **Pamela L. Alebna:** Writing – review & editing. **Dave L. Dixon:** Writing – review & editing. **Michael D. Shapiro:** Writing – review & editing. **Erin D. Michos:** Writing – review & editing. **Laurence S. Sperling:** Writing – review & editing. **Ambarish Pandey:** Conceptualization, Methodology, Writing – review & editing. **Anurag Mehta:** Conceptualization, Methodology, Supervision, Writing – review & editing.

Declaration of competing interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2024.100673.

References

[1] Grundy 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). https://doi.org/10.1161/cir.0000000000000625.

[2] Lloyd-Jones DM, Morris PB, Ballantyne CM, 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. J Am Coll Cardiol 2022;80(14):1366–418. https://doi.org/10.1016/j.jacc.2022.07.006.

[3] Aggarwal R, Chiu N, Libby P, Boden WE, Bhatt DL. Low-Density Lipoprotein Cholesterol Levels in Adults With Coronary Artery Disease in the US, January 2015 to March 2020. JAMA 2023;330(1):80. https://doi.org/10.1001/jama.2023.8646.

[4] Kim CJ, Sussman JB, Mukamal KJ, Eades M, Anderson TS. Trends in Primary Prevention Statin Use by Cardiovascular Risk Score From 1999 to 2018: a Repeated

Cross-Sectional Study. Ann Intern Med 2023;176(12):1684–8. https://doi.org/10.7326/m23-1915 [PMID: 38048586].
[5] Vega GL, Grundy SM. Current trends in non–HDL cholesterol and LDL cholesterol levels in adults with atherosclerotic cardiovascular disease. J Clin Lipidol 2019;13(4):563–7. https://doi.org/10.1016/j.jacl.2019.05.012.
[6] Zipf G, Chiappa M, Porter KS, Ostchega Y, Lewis BG, Dostal J. National health and nutrition examination survey: plan and operations, 1999-2010. Vital Health Stat 2013;1(56):1–37 [PMID: 25078429].
[7] National Health and Nutrition Examination Survey. Prepandemic file: sample design, estimation, and analytic guidelines, vital and health statistics series(2022). 2020.
[8] Minhas AMK, Ijaz SH, Javed N, et al. National trends and disparities in statin use for ischemic heart disease from 2006 to 2018: insights from National Ambulatory Medical Care Survey. Am Heart J 2022;252:60–9. https://doi.org/10.1016/j.ahj.2022.05.015 [PMID: 35644222].
[9] Jacobs JA, Addo DK, Zheutlin AR, et al. Prevalence of Statin Use for Primary Prevention of Atherosclerotic Cardiovascular Disease by Race, Ethnicity, and 10-Year Disease Risk in the US. JAMA Cardiol 2023;8(5):443. https://doi.org/10.1001/jamacardio.2023.0228.
[10] Chobufo MD, Regner SR, Zeb I, Lacoste JL, Virani SS, Balla S. Burden and predictors of statin use in primary and secondary prevention of atherosclerotic vascular disease in the US: from the National Health and Nutrition Examination Survey 2017–2020. Eur J Prev Cardiol 2022;29(14):1830–8. https://doi.org/10.1093/eurjpc/zwac103.
[11] Lowenstern AM, Li S, Navar AM, et al. Measurement of Low-Density Lipoprotein Cholesterol Levels in Primary and Secondary Prevention Patients: insights From the PALM Registry. J Am Heart Assoc 2018;7(18). https://doi.org/10.1161/jaha.118.009251.
[12] Kim BK, Hong SJ, Lee YJ, et al. Long-term efficacy and safety of moderate-intensity statin with ezetimibe combination therapy versus high-intensity statin monotherapy in patients with atherosclerotic cardiovascular disease (RACING): a randomised, open-label, non-inferiority trial. Lancet 2022;400(10349):380–90. https://doi.org/10.1016/s0140-6736(22)00916-3 [PMID: 35863366].
[13] Peters SAE, Colantonio LD, Zhao H, et al. Sex Differences in High-Intensity Statin Use Following Myocardial Infarction in the United States. J Am Coll Cardiol 2018;71(16):1729–37. https://doi.org/10.1016/j.jacc.2018.02.032 [PMID: 29673463].
[14] Bradley CK, Wang TY, Li S, et al. Patient-Reported Reasons for Declining or Discontinuing Statin Therapy: insights From the PALM Registry. J Am Heart Assoc 2019;8(7). https://doi.org/10.1161/jaha.118.011765.
[15] Nanna MG, Wang TY, Xiang Q, et al. Sex Differences in the Use of Statins in Community Practice. Circulation 2019;12(8). https://doi.org/10.1161/circoutcomes.118.005562.
[16] Rodriguez F, Maron DJ, Knowles JW, Virani SS, Lin S, Heidenreich PA. Association Between Intensity of Statin Therapy and Mortality in Patients With Atherosclerotic Cardiovascular Disease. JAMA Cardiol 2017;2(1):47. https://doi.org/10.1001/jamacardio.2016.4052.
[17] Association AD. Standards of Medical Care in Diabetes. Diabetes Care 2005;28(suppl_1):s4–36. https://doi.org/10.2337/diacare.28.suppl_1.S4.
[18] Huebschmann AG, Huxley RR, Kohrt WM, Zeitler P, Regensteiner JG, Reusch JEB. Sex differences in the burden of type 2 diabetes and cardiovascular risk across the life course. Diabetologia 2019;62(10):1761–72. https://doi.org/10.1007/s00125-019-4939-5 [PMID: 31451872].
[19] Devareddy A, Sarraju A, Rodriguez F. Health Disparities Across the Continuum of ASCVD Risk. Curr Cardiol Rep 2022;24(9):1129–37. https://doi.org/10.1007/s11886-022-01736-y [PMID: 35788894].
[20] Piercy KL, Troiano RP, Ballard RM, et al. The Physical Activity Guidelines for Americans. JAMA 2018;320(19):2020. https://doi.org/10.1001/jama.2018.14854.
[21] Inker LA, Eneanya ND, Coresh J, et al. New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race. N Engl J Med 2021;385(19):1737–49. https://doi.org/10.1056/nejmoa2102953.