Research Square

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Temporal Trends in Hyperlipidemia and Atrial Fibrillation–Related Mortality in the United States: A Population-Based Study Using CDC WONDER, 2001–2024

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Research Article

Keywords: Hyperlipidemia, atrial fibrillation, mortality, sex, race, disparities

Posted Date: April 30th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9204314/v1

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Additional Declarations: No competing interests reported.

Abstract

Background

Hyperlipidemia is a comorbid condition of atrial fibrillation (AF) and may enhance cardiovascular mortality. We quantified national mortality trends and inequities for AF and hyperlipidemia decedents in the United States.

Methods

We extracted CDC WONDER Multiple Cause of Death records 2001–2024) for adults aged ≥ 25 years with AF (ICD-10: I48) and hyperlipidemia (ICD-10: E78) as an underlying or contributing causes. We calculated age-adjusted mortality rates (AAMR; 2000 US standard; per 100,000) using Joinpoint regression to approximate annual percent change (APC) and average annual percent change (AAPC) and 95% CIs. Stratifications included sex, race/ethnicity, census region, state, prevalence of urban characteristics (rural compared with urban), and place of death.

Results

From 2001–2024, 214,585 deaths involved AF with hyperlipidemia. National AAMR rose from 0.6 to 8.9, with segment APCs: 2001–2010: 15.6%; 2010–2018: 7.8%; 2018–2021: 18.5%; 2021–2024: 5.1%. Men exceeded women (4.6 vs 2.9). By race/ethnicity, Whites had the highest mean AAMR (4.0), followed by Blacks (2.3), Other (2.0), and Hispanic (1.9). The West had the highest regional burden (4.0) and the Northeast the lowest (3.3). Rural areas exceeded urban (3.1 vs 2.6). States varied widely (Vermont 6.8 vs Georgia 1.1). Most deaths occurred at home (34.3%), then medical facilities (33.0%), nursing homes (23.1%), and hospice (4.6%).

Conclusion

Mortality linked to AF and hyperlipidemia increased substantially from 2001–2024, with a pronounced surge during 2018–2021 and persistent disparities across sex, race, region, and state. Strengthening lipid management, improving AF risk assessment, and ensuring equitable access to cardiovascular care may help curb this growing national burden.

INTRODUCTION

Hyperlipidemia is a well-established risk factor for atherosclerosis and coronary artery disease (CAD), which in turn are important contributors to the development of (AF) (1). AF is the most common symptomatic arrhythmia globally, and its burden is set to rise over twice within the next three decades (2).

It contributes importantly to morbidity and mortality by its connections with stroke, heart failure, and reduced quality of life (3).

Despite the strong links between hyperlipidemia and vascular disease, the direct relationship between lipid disorders and AF has proven paradoxical and ambiguous. While raised total cholesterol and low-density lipoprotein cholesterol (LDL-C) levels have the strongest relationship to vascular disease, several population-based studies have demonstrated that these lipid fractions do not have universal associations with AF prevalence and, in certain cohorts, have even reverse correlations (4). This type of deviation from anticipated pattern has come to be called part of a "lipid paradox," which defies the accepted wisdom of cardiovascular risk factors for AF (5). In contrast, other lipid dysfunctions have provided more consistent correlations with AF risk. Specifically, lower HDL-C levels and increased triglyceride-to-HDL ratios are reproducibly and strongly correlated with an increased incidence of AF (6). These findings suggest that several elements of the lipid profile exert distinct and possibly counterintuitive effects on atrial remodeling and arrhythmogenesis.

The complexity of these associations underscores the need for large-scale, population-based cohorts to define further the relationship between hyperlipidemia and AF. Employment of national databases such as the Centers for Disease Control and Prevention – Wide-ranging Online Data for Epidemiologic Research system (CDC WONDER) provides a significant avenue through which population trends, demographic disparities, and temporal patterns in co-occurrence of these conditions can be evaluated. Therefore, for this research, the CDC WONDER database will be employed to analyze these trends and generate evidence that can be utilized to advocate for improved AF risk stratification, prevention, and management among hyperlipidemic patients.

METHODOLOGY

Study Setting

CDC WONDER Multiple Cause of Death data set was used for death certificate data reporting Hyperlipidemia and AF as an underlying or contributing cause of death between 2001 and 2024 (7). The study used the International Classification of Diseases, Tenth Revision code E78 for Hyperlipidemia and I48 for AF to identify cases. Similar codes have been used for hyperlipidemia and AF in prior studies (8)(9). Notably, our study did not necessitate approval from an Institutional Review Board (IRB) as it relied on anonymized and publicly available data. Furthermore, the research strictly adhered to the STROBE guidelines (10).

Data Extraction

Data were stratified according to demographic variables like sex, race or ethnicity, and geographic variables like states, census region, and urbanization. Racial and ethnic populations were classified as Hispanic or Latino, non-Hispanic (NH) White, NH Black or African American and NH others. Trends in

mortality according to urbanization status were classified according to the National Center for Health Statistics' Urban-Rural Classification Scheme. Urban was characterized as big metro cities (populations > 1 million) and small and medium metro areas (50,000–999,999), and rural was characterized as locations with populations < 50,000 (11). Census regions were categorized according to the US Census Bureau as Northeast, Midwest, South, and West. Places of death (medical facility-inpatient, decedent's family; hospice facility; nursing home, and others) were also included in the analysis as a categorical variable.

Statistical Analysis

Age-standardized death rates (AAMR) for hyperlipidemia and AF were pulled from database, age-standardized to the 2000 US standard population. Trends in age-standardized mortality from 2001 through 2024 were examined by the Joinpoint Regression Program (12). The program utilizes serial permutation tests to examine repeated time trends and can identify up to one inflection point where the rate of change of mortality is statistically significantly different. The program then calculates the weighted average annual percent change (APC) for each time interval in the AAMR, as well as corresponding 95% confidence intervals (CIs). The APC estimate was calculated to define an increase or decrease if the slope of the trend was significantly different from zero; otherwise, the trend was characterized as stable. Pairwise comparison was made to determine whether the APC differences varied significantly between various subgroups (sex, race, census regions, state and urbanization. Statistical significance was set at $p < 0.05$.

RESULTS

Between 2001 and 2024, there was a total 214,585 deaths related to hyperlipidemia and AF-related mortality. **(Supplementary Table 1)**.

Annual trends

Throughout the study period from 2001 to 2024, AAMR increased from 0.6 (95% CI: 0.6 to 0.6) in 2001 to 8.9 (95% CI: 8.8 to 9.0) in 2024.

The AAMR demonstrated a consistent upward trend across all four segments, with varying rates of increase. From 2001 to 2010, there was a steep rise with an APC of 15.6 (95% CI: 14.0 to 18.2; $p < 0.001$). From 2010 to 2018, the upward trend persisted but at a slower pace APC of 7.8 (95% CI: 5.0 to 8.8; $p < 0.001$). The period from 2018 to 2021 experienced the most rapid increase, with an APC of 18.5 (95% CI: 14.5 to 20.7; $p < 0.001$). From 2021 to 2024, the upward trend continued but at a slower pace, with an APC of 5.1 (95% CI: 2.2 to 6.9; $p = 0.011$). **(**Fig. 1, **Supplementary Table 3, Supplementary Table 4)**

Sex

Throughout the study period from 2001 to 2024, the AAMR was consistently higher for men than for women. Specifically, the mean AAMRs were 4.6 (95% CI: 4.5 to 4.7) for men and 2.9 (95% CI: 2.8 to 3.0) for women. **(Supplementary Table 4)**

In men, the AAMR demonstrated a pattern with four distinct phases. From 2001 to 2009, there was a substantial increase with an APC of 17.0 (95% CI: 15.1 to 19.8; p < 0.001). The rate slowed from 2009 to 2018, showing an APC of 8.4 (95% CI: 7.0 to 9.3; p < 0.001). From 2018 to 2021, a sharp rise was seen with an APC of 18.8 (95% CI: 15.4 to 20.7; p < 0.001), followed by a decline from 2021 to 2024 with an APC of 4.4 (95% CI: 2.3 to 6.1; p = 0.004). Females displayed analogous trajectories, with increasing AAMR throughout the study period. **(**Fig. 1, **Supplementary Table 3)**

Race

NH White populations had the highest mean AAMR of 4.0 (95% CI: 3.9 to 4.1), followed by NH Black or African Americans with 2.3 (95% CI: 2.1 to 2.5), NH others with 2.0 (95% CI: 1.8 to 2.3), and Hispanic or Latino populations with the lowest AAMR at 1.9 (95% CI: 1.7 to 2.1). **(Supplementary Table 5)**

The trends for NH White demonstrated five segments with varying rates of increase. From 2001 to 2006, there was a steep increase with an APC of 19.5 (95% CI: 17.1 to 26.5; p < 0.001). From 2006 to 2012, the rate of increase slowed to an APC of 12.6 (95% CI: 10.4 to 14.2; p < 0.001). From 2012 to 2018 AAMR showed further slowing with an APC of 7.4 (95% CI: 5.3 to 8.2; p < 0.001). From 2018 to 2021, there was acceleration with an APC of 19.3 (95% CI: 17.4 to 21.0; p < 0.001). Finally, from 2021 to 2024, the rate slowed again with an APC of 5.0 (95% CI: 3.6 to 6.4; p < 0.001). Hispanic or Latino, NH Black or African American, and NH others all showed consistent single-segment upward trends throughout 2001–2024, with APCs of 11.9 (95% CI: 11.1 to 13.4; p < 0.001), 12.9 (95% CI: 12.3 to 14.1; p < 0.001), and 8.2 (95% CI: 7.5 to 9.7; p < 0.001) respectively. **(**Fig. 2, **Supplementary Table 3)**

Geographic regions

States exhibited significant differences in AAMR, with values ranging from 6.8 in Vermont to 1.1 in Georgia. States in the upper 90th percentile of AAMRs for hyperlipidemia and AF-related patients included Vermont (6.8), Minnesota (4.9), North Dakota (4.8), Oregon (4.8), and Nebraska (4.7). These states had AAMRs that were nearly six to seven times higher than those in the lower 10th percentile, which included Georgia (1.1), Alabama (1.5), Nevada (1.5), District of Columbia (1.6), and New Mexico (1.6). **(Supplementary Table 6).**

Throughout the period from 2001 to 2020, the mean AAMRs were 3.1 (95% CI: 2.9 to 3.3) for rural areas and 2.6 (95% CI: 2.6 to 2.7) for urban areas. The trend for rural areas displayed a three-segment pattern. From 2001 to 2007, there was an increase with an APC of 19.6 (95% CI: 15.4 to 27.8; p < 0.001). From 2007 to 2018, the rate slowed with an APC of 9.4 (95% CI: 6.4 to 10.4; p = 0.002). The final segment from 2018 to 2020 showed acceleration with an APC of 23.2 (95% CI: 15.0 to 27.9; p < 0.001). Urban areas showed a similar four-segment pattern with initial steep increases, followed by gradual slowing, and acceleration in the final 2018–2020 period **(Supplementary Fig. 1, Supplementary Table 3, Supplementary Table 8).**

During the period from 2001 to 2024, the West region had the highest mean AAMR at 4.0 (95% CI: 3.9 to 4.2), followed by the Midwest at 3.7 (95% CI: 3.6 to 3.8), the South at 3.4 (95% CI: 3.3 to 3.5), and the Northeast with the lowest AAMR at 3.3 (95% CI: 3.2 to 3.4) **(Supplementary Table 7).**

The West demonstrated four segments. From 2001 to 2010, there was a steep increase with an APC of 16.0 (95% CI: 13.6 to 19.7; $p < 0.001$). From 2010 to 2018, the rate slowed with an APC of 6.0 (95% CI: 1.0 to 7.4; $p = 0.025$). From 2018 to 2021, there was acceleration with an APC of 15.7 (95% CI: 11.1 to 18.7; $p < 0.001$). The final segment from 2021 to 2024 showed a continued increase with an APC of 4.4 (95% CI: -0.4 to 7.1; $p = 0.057$, **non-significant**). The Midwest region displayed two segments. From 2001 to 2007, there was an increase with an APC of 19.8 (95% CI: 14.6 to 37.4; $p < 0.001$), followed by a steady increase from 2007 to 2024 with an APC of 9.2 (95% CI: 8.5 to 9.8; $p < 0.001$). The Southern region showed four segments. From 2001 to 2010, there was an increase with an APC of 15.1 (95% CI: 13.8 to 17.2; $p < 0.001$). From 2010 to 2017, the rate slowed with an APC of 8.0 (95% CI: 5.6 to 9.1; $p < 0.001$). The segment from 2017 to 2021 showed acceleration with an APC of 20.3 (95% CI: 18.7 to 23.5; $p < 0.001$), followed by relatively slower incline from 2021 to 2024 with an APC of 5.8 (95% CI: 3.9 to 7.5; $p < 0.001$). The Northeastern region showed similar trends as Southern region with increasing AAMR throughout the study period with varying trajectories. **(Supplementary Fig. 2, Supplementary Table 3).**

Place of death

Most of these deaths (34.3) occurred in decedent's home, followed by deaths at the medical facilities (33.0%), nursing homes or long-term care facilities (23.1%), and hospice facilities (4.6%). A small number of cases (4.6%) had other places of death. **(Supplementary Table 2).**

DISCUSSION

This study provides a comprehensive analysis of mortality related to hyperlipidemia and AF among adults aged ≥ 25 years in the United States from 2001 to 2024, elucidating crucial temporal trends and demographic disparities. Our findings reveal a substantial and concerning escalation in the age-adjusted mortality rate (AAMR), which increased nearly fifteen-fold over the study period, with a particularly sharp acceleration observed between 2018 and 2021. The largest proportion of these deaths occurred in the decedent's home, followed closely by medical facilities. The analysis underscores persistent disparities: men consistently experienced higher mortality rates than women, and Non-Hispanic White individuals bore the highest mortality burden among all racial and ethnic groups. Geographically, the highest mortality rates were observed in the Western US and in rural areas, which exhibited a greater mortality burden than their urban counterparts.

The link between hyperlipidemia and fatal AF is a synergy of pathological processes. First, hyperlipidemia accelerates atherosclerosis, causing the structural remodeling and fibrosis in the atria that creates a vulnerable substrate for the arrhythmia (13)(14). Beyond large-vessel disease, dyslipidemia also inflicts direct molecular damage by unleashing systemic inflammation and oxidative stress, which injures atrial cells and compromises the heart's electrical stability (15). The ultimate lethal factor is thrombosis. AF

promotes blood stasis, while the underlying atherosclerotic disease fosters a hypercoagulable state. This dangerous combination of stagnant blood and pro-clotting factors dramatically elevates the risk of a catastrophic thromboembolic event, providing the mechanism for a terminal outcome (16).

The observed mortality trend reflects a multi-phase evolution of risk. The initial increase was likely driven by the surging prevalence of obesity and metabolic syndrome, which expanded the pool of at-risk individuals (17)(18). This was followed by a period of moderation, likely due to therapeutic advances like widespread statin use and the introduction of novel oral anticoagulants (NOACs) that improved stroke risk management (19). This trajectory was shattered by the 2018–2021 spike, which points to the COVID-19 pandemic; the SARS-CoV-2 virus, a potent trigger of thrombo-inflammation and cardiac injury, disproportionately harmed this already vulnerable population (20). The trend is thus best understood as a worsening baseline of chronic disease that was briefly tempered by better therapies, only to be catastrophically accelerated by the acute shock of the pandemic (21).

The persistently higher mortality rate in men reflects a fundamental disparity in baseline cardiovascular risk. Men tend to develop conditions like hypertension and coronary artery disease earlier in life, leading to a greater cumulative burden of cardiac damage that creates a substrate for lethal arrhythmias (22)(23). This vulnerability is compounded by the absence of estrogen's long-term cardioprotective effects, which benefit women (24). Since both sexes followed analogous mortality trajectories, the data suggest that the public health crises driving the overall increase, rising metabolic disease and the COVID-19 pandemic, did not create this sex gap. Instead, these factors disproportionately exacerbated mortality in a male population already predisposed to adverse cardiovascular outcomes (25). The racial disparities in mortality present a paradoxical dual narrative. Unusually for a cardiovascular condition, Non-Hispanic (NH) White populations had the highest overall death rate, a finding likely explained by the higher underlying prevalence of AF in this group (26). However, a more alarming trend is the steep and unrelenting rise in mortality among NH Black and Hispanic populations. This climb suggests a worsening burden of risk factors like hypertension and diabetes, which is compounded by systemic inequities in healthcare that limit access to effective treatments (27). While therapeutic advances appeared to temper the death rate for the NH White population in the 2010s, the unabated rise in minority communities signals a failure to achieve these gains equitably. This creates a dual challenge: a high-volume burden in the NH White population and an accelerating crisis of disparity affecting minority communities (28).

The geography of this mortality crisis is marked by two key features: a disproportionate burden on rural populations and a notable concentration of deaths in the West and Midwest. The elevated mortality in rural settings is a familiar story of healthcare disparity, likely reflecting scarcer access to specialized cardiovascular providers and longer delays in obtaining emergency care for acute events like stroke (29)(30). The clustering of risk in the West and Midwest, however, appears to be a demographic signature. It aligns with the finding that older, Non-Hispanic White individuals face the highest absolute risk, and these regions contain large populations with that specific demographic profile (31).

This regional picture, however, simplifies a more complex reality at the state level, revealing a patchwork of localized risk profiles. There is no single archetype for a high-burden state; instead, places like Vermont

and Minnesota, though geographically distant, both have populations with the demographic characteristics known to be associated with high AF prevalence (32). Perhaps more telling are the low-mortality outliers. The unexpectedly low rates in states like Georgia and Alabama, epicenters of other cardiovascular diseases, suggest that their younger, more diverse populations may be a protective factor, though variations in death certificate coding cannot be ruled out (33). Ultimately, these sharp state-level contrasts demonstrate that geography serves as a proxy for a deeply interwoven set of factors, including population structure, health system performance, and data reporting practices.

The place of death data reveals two distinct terminal scenarios. The high proportion of deaths occurring at home strongly suggests that sudden, catastrophic events like a major stroke or arrhythmia are a primary failure mode, highlighting a critical gap in outpatient risk stratification (34)(35). In contrast, the large number of deaths in medical and nursing facilities points to a different pathway: patients with a high comorbidity burden who suffer a fatal complication during hospitalization or as the culmination of a decline in long-term care (36). This pattern presents a dual challenge: preventing sudden death in the community while also improving the management of acute complications in institutionalized patients.

Collectively, these multifaceted disparities across demographics, geography, and clinical settings demand a transition from observation to action, compelling a new focus on targeted recommendations for clinicians, policymakers, and researchers. Given the high proportion of sudden deaths at home, clinicians must adopt more aggressive outpatient risk stratification, particularly for male patients, who face the highest mortality burden, and intensify efforts to ensure medication adherence (37). Policymakers must address the stark geographic and racial disparities through targeted investments to improve rural access to care and a firm commitment to health equity to reverse the crisis in minority communities (38). The research community should prioritize developing risk models that better integrate these demographic factors, while using implementation science to ensure effective interventions equitably reach all populations (39). The overarching goal is to integrate these clinical, policy, and research efforts into routine primary care to proactively manage this lethal comorbidity across all affected groups (40).

Limitations

These findings should be interpreted within the context of limitations inherent to the CDC WONDER database. Our analysis depends on the accuracy of death certificates, which are subject to misclassification and underreporting of comorbidities, potentially misestimating the true mortality burden. The observed increase may also be partly influenced by a surveillance artifact, as growing clinical awareness of both conditions could have led to more frequent documentation over time, a "coding drift" that inflates the trend. As an ecological study, our findings identify population-level associations, not individual causality. This is compounded by a lack of granular clinical data, such as medication adherence or disease severity, which precludes a more detailed, risk-adjusted analysis. Despite these constraints, the study’s strength remains its large, population-based design, which provides a robust view of broad epidemiological trends that warrant urgent attention.

CONCLUSION

In conclusion, this study documents a nearly fifteen-fold surge in mortality from the combined burden of hyperlipidemia and atrial fibrillation, signaling an escalating public health crisis over the past two decades. This trend appears to be the fatal result of a worsening baseline of national metabolic health that was catastrophically exploited by the COVID-19 pandemic. Our findings reveal that this crisis is profoundly inequitable, with deep and multifaceted disparities that expose systemic gaps in care. These results should serve as a mandate to stop treating these as separate risk factors and to implement a new, integrated standard of care that confronts the inequities driving this lethal epidemic.

Abbreviations

Atrial Fibrillation (AF)

Age-Adjusted Mortality Rates (AAMR)

Average Annual Percentage Changes (AAPC)

Annual Percent Change (APC)

Non-Hispanic (NH)

Centers for Disease Control and Prevention's Wide-ranging Online Data for Epidemiologic Research (CDC-WONDER)

Declarations

Conflicts of Interests: The authors declare no conflicts of interest.

Funding: The authors received no funds, grants, or financial support for this study.

Acknowledgments: Not applicable.

Ethics Approval: Not applicable.

Disclosures: All other authors have no conflicts of interest to declare.

Patient consent: Not required

Author Contribution

Ammad Uddin: conceptualized the study, supervised the project, and critically revised the manuscript.Muhammad Salik Uddin: contributed to study design, data acquisition, and drafting of the manuscript.Asim Sajjad: performed data analysis and interpretation using CDC WONDER and assisted in manuscript writing.Asma Naz: contributed to literature review, data interpretation, and manuscript drafting.Muhammad Tahir: assisted in statistical analysis and interpretation of results.Faisal Islam:

contributed to data collection, validation, and manuscript editing.Arsheen Khudadad: assisted in data extraction and preparation of tables and figures.Aroosa Zafar: contributed to methodology development and critical revision of the manuscript.Hudaifa Hassan Salad: contributed to literature review, manuscript editing, and final approval of the version of manuscriptMohid Zulfiqar: contributed to study design, supervised data analysis, finalized the manuscript

Data Availability

The data supporting the findings of this study were obtained from the CDC WONDER online database (Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research). The datasets used and analyzed during the current study are publicly available and can be accessed at CDC Wonder Website (https://wonder.cdc.gov/).

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Figures

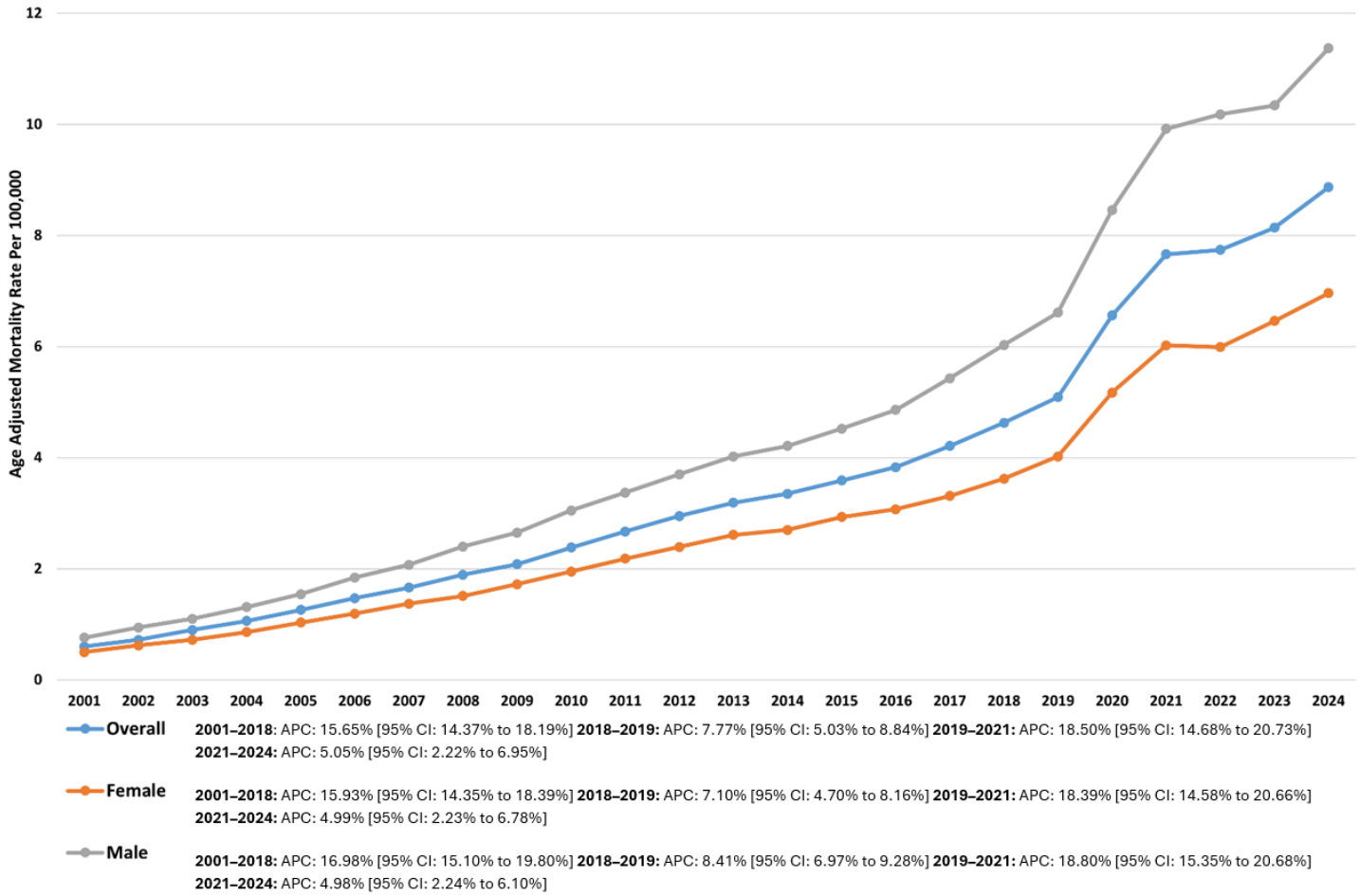


Figure 1

Trends in Hyperlipidemia and AF-related AAMR per 100,000, stratified by sex, in the United States from 2001-2024.

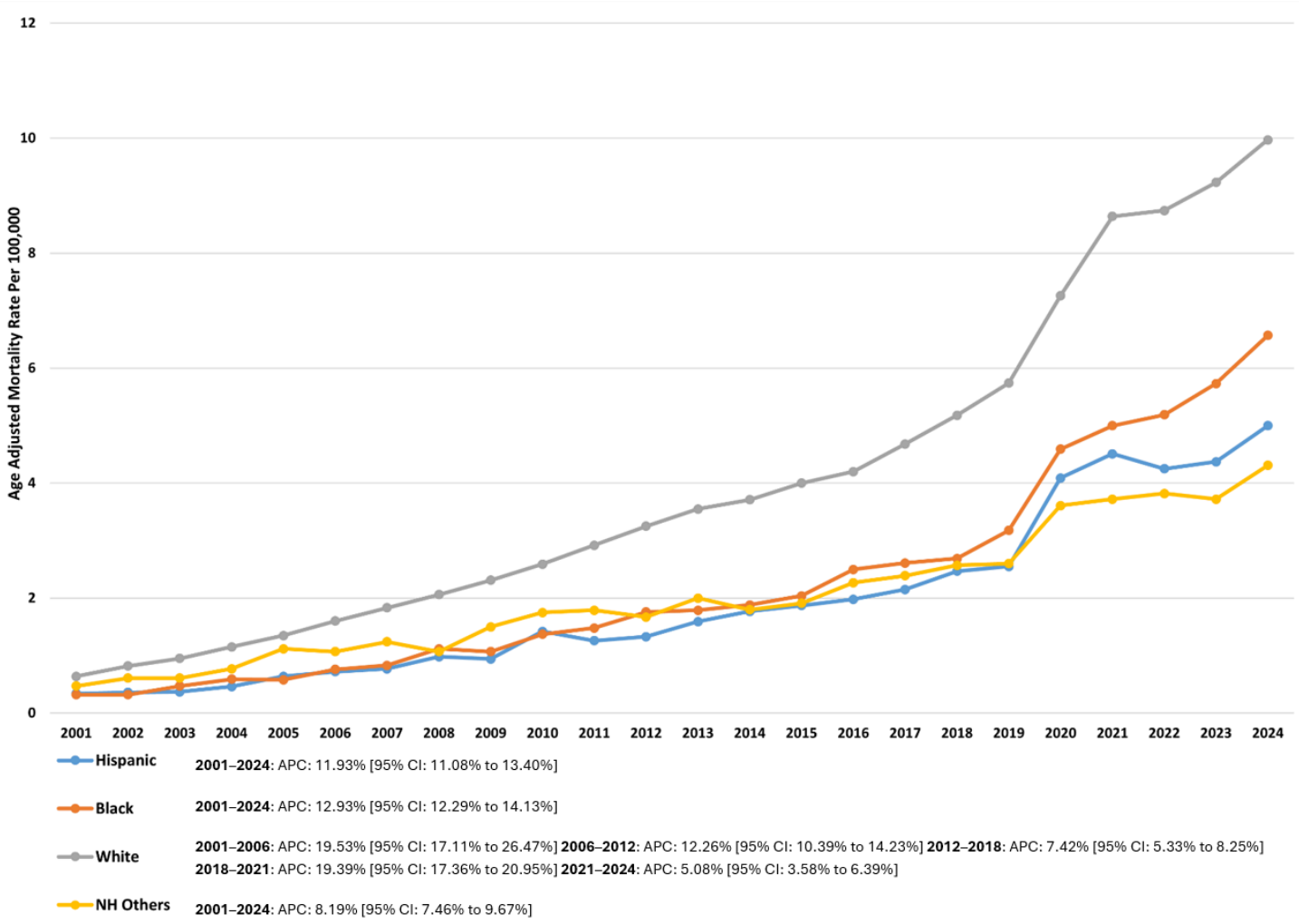


Figure 2

Trends in Hyperlipidemia and AF-related AAMR per 100,000, stratified by race, in the United States from 2001-2024.

Supplementary Files

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- supplementarytablesandfigures.docx
- SupplementaryFigure12.docx
- floatimage1.jpeg