

Mortality Trends Involving Hyperlipidemia and Hypertension in US Adults, 1999-2020: A CDC WONDER Multiple-Cause-of-Death Analysis

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Abstract

Background

Hypertension and hyperlipidemia are leading chronic conditions in the United States, collectively driving substantial cardiovascular mortality. Nearly 48% of U.S. adults have hypertension and tens of millions are affected by dyslipidemia, yet national mortality trends associated with their co-occurrence among older adults remain insufficiently characterized.

Objective

This study examined temporal trends and demographic disparities in mortality associated with hypertension and hyperlipidemia among U.S. adults aged 45 years and older from 1999 to 2020.

Methods

CDC WONDER multiple cause-of-death data were analyzed for adults aged 45 and older using ICD-10 codes I10–I15 and E78.0–E78.5. Age-adjusted mortality rates (AAMRs) per 100,000 were standardized to the 2000 U.S. population. Joinpoint regression was used to calculate APC and AAPC, stratified by sex, race/ethnicity, urbanization, census region, and state.

Results

Between 1999 and 2020, 822,127 deaths were recorded. The overall AAMR rose from 2.94 to 58.68 (AAPC: 12.45; 95% CI: 9.63–15.32; $p < 0.001$), with the sharpest rise from 1999 to 2001 (APC: 71.79) and a renewed surge from 2018 to 2020 (APC: 16.94). Men had higher AAMRs than women (36.25 vs. 24.94). while NH White individuals showed the steepest increase (AAPC: 11.93). Rural areas exceeded urban areas (33.54 vs. 29.35). Vermont recorded the highest state-level AAMR (62.34) and Nevada the lowest (14.61).

Conclusion

Mortality associated with hypertension and hyperlipidemia has risen markedly over two decades, with significant disparities across sex, race/ethnicity, geography, and urbanization. Targeted, equity-focused public health strategies are urgently needed to reduce preventable cardiovascular mortality in high-risk populations.

1. INTRODUCTION

Hyperlipidemia and hypertension are among the most prevalent chronic conditions worldwide and represent leading contributors to cardiovascular disease and mortality. The World Health Organization reports that approximately 1.28 billion adults between the ages of 30 and 79 live with hypertension [1], while roughly one-fourth of adults are affected by elevated cholesterol levels [2]. Together, these conditions account for a substantial share of the global cardiovascular disease burden. Evidence from global burden analyses demonstrates that elevated low-density lipoprotein (LDL) cholesterol remains a significant driver of cardiovascular mortality and has shown a notable rise in attributable disease burden over time [5]. The epidemiologic burden within the United States is comparably high. Recent estimates indicate that nearly 48% of U.S. adults have hypertension [3], and tens of millions are affected by dyslipidemia. Both conditions significantly contribute to ischemic heart disease, stroke, and related cardiovascular outcomes, particularly among middle-aged and older adults. Given their high prevalence and frequent co-occurrence, they represent critical public health priorities.

Hypertension and hyperlipidemia frequently coexist as components of the metabolic syndrome, sharing common underlying risk factors such as obesity and insulin resistance. Dyslipidemia characterized by elevated LDL cholesterol and triglycerides alongside reduced high-density lipoprotein (HDL) cholesterol promotes the formation of atherosclerotic plaques, while hypertension exerts mechanical stress on blood vessels and impairs endothelial function. This study does not seek to establish the biological basis for their co-occurrence; rather, their simultaneous presence reflects a clinically meaningful accumulation of risk factors commonly identified in population-based data, particularly among older adults. Through shared pathways including inflammation, endothelial dysfunction, and accelerated atherosclerosis, the concurrent presence of these risk factors is associated with a substantially elevated risk of cardiovascular disease [4].

The present study focuses on individuals aged 45 years and older, as the concurrent prevalence of hypertension and hyperlipidemia becomes increasingly frequent and clinically significant after midlife. The upper age threshold is consistent with prior mortality studies utilizing CDC WONDER, facilitating comparability across the literature. To characterize dyslipidemia, ICD-10 codes E78.0–E78.5 were applied to capture a broad spectrum of lipid disorders, in line with established epidemiologic approaches [6, 7].

The primary objective of this study is to describe temporal trends in U.S. death certificates documenting both hypertension and hyperlipidemia among adults aged 45 years and older, using the CDC WONDER database from 1999 to 2020. The analysis is descriptive in nature, as the database does not provide a denominator for these coexisting chronic conditions. Accordingly, this study does not aim to determine the prevalence, incidence, or causation of either condition; rather, it characterizes how mortality trends associated with these commonly co-occurring chronic diseases have evolved over time.

2. METHODOLOGY

2.1 Data Source:

This study utilized the U.S. Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) database [8]. The data are compiled from official death certificates of U.S. residents and curated by the National Center for Health Statistics (NCHS). Mortality data were extracted from the multiple cause-of-death coding fields, meaning that hypertension or hyperlipidemia could appear either as the underlying cause of death or as a contributing cause listed anywhere on the death certificate. This provided detailed demographic and epidemiologic information, including age-adjusted mortality rates (AAMRs), sex, race/ethnicity, geographic distribution, and cause-of-death codes.

2.2 Study Population and ICD-10 Code Definition

All adult decedents aged 45 years and older in the United States from January 1, 1999 to December 31, 2020 were identified from the multiple cause-of-death files. Causes of death were classified according to the International Classification of Diseases, 10th Revision (ICD-10) [9]. Deaths attributed to hypertension were identified using codes I10–I15, while hyperlipidemia was defined using codes E78.0, E78.1, E78.2, E78.3, E78.4, and E78.5, consistent with prior studies [10,11] (Table S1).

2.3 Data Extraction and Geographic Classification:

Mortality data were extracted from CDC WONDER using predefined demographic and geographic variables, including age, sex, race/ethnicity, place of residence, and place of death. Geographic analyses based on state, census region, and urban–rural classification was assigned according to the decedent's place of residence as recorded on the death certificate. Census regions were categorized into four groups as defined by the U.S. Census Bureau: Northeast, Midwest, South, and West [12]. Place-of-death analyses were conducted separately based on the reported location where death occurred, with categories including medical facility, decedent's home, hospice facility, nursing home or long-term care facility, and other locations.

2.4 Race/Ethnicity Stratification

The following race and ethnicity categories were applied: non-Hispanic (NH) White, NH Black or African American, NH American Indian or Alaska Native, NH Asian or Pacific Islander, and Hispanic or Latino. These classifications are widely used in epidemiologic studies utilizing CDC WONDER data [13]. Of note, CDC WONDER data reflect a transition from bridged-race categories (1999–2002) to single-race categories (2003 onward), following revisions to federal race classification standards [14]. Although CDC provides harmonized estimates to improve cross-year comparability, this transition may introduce minor temporal inconsistencies in race-stratified analyses and is acknowledged as a limitation.

2.5 Urban–Rural Classification:

Urban–rural status was determined using the NCHS 2013 Urban–Rural Classification Scheme for Counties [15], applied uniformly across all study years (1999–2020) to ensure consistency in geographic categorization. As this scheme reflects county urbanization status at a single point in time, some

counties may have undergone changes in population density or urban development during the study period, which may introduce minor temporal misclassification.

2.6 Statistical Analysis:

Crude and age-adjusted mortality rates per 100,000 population were calculated for hypertension- and hyperlipidemia-related deaths. Age-adjusted mortality rates were standardized to the 2000 U.S. standard population using the direct method to allow comparisons across demographic groups and time periods [16]. Finalized data were downloaded and imported into Microsoft Excel for organization and preliminary descriptive analysis.

Mortality trend analyses were conducted using the Joinpoint Regression Program (version 5.0.2; National Cancer Institute) [17]. Joinpoint regression identifies statistically significant changes in temporal trends by fitting segmented regression models to annual mortality rates. A maximum of one joinpoint per model was permitted, in accordance with the number of study years and standard modeling recommendations. The optimal number of joinpoints was determined using the Monte Carlo permutation test, and statistical significance was assessed using two-sided tests with a threshold of $p < 0.05$. Annual Percent Change (APC) and Average Annual Percent Change (AAPC) were calculated with corresponding 95% confidence intervals, and APC segments that did not reach statistical significance were reported accordingly.

CDC WONDER suppresses mortality counts fewer than 10 to protect confidentiality; suppressed or unreliable cells were excluded from trend analyses where necessary. Overall summary AAMRs were calculated as the arithmetic mean of annual age-adjusted mortality rates across the study period.

2.7 Ethical Approval:

This study used de-identified, publicly available data provided by the U.S. government and adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines [18]. Accordingly, institutional review board approval was not required.

3. RESULTS

Between 1999 and 2020, hypertension with hyperlipidemia accounted for a total of 822,127 deaths among adults aged 45 years and older in the United States (Supplemental Table). These deaths were distributed across various settings, with the majority occurring at the decedent's home (38.86%), followed by medical facilities (35.73%), nursing home or long-term care facilities (18.26%), other locations (4.38%), hospice facilities (2.59%), and unknown places of death (0.18%) (Supplemental Table).

3.1. Annual Trends in Hypertension with Hyperlipidemia-Related Age-Adjusted Mortality Rate (AAMR)

The overall AAMR for hypertension with hyperlipidemia-related deaths among adults increased from 2.94 in 1999 to 58.68 in 2020, with an AAPC of 12.45 (95% CI: 9.63 to 15.32; $p < 0.001$). The AAMR

demonstrated a significant rise between 1999 and 2001 (APC: 71.79; 95% CI: 29.59 to 127.74; $p = 0.001$), followed by a notable increase from 2001 to 2010 (APC: 10.63; 95% CI: 9.22 to 12.05; $p < 0.001$). A more modest rise was observed from 2010 to 2018 (APC: 2.007; 95% CI: 0.93 to 3.09; $p = 0.001$), after which the AAMR experienced a sharp increase from 2018 to 2020 (APC: 16.94; 95% CI: 9.43 to 24.95; $p = 0.002$) (Figure 1).

3.2. Hypertension with Hyperlipidaemia-Related AAMR Stratified by Sex

Throughout the study period, adult men exhibited considerably higher AAMRs compared to adult women (mean AAMR: men 36.25, 95% CI: 35.74 to 36.77; women 24.94, 95% CI: 24.57 to 25.30). The AAMR increased for both sexes from 1999 to 2020 (AAPC: men 13.24, 95% CI: 9.72 to 14.98, $p < 0.001$; women 12.32, 95% CI: 9.72 to 14.98, $p < 0.001$).

Among men, the AAMR rose sharply from 1999 to 2001 (APC: 83.01; 95% CI: 36.11 to 146.08; $p = 0.009$), followed by a steady increase from 2001 to 2010 (APC: 10.77; 95% CI: 9.29 to 12.26; $p < 0.001$). A more gradual rise was observed from 2010 to 2018 (APC: 2.12; 95% CI: 0.98 to 3.28; $p = 0.001$), with a subsequent sharp increase from 2018 to 2020 (APC: 17.03; 95% CI: 9.41 to 25.19; $p = 0.003$). Among women, the AAMR similarly increased from 1999 to 2001 (APC: 72.23; 95% CI: 33.10 to 122.88; $p = 0.007$), followed by a steady rise from 2001 to 2010 (APC: 10.53; 95% CI: 9.13 to 11.95; $p < 0.001$). A modest further increase occurred from 2010 to 2018 (APC: 1.81; 95% CI: 0.71 to 2.92; $p = 0.003$), with a pronounced rise from 2018 to 2020 (APC: 16.67; 95% CI: 9.18 to 24.66; $p = 0.003$) (Figure 1).

3.3 Hypertension with Hyperlipidaemia-Related AAMR Stratified by Race/Ethnicity

From 1999 to 2020, the AAMR increased across all racial and ethnic groups, rising from 3.37 (95% CI: 2.97 to 3.78) to 73.76 (95% CI: 72.31 to 75.21) among NH Black individuals; from 2.95 (95% CI: 2.83 to 3.07) to 57.84 (95% CI: 57.39 to 58.30) among NH White individuals; from 3.20 (95% CI: 2.50 to 4.00) to 45.60 (95% CI: 44.10 to 47.00) among NH Other individuals; and from 1.95 (95% CI: 1.55 to 2.41) to 55.76 (95% CI: 54.46 to 57.06) among Hispanic individuals. The highest mean AAMR was observed among NH Black individuals (34.28; 95% CI: 33.71 to 35.93), followed by NH White (30.41; 95% CI: 30.07 to 30.75), NH Other (24.93; 95% CI: 23.50 to 26.35), and Hispanic individuals (22.67; 95% CI: 21.66 to 23.69). (Figure 3).

The greatest AAPC was observed among NH White individuals, followed by Hispanics, NH Black, and NH Other groups (NH White: AAPC 11.93, 95% CI: 5.97 to 18.22, $p = 0.005$; Hispanic: AAPC 10.55, 95% CI: 8.11 to 13.03, $p < 0.001$; NH Black: AAPC 9.88, 95% CI: 7.27 to 12.56, $p < 0.001$; NH Other: AAPC 8.33, 95% CI: 6.09 to 10.62, $p < 0.001$).

Among NH Black individuals, the AAMR showed a modest increase from 1999 to 2007 (APC: 17.27; 95% CI: 11.72 to 23.09; $p = 0.006$), followed by a gradual rise from 2007 to 2018 (APC: 3.02; 95% CI: 1.17 to 4.91; $p = 0.003$), and a sharp increase from 2018 to 2020 (APC: 20.78; 95% CI: 1.84 to 43.24; $p = 0.032$). Among NH White individuals, the AAMR increased from 1999 to 2001 (APC: 67.37; 95% CI: -7.73 to

203.60; $p = 0.084$), followed by a rise from 2001 to 2007 (APC: 13.53; 95% CI: 6.56 to 20.95; $p = 0.007$), and a continued increase from 2007 to 2020 (APC: 4.53; 95% CI: 3.52 to 5.54; $p < 0.001$). Among NH Other individuals, a modest increase was observed from 1999 to 2007 (APC: 16.33; 95% CI: 11.34 to 21.56; $p = 0.003$), followed by a gradual rise from 2007 to 2018 (APC: 1.45; 95% CI: -0.02 to 2.94; $p = 0.053$), and a sharp increase from 2018 to 2020 (APC: 16.89; 95% CI: 1.34 to 34.82; $p = 0.034$). Among Hispanic individuals, the AAMR rose steadily from 1999 to 2009 (APC: 14.95; 95% CI: 10.91 to 19.13; $p = 0.001$), followed by a more gradual increase from 2009 to 2018 (APC: 1.78; 95% CI: -0.53 to 4.16; $p = 0.121$), and a pronounced rise from 2018 to 2020 (APC: 31.84; 95% CI: 13.46 to 53.20; $p = 0.001$) (Figure 2).

3.4. Hypertension with Hyperlipidemia-Related AAMR Stratified by Geographical Region

Stratified by State:

Notable variation in AAMRs was observed across states, ranging from a low of 14.61 (95% CI: 14.05 to 15.17) in Nevada to a high of 62.34 (95% CI: 60.30 to 64.38) in Vermont. States in the top 90th percentile – including Oregon, North Dakota, Minnesota, Nebraska, Ohio, West Virginia, Maryland, Vermont, Hawaii, and Rhode Island exhibited AAMRs approximately 50% higher than those in the lowest 10th percentile, which included Nevada, Utah, Arizona, Arkansas, Mississippi, Alabama, Georgia, New York, Connecticut, Massachusetts, and Illinois (Supplemental Table).

Stratified by Census Region:

From 1999 to 2020, the AAMR increased across all four census regions, rising from 4.01 (95% CI: 3.72 to 4.29) to 57.66 (95% CI: 56.84 to 58.49) in the West; from 3.36 (95% CI: 3.12 to 3.60) to 60.12 (95% CI: 59.25 to 60.98) in the Midwest; from 2.81 (95% CI: 2.58 to 3.04) to 56.08 (95% CI: 55.18 to 56.97) in the Northeast; and from 2.17 (95% CI: 2.01 to 2.33) to 59.72 (95% CI: 59.07 to 60.37) in the South. The highest mean AAMR was observed in the West (33.22; 95% CI: 32.52 to 33.91), followed by the Midwest (32.70; 95% CI: 32.04 to 33.37), the South (28.61; 95% CI: 28.13 to 29.10), and the Northeast (26.27; 95% CI: 25.64 to 26.91). The most pronounced AAPC was observed in the Northeast, followed by the West, South, and Midwest (Northeast: AAPC 13.23, 95% CI: 10.57 to 15.96, $p < 0.001$; West: AAPC 11.51, 95% CI: 8.47 to 14.64, $p < 0.001$; South: AAPC 10.26, 95% CI: 7.28 to 13.23, $p < 0.001$; Midwest: AAPC 9.09, 95% CI: 6.76 to 11.48, $p < 0.001$) (Supplemental Table) (Figure).

Stratified by Urbanization:

From 1999 to 2020, the AAMR increased in both urban and rural areas, rising from 3.02 (95% CI: 2.90 to 3.15) to 56.49 (95% CI: 56.07 to 56.92) in urban areas, and from 2.65 (95% CI: 2.42 to 2.89) to 69.96 (95% CI: 68.89 to 71.03) in rural areas. The mean AAMR was higher in rural areas (33.54; 95% CI: 32.78 to 34.29) compared to urban areas (29.35; 95% CI: 29.02 to 29.69). The overall increase in AAMR was more pronounced in rural areas than urban areas (Rural: AAPC 13.99, 95% CI: 11.37 to 16.66, $p < 0.001$; Urban: AAPC 12.58, 95% CI: 9.82 to 15.42, $p < 0.001$) (Supplemental Table) (Figure 4).

4. DISCUSSION

This nationwide analysis of CDC WONDER mortality data from 1999 to 2020 highlights several significant findings. Among adults aged 45 years and older in the United States, deaths associated with hypertension and comorbid hyperlipidemia totaled over 822,000, with age-adjusted mortality rates demonstrating a dramatic and sustained escalation over the study period. The most prominent finding was a significant rise in AAMR between 1999 and 2001, followed by a continued increase from 2001 to 2010, a more modest rise between 2010 and 2018, and a sharp escalation from 2018 to 2020. Overall, the trend reflected a consistent upward trajectory in AAMR across two decades. The majority of these deaths occurred at the decedent's home. Beyond annual trends, notable variation was observed across demographic and geographic parameters. Under sex-based stratification, adult men consistently exhibited higher AAMRs than adult women. Significant disparities were identified across racial and ethnic groups, with the highest AAMR recorded among non-Hispanic Black or African American individuals. At the state level, Vermont recorded the highest AAMR, while the highest mortality rates by census region were observed in the Midwest. Similarly, AAMRs were higher in non-metropolitan areas compared to metropolitan regions.

A defining feature of this study is the marked increase in mortality observed between 2018 and 2020. This sharp rise likely reflects the multifactorial impact of the COVID-19 pandemic on individuals with chronic hypertension and hyperlipidemia. Beyond its direct physiological burden, SARS-CoV-2 infection can exacerbate cardiometabolic instability through systemic inflammation and ACE-2 receptor signaling. Given the high expression of the ACE2 receptor in cardiac tissue and the vascular endothelium which serves as the primary viral entry point individuals with pre-existing hypertension are particularly vulnerable [19,20]. The renin-angiotensin system (RAS), which is frequently dysregulated in patients with chronic hypertension, undergoes functional downregulation of ACE2 upon viral binding, resulting in a hazardous accumulation of Angiotensin II [21]. This imbalance triggers a cascade of pro-inflammatory signaling, vasoconstriction, and oxidative stress that can seriously destabilize blood pressure control and precipitate cardiac injury [19,22]. In the context of hyperlipidemia, the resulting cytokine storm promotes endothelitis and destabilizes atherosclerotic plaques, heightening the risk of microvascular thrombosis and plaque rupture observed during the pandemic [20,23]. Compounding these biological mechanisms, disruption of routine clinical care led high-risk patients to forgo regular appointments, resulting in deteriorating lipid control and a considerable rise in out-of-hospital mortality [24]. Furthermore, over 97% of COVID-19-related death certificates in 2020 documented at least one co-occurring condition, suggesting that shifts in documentation practices also influenced these figures [25]. While a sensitivity analysis excluding 2020 reveals a steadily rising trend from 2014 onward, the steepness of the 2020 curve remains an exceptional anomaly driven by the convergence of acute viral stress and systemic changes in coding practices and care-seeking behavior [20,26].

Sex-based disparities in cardiovascular mortality were also prominent, with men exhibiting overall higher AAMRs while women demonstrated a steeper rate of increase over time. These findings likely reflect several contributing factors, including historical under-representation of women in cardiovascular

research, variations in statin prescribing patterns, and sex-specific differences in symptom recognition. Recent evidence indicates that cardiometabolic risk factors including diabetes, obesity, and metabolic syndrome are increasingly prevalent among women and substantially amplify the burden of cardiovascular disease [27]. Women are also more likely to present with atypical or underrecognized cardiovascular symptoms, which may delay timely diagnosis and treatment and contribute to worse outcomes. Moreover, despite well-established evidence of benefit, women are less likely to receive guideline-directed therapies such as statins and are often managed at lower treatment intensities [28]. These management gaps are further compounded by lower risk recognition and delays in preventive care, which have been associated with rising hospitalization and mortality rates among younger women. The longstanding under-representation of women in cardiovascular clinical trials has additionally limited the development of sex-specific data and may perpetuate persistent inequalities in treatment and outcomes [29]. Collectively, these factors may help explain the more pronounced rise in female mortality and underscore the urgent need for more equitable and targeted cardiovascular prevention strategies.

Significant racial and ethnic disparities were observed in cardiovascular mortality, with the highest overall burden recorded among non-Hispanic Black and African American individuals. This disparity likely reflects the compounding effect of multiple systemic inequities rather than any single factor. Black adults face a disproportionately elevated cardiovascular risk, characterized by higher prevalence, earlier onset, and poorer blood pressure control [30]. These trends are closely associated with inequities in healthcare access and quality, including lower rates of preventive care, delayed diagnosis, and reduced utilization of guideline-directed therapies [31]. Chronic psychosocial stress including the physiological consequences of structural racism alongside socioeconomic factors such as income inequality, residential segregation, and limited access to health-promoting environments, further compounds cardiovascular risk [32]. Prior research has also demonstrated lower rates of screening and disease control, along with higher prevalences of hypertension and hyperlipidemia, among Black and Hispanic populations [33]. Taken together, these factors likely contribute substantially to the observed mortality burden and emphasize the necessity of structural, equity-focused public health interventions.

Adults in rural areas of the United States are experiencing a growing burden of cardiovascular disease mortality relative to their urban counterparts. In 2021, high-poverty rural counties in the South exhibited the largest rural-urban disparity, with approximately 191 cardiovascular deaths per 100,000 middle-aged adults [34]. Contributing factors include limited access to primary care and specialty services, which leads to delays in the diagnosis and management of chronic conditions, as well as reduced pharmacy availability and transportation barriers that impair adherence to essential medications. Higher prevalence of uncontrolled hypertension, hyperlipidemia, obesity, and diabetes further accelerates disease progression in these communities [35]. When compounded by socioeconomic pressures and low health literacy, these structural disadvantages significantly constrain opportunities for preventive care and worsen outcomes. Urban cardiovascular mortality declined between 2010 and 2022, whereas rural rates continued to rise particularly among younger individuals widening the mortality gap [36]. The West recorded the highest absolute age-adjusted mortality, likely reflecting the challenges posed by sparse populations and limited healthcare access, while the South demonstrated the fastest rate of

mortality increase, attributable to concentrated socioeconomic disadvantage, poor baseline cardiovascular health, and weaker healthcare infrastructure [34,35]. It is also worth noting that geographic analyses in this study relied on the 2013 NCHS urban-rural classification scheme, which may introduce county-level misclassification over time. Collectively, these findings underscore that structural, socioeconomic, and healthcare access inequities remain the principal drivers of elevated cardiovascular mortality in rural communities.

IMPLICATIONS:

The sustained rise in mortality associated with hypertension and hyperlipidemia underscores the urgent need for more aggressive and targeted cardiovascular risk factor management strategies at both the population and clinical levels. The disparities observed at the sex level suggest that existing prevention and treatment strategies may be insufficient to address the unique risk profiles and clinical presentations seen in women, highlighting the necessity for sex-specific guidelines and greater investment in women-focused cardiovascular research. The significant role of structural inequities in shaping health outcomes is further reflected in the divergent temporal trends observed across racial and ethnic groups [37]. Expanding access to preventive care, fostering culturally competent healthcare delivery, and implementing policies aimed at reducing socioeconomic disparities are essential steps toward narrowing these gaps.

The widening rural-urban mortality divide points to entrenched systemic barriers in healthcare accessibility, including shortages of healthcare providers, underdeveloped infrastructure, and limited availability of tertiary care services in rural communities [38]. Strengthening healthcare delivery systems in underserved regions should therefore be regarded as a pressing public health priority. Finally, the surge in mortality observed during the COVID-19 pandemic underscores the heightened vulnerability of patients with underlying cardiometabolic conditions to external health system disruptions and emphasizes the critical importance of maintaining continuity of care during public health crises.

LIMITATIONS:

Several limitations of this study warrant acknowledgment. First, death certificates obtained from CDC WONDER are subject to reporting bias, as the accuracy of cause-of-death attribution depends on the certifying physician. Conditions such as hypertension and hyperlipidemia are known to be underreported or inconsistently documented on death certificates. Second, the use of multiple cause-of-death data limits this analysis to a descriptive characterization of disease associations rather than the establishment of direct causal relationships [39]. While this approach captures the broader burden of these conditions, it does not confirm that hypertension or hyperlipidemia directly caused the reported comorbidities.

Third, the increasing frequency of ICD coding over time may partly reflect evolving documentation and recording practices rather than a true escalation in disease burden [40]. Additionally, AAMRs are calculated using the general population as the denominator and may therefore not accurately reflect the

true mortality risk among individuals specifically diagnosed with both hypertension and hyperlipidemia. Consequently, these estimates describe population-level mortality burden rather than disease-specific risk. Furthermore, CDC WONDER suppresses mortality counts below 10 to protect confidentiality, which may introduce bias in stratified analyses and underrepresent lower-density population groups [41]. This study also lacks individual-level clinical data including treatment adherence, lipid levels during therapy, and blood pressure control which limits the ability to adjust for confounding factors and fully explain the observed trends. Finally, evolving death certification practices and the impact of the COVID-19 pandemic may have introduced temporal inconsistencies across the study period [42][43].

FUTURE DIRECTIONS:

Future research should prioritize the use of clinical datasets that more precisely capture cause-of-death relationships and their associated factors, including hypertension, hyperlipidemia, and cardiac comorbidities. Linking electronic health record (EHR) data with national death indices would yield more granular and clinically meaningful insights. Additionally, studies examining post-pandemic mortality trajectories beyond 2020 are needed to determine whether the observed surge represents a transient disruption or a sustained shift in cardiometabolic risk. Targeted investigations addressing sex- and race-based differences in disease trajectories, treatment accessibility, and post-treatment prognosis would further refine our understanding of these disparities. Incorporating social determinants of health including income, educational attainment, and environmental exposures into geospatial analyses would strengthen the interpretation of geographic and regional disparities. Finally, evaluating the impact of public health interventions and policy changes directed at improving cardiovascular risk factor control, particularly in vulnerable and underserved populations, represents an important area for future inquiry.

CONCLUSION

In conclusion, this analysis documents a persistent and concerning rise in mortality associated with hypertension and hyperlipidemia among adults in the United States from 1999 to 2020. Despite advances in cardiovascular prevention and treatment, the overall burden continued to increase throughout the study period, revealing significant gaps in risk factor control and long-term disease management. The variation in mortality trends across sex, race/ethnicity, state, and urban-rural status reflects an unequal distribution of burden and points to underlying structural, socioeconomic, and healthcare access inequities. The sharp rise in mortality observed in 2020 further highlights the vulnerability of patients with cardiometabolic conditions to external disruptions of the health system, as exemplified by the COVID-19 pandemic.

Our findings affirm that hypertension and hyperlipidemia remain critical and interrelated drivers of cardiovascular mortality at the population level. Addressing this growing burden demands comprehensive strategies aimed at improving early detection, mitigating long-term risk factors, and ensuring equitable access to preventive and therapeutic care particularly among high-risk and underserved populations. Ultimately, reversing current trends will require coordinated efforts across

public health systems and clinical care settings to bridge existing gaps and meaningfully reduce disparities in cardiovascular outcomes.

Declarations

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Competing Interests:

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval and consent to participate:

Ethics approval is deemed unnecessary according to national regulations as our study did not involve any human/ animal test subject (<http://nbcPakistan.org.pk/nbc-r.html>). The need for consent to participate is deemed unnecessary according to national regulations as our study did not involve any human/ animal test subject (<http://nbcPakistan.org.pk/nbc-r.html>). We ensured adherence to the ethical principles outlined in the Declaration of Helsinki. This has been clearly stated under the Declarations section in the manuscript.

Availability of data and materials:

Data is provided within the manuscript or supplementary information files. Any extra data required will be provided on further request to the author.

Author's Contributions:

Conception & Design: SMA

Data Extraction: SMA

Analysis: SMA

Main Manuscript Writing: UA, HYI, MM, RM, SA, BM, NAY, MW, JHJA, AZ

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