Brief Report

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Prevalence of clinically suspected familial hypercholesterolemia in the United States, 2009–2018

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Graphical abstract



*Modified Dutch Lipid Clinic Network (DLC) criteria

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1. Introduction

Familial hypercholesterolemia (FH) is a common inherited lipid disorder that confers a markedly increased risk of premature atherosclerotic cardiovascular disease (ASCVD).[1] In the United States, prior analyses applying clinical diagnostic criteria to the 1999–2012 National Health and Nutrition Examination Survey (NHANES) estimated a prevalence of approximately 0.40% for definite or probable FH.[2] However, prior research has predominantly focused on these strict diagnostic categories, potentially omitting a broader spectrum of individuals with clinically suspected FH. This includes those classified as having "possible" FH, who may still face substantial cardiovascular risk. Therefore, this study aims to characterize temporal trends and sociodemographic patterns of clinically suspected FH, encompassing definite, probable, and possible cases, among United States adults from 2009 to 2018, thereby providing a more comprehensive population-level assessment.

2. Methods

NHANES uses a multistage probability sampling design to generate nationally representative cross-sectional data for the US population. We utilized data from 2-year cycles of United States adults aged ≥ 20 years, excluding pregnant women, from 2009 to 2018. FH was identified using a modified Dutch Lipid Clinic (DLC) scoring system, chosen for its applicability to population-based surveys and comparability with prior studies. The standard DLC algorithm is a validated clinical tool that classifies FH based on low-density lipoprotein cholesterol (LDL-C) levels, physical findings, genetic testing, and personal and family history of premature ASCVD. Because NHANES does not collect genetic data or FH-relevant physical examination findings, we applied a modified DLC score incorporating only variables consistently available in the dataset, including LDL-C levels, personal history of ASCVD, and family history of early ASCVD in first-degree relatives. Personal ASCVD was defined as a self-reported history of coronary heart disease, angina, myocardial infarction, or stroke occurring before age 55 years in men and 60 years in women. Family history of ASCVD was defined as a report of a heart attack or angina occurring before age 50 years in a first-degree relative. We also analyzed trends in statin utilization among individuals with clinically suspected FH over the study period. Statin use was defined as a self-reported positive response to the NHANES questionnaire on prescription cholesterol-lowering medication use, verified through matching drug names in the prescription medication files.

Prevalence estimates and corresponding 95% confidence intervals (CIs) were calculated for the overall population and stratified by sex, age group, race/ethnicity, education level, and family poverty-income ratio. All estimates were age- and sex-standardized to the 2010 US Census population using the direct method to ensure comparability across survey cycles and subgroups. Temporal trends in age- and sex-standardized prevalence were assessed using weighted linear regression models, with survey cycles treated as a continuous predictor and adjustments made for age and sex as appropriate. Statistical significance was defined as a 2-sided p-value < 0.05. To account for multiple comparisons across subgroups and survey cycles, the Benjamini–Hochberg procedure was applied to control the false discovery rate. All analyses incorporated the complex survey design of NHANES, including stratification, clustering, and sample weights (wtsaf2yr). Survey-weighted χ^2 tests were used for categorical comparisons. Statistical analyses were performed using R version 4.4.0. Since only de-identified, publicly available data were used, no additional ethics approval was required.

3. Results

Among the 11,784 adults included, the weighted mean age of participants was 50.01 years, of whom 5,698 (48.35%) were male. From 2009 to 2018, the prevalence of FH exhibited mild, nonlinear fluctuations rather than a consistent trend. Specifically, the prevalence rose slightly from 5.11% in 2009–2010 to 5.26% in 2011–2012, then experienced a modest decline to 4.99% in 2013–2014, reflecting a temporary dip in mid-period prevalence. However, this decline was followed by a gradual rebound, with prevalence increasing to 5.22% in 2015–2016 and reaching 5.37% in 2017–2018 (Table 1).

Women generally showed slightly higher FH rates than men, except in 2015–2016. Disparities were also evident across subgroups. Middle-aged adults (45–64 years) consistently exhibited the highest prevalence. Racial differences emerged as well, with non-Hispanic Black adults displaying slightly higher prevalence in most cycles. Significant socioeconomic gradients were observed: individuals with a high school diploma or less and those with low income had substantially higher prevalence compared with their more educated or affluent counterparts.

Our analysis of statin utilization revealed significant temporal variation. Age- and sex-standardized statin use was 44.85% in 2009–2010, peaked at 55.70% in 2011–2012, then declined to 42.74% in 2013–2014. A partial rebound occurred in 2015–2016, with utilization rising to 44.14%, before declining again to 35.92% in 2017–2018. Notably, the pronounced peak in statin use during 2011–2012 and subsequent decline in 2013–2014 align temporally with the transient dip in FH prevalence observed in the same 2013–2014 cycle (Figure S1, Supplemental Digital Content, https://links.lww.com/CARES/A15).

4. Discussion

The prevalence of clinically suspected FH among US adults from 2009 to 2018 followed a nonlinear trajectory, characterized by an initial rise, a mid-period decline, and a subsequent rebound. This pattern suggests that recorded prevalence was shaped by evolving clinical detection and management practices rather than a true change in genetic burden.

Table 1

Estimated prevalence of clinically suspected familial hypercholesterolemia among the US population ≥ 20 years of age by sociodemographic factors

Characteristic	Participants, No. (%)	Age standard prevalence, % (95% CI)* (*N* = 11,784)†					*p* for Trend‡	FDR
		2009–2010 (*n* = 2,595)	2011–2012 (*n* = 2,294)	2013–2014 (*n* = 2,370)	2015–2016 (*n* = 2,246)	2017–2018 (*n* = 2,279)		
Overall		5.11 (3.94–6.28)	5.26 (3.98–6.53)	4.99 (4.20–5.79)	5.22 (3.48–6.95)	5.37 (3.94–6.80)	0.819	0.819
Sex								
Female	6,086 (51.65)	5.56 (4.39–6.73)	5.84 (4.17–7.51)	5.13 (3.84–6.43)	5.03 (3.30–6.77)	5.65 (4.17–7.13)	0.857	0.857
Male	5,698 (48.35)	4.63 (3.26–5.99)	4.63 (2.60–6.67)	4.85 (3.25–6.45)	5.41 (2.96–7.85)	5.07 (3.03–7.11)	0.597	0.857
Age group, year								
20–44	4,782 (40.58)	2.91 (2.03–3.80)	2.28 (0.98–3.57)	2.27 (1.27–3.26)	2.02 (0.93–3.12)	2.26 (1.08–3.43)	0.531	0.700
45–64	4,183 (35.50)	7.62 (5.03–10.21)	8.45 (5.86–11.04)	8.35 (6.03–10.68)	8.75 (4.24–13.26)	8.73 (5.17–12.29)	0.700	0.700
65	2,819 (23.92)	5.68 (4.36–7.01)	6.47 (4.16–8.78)	5.23 (4.06–6.40)	6.29 (4.20–8.37)	6.59 (4.25–8.94)	0.633	0.700
Race/ethnicity								
Mexican American	1,762 (14.95)	3.52 (2.12–4.91)	3.16 (1.19–5.14)	4.75 (1.59–7.90)	3.15 (1.84–4.46)	4.39 (2.00–6.79)	0.800	0.800
Non–Hispanic Black	2,365 (20.07)	6.52 (4.02–9.02)	4.68 (2.83–6.53)	4.97 (3.18–6.77)	7.99 (6.60–9.39)	8.51 (6.69–10.33)	0.082	0.328
Non–Hispanic White	4,697 (39.86)	5.16 (3.87–6.44)	5.50 (3.47–7.54)	5.23 (4.26–6.21)	4.84 (2.52–7.16)	4.75 (2.71–6.79)	0.631	0.800
Others§	2,960 (25.12)	4.40 (1.62–7.18)	5.48 (3.18–7.77)	3.81 (2.26–5.36)	5.91 (3.41–8.41)	6.29 (3.27–9.32)	0.441	0.800
Education level								
Less than high school	2,809 (23.84)	6.83 (5.03–8.64)	5.87 (3.11–8.63)	5.60 (3.24–7.96)	7.71 (3.17–12.24)	6.44 (2.77–10.11)	0.550	0.733
High school graduate or GED	2,603 (22.09)	5.03 (3.81–6.26)	8.36 (2.54–14.18)	4.39 (2.98–5.81)	6.96 (4.27–9.65)	7.64 (3.70–11.59)	0.417	0.733
Some college or associate degree	3,496 (29.67)	4.96 (3.20–6.71)	5.55 (2.30–8.79)	4.45 (2.65–6.25)	3.94 (2.35–5.52)	5.28 (3.36–7.19)	0.794	0.794
College graduate or above	2,876 (24.40)	4.32 (2.14–6.51)	2.99 (1.09–4.89)	5.59 (4.28–6.91)	4.16 (2.04–6.29)	2.73 (0.99–4.47)	0.424	0.733
Family PIR								
Low income (< 1.30)	3,904 (33.13)	7.17 (5.03–9.32)	7.22 (4.03–10.41)	6.19 (2.90–9.47)	9.14 (4.91–13.37)	8.69 (5.60–11.78)	0.209	0.355
Middle income (1.30–3.49)	4,457 (37.82)	5.12 (3.74–6.51)	4.51 (2.84–6.19)	3.78 (2.21–5.35)	6.26 (3.22–9.31)	5.45 (3.77–7.14)	0.355	0.355
High income (≥ 3.50)	3,423 (29.05)	4.30 (2.61–6.00)	5.25 (2.93–7.57)	5.25 (4.22–6.27)	3.08 (1.87–4.30)	3.63 (1.56–5.70)	0.298	0.355

CI = confidence interval; Family PIR = family income-to-poverty ratio; FDR = false discovery rate; GED = General Educational Development.

*The percentage values (95% CI) are weighted using National Health and Nutrition Examination Survey sample weights (wtsaf2yr) to be nationally representative and standardized to the overall sample-weighted age and sex distribution.

†The number of the unweighted population.

‡*p* values for the trend from 2009 to 2018 are age- and sex-adjusted.

§"Others" includes groups designated as"other"in NHANES, including multiracial individuals.

The increase from 2009–2010 to 2011–2012 likely reflects growing clinical recognition, improved diagnostic practices, and heightened awareness driven by emerging guidelines. The subsequent decline in 2013–2014 coincided with the release of the 2013 American College of Cardiology/ American Heart Association cholesterol guidelines, which promoted more intensive, risk-based treatment.[3] This shift may have lowered measured LDL-C levels in high-risk individuals, thereby reducing the proportion meeting LDL-C–based FH criteria in cross-sectional surveys like NHANES, despite an unchanged underlying genetic prevalence. The observed synchronous decline in statin use supports this interpretation.

The rebound from 2015 to 2018 aligns with advances in genetic testing, wider adoption of standardized diagnostic criteria (e.g., Dutch Lipid Clinic Network), increased cascade screening, and improved documentation in electronic health records. Growing emphasis on FH in professional guidelines and public health initiatives further enhanced case identification during this period.

Demographic disparities persisted throughout the decade. The prevalence was generally slightly higher among women, which may be influenced by biological factors, including androgen and estrogen-mediated regulation of lipid metabolism and Proprotein Convertase Subtilisin/ Kexin Type 9 (*PCSK9*) expression,[4–6] as well as clinical disparities such as later diagnosis, less intensive treatment, and pregnancy-related therapy interruptions in women.[5] Middle-aged adults (45–64 years) had the highest prevalence, likely due to underdiagnosis in youth and the accumulation of clinical manifestations by midlife.[7] Non-Hispanic Black adults consistently experienced among the highest prevalence rates, linked to structural barriers, healthcare inequities, and gaps in preventive care.[8] Socioeconomically, individuals with a college education maintained a low prevalence (< 3%), suggesting a protective effect from higher health literacy and better healthcare access, whereas prevalence peaked among low-income groups, potentially due to reduced screening access.[9]

FH is most commonly caused by pathogenic variants in the LDL receptor, Apolipoprotein *B*, or *PCSK9* genes, which impair LDL-C clearance via disruption of the LDL receptor pathway and lead to markedly elevated plasma LDL-C concentrations. Individuals with more severe mutations face a substantially elevated risk of premature cardiovascular mortality in the absence of treatment. Given that FH is frequently diagnosed during middle age,[8] initiating lipid-lowering therapy upon diagnosis represents a critical intervention to mitigate this additional risk and improve long-term prognosis.[1]

This study has several limitations. The analysis is restricted to 2009–2018, preventing assessment of post-COVID-19 trends. The use of a modified clinical criteria score without genetic confirmation may lead to misclassification and likely underestimates the true FH burden. While trends in statin use provide context, they do not fully capture changes in screening, diagnosis, or use of nonstatin therapies.

In conclusion, the fluctuating prevalence of clinically suspected FH from 2009 to 2018 highlights the dynamic interplay between improved case detection and evolving treatment strategies. The transient dip following the 2013 guidelines emphasizes how intensive treatment can temporarily influence cross-sectional prevalence estimates. The persistence of elevated prevalence, particularly among underserved groups, underscores ongoing challenges in equitable FH detection and management. Future efforts should focus on equitable screening, timely intervention, and sustained public health initiatives to reduce the burden of FH across all populations.

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Ethical statement

This study was conducted in accordance with the Declaration of Helsinki. The study protocol received approval from the National Center for Health Statistics Research Ethics Review Board, and all participants provided written informed consent. Since only de-identified data were used in this study, no additional ethics approval was required.

Conflicts of interest

The authors have no conflicts of interest to disclose.

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Data availability statement

The datasets generated during and/or analyzed during the current study are available in the National Health and Nutrition Examination Survey (NHANES) repository.

Author contributions

All the authors gave substantial contributions to the conception or design of the work, acquisition, analysis or interpretation of data, drafting the work or revising it critically for important intellectual content, and final approval of the version to be published.

AI statement

Generative AI tools, specifically ChatGPT, were used solely for language editing during the preparation of this manuscript.

References

[1] Sniderman AD, Tsimikas S, Fazio S. The severe hypercholesterolemia phenotype: clinical diagnosis, management, and emerging therapies. *J Am Coll Cardiol*. 2014;63:1935–47.

[2] de Ferranti SD, Rodday AM, Mendelson MM, Wong JB, Leslie LK, Sheldrick RC. Prevalence of familial hypercholesterolemia in the 1999 to 2012 United States National Health and Nutrition Examination Surveys (NHANES). *Circulation*. 2016;133:1067–72.

[3] Stone NJ, Robinson JG, Lichtenstein AH, et al.; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:S1–45.

[4] Li F, Xing X, Jin Q, et al. Sex differences orchestrated by androgens at single-cell resolution. *Nature*. 2024;629:193–200.

[5] Klevmoen M, Mulder JWCM, Roeters van Lennep JE, Holven KB. Sex differences in familial hypercholesterolemia. *Curr Atheroscler Rep*. 2023;25:861–8.

[6] Guan Y, Liu X, Yang Z, et al. PCSK9 promotes LDLR degradation by preventing SNX17-mediated LDLR recycling. *Circulation*. 2025;151:1512–26.

[7] EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC). Global perspective of familial hypercholesterolaemia: a cross-sectional study from the EAS familial hypercholesterolaemia studies collaboration (FHSC). *Lancet*. 2021;398:1713–25.

[8] Amrock SM, Duell PB, Knickelbine T, et al. Health disparities among adult patients with a phenotypic diagnosis of familial hypercholesterolemia in the CASCADE-FH™ patient registry. *Atherosclerosis*. 2017;267:19–26.

[9] Hagger MS, Hardcastle SJ, Hu M, et al. Health literacy in familial hypercholesterolemia: a cross-national study. *Eur J Prev Cardiol*. 2018;25:936–43.