Global, Regional and National Burden of Elevated Low-Density Lipoprotein Cholesterol, 1990–2023: Findings from the Global Burden of Disease Study 2023

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Key points (97/75-100 words)

Question:

What is the global disease burden attributable to low-density lipoprotein cholesterol (LDL-c)?

Findings:

From 1990 to 2023, the number of adults aged 25 plus with LDL-c ≥1.4 mmol/L increased from 21 million to 147 million. In 2023, high LDL-c caused 3.6 million deaths and 90.7 million DALYs, accounting for 6.0% of global deaths and 3.3% of all DALYs. LDL-c-related all-age mortality and DALY rates remained stable, while age-standardized death and DALY rates declined by 45.5% and 39.5%, respectively.

Meaning:

The persistent burden of high LDL-c highlights the need for stronger prevention, diagnosis, treatment, and control strategies.

Abstract (3/350 words)

Importance:

Elevated low-density lipoprotein cholesterol (LDL-c) is a key modifiable risk factor for cardiovascular disease (CVD), the leading cause of premature death worldwide. Quantifying its burden is critical for informing health policies.

Objective:

To estimate the global burden attributable to elevated LDL-c (relative to the theoretical minimum risk exposure level of 0.9-1.4 mmol/L).

Design, setting, and participants:

As part of the Global Burden of Disease study 2023, a comparative risk assessment of health loss related to elevated LDL-c was conducted. Mean LDL-c levels were estimated based on 806 population-based studies across 161 countries. Relative risks of CVD outcomes were derived from a meta-analysis of 52 randomized controlled trials. LDL-c population attributable fractions (PAFs) of deaths and disability-adjusted life years (DALYs) were estimated by age, sex, and year from 1990 to 2023 for adults aged ≥25 in 204 countries and territories.

Exposures:

Population-level exposure to LDL-c.

Main outcomes and measures:

PAFs, LDL-c-attributable deaths, and DALYs from ischemic heart disease and ischemic stroke, with corresponding rates and 95% uncertainty intervals (UI) for the years 1990–2023 in all countries.

Results:

From 1990 to 2023, the number of adults with LDL-c ≥1.4 mmol/L increased from 21 million (95% UI: 18–25) to 147 million (95% UI: 130–165). In 2023, LDL-c accounted for 3.6 (95% UI: 2.2–5.4) million deaths and 90.7 (95% UI: 58.9–123.3) million DALYs—6.0% of global deaths and 3.3% of DALYs. Global all-age rates per 100,000 remained stable at 49 (95% UI: 28.9–71.3) in 1990 and at 45 (95% UI: 27.6–66.5) in 2023 for deaths and 1,226.8 95% UI: 688–1,629) and 1,177 (95% UI: 688–1,629) for DALYs. Age-standardized rates declined from 90 (95% UI: 55–123) to 57 (95% UI: 34–79) deaths per 100,000 and from 1,657 (95% UI: 981–2,251) to

1,610 (95% UI: 650–1,532) DALYs per 100,000. In 2023, age-standardized LDL-c-attributable DALYs were highest in Eastern Europe, Central Asia, and North Africa and the Middle East, and lowest in high-income Asia Pacific and Andean Latin America.

Conclusions and relevance:
Between 1990 and 2023, the population with elevated LDL-c increased substantially, along with the associated burden. This burden was partly driven by population growth and aging and has shifted from high- to middle-income countries. Measurement limitations and surveillance gaps should be considered when interpreting trends. Scalable, population-level strategies are essential to reduce the LDL-c burden.

Introduction (140/150-250 words)

Elevated low-density lipoprotein cholesterol (LDL-c) is a well-established, modifiable risk factor for atherosclerotic cardiovascular disease (CVD), primarily ischemic heart disease (IHD) and ischemic stroke.[1,2] These conditions are the leading causes of premature mortality worldwide,[3–6] accounting for 22% of global deaths and 10% of disability-adjusted life years (DALYs) in 2023.[7–9]

LDL-c is key in CVD risk prediction models and a primary therapeutic target in prevention and treatment guidelines.[10–16] It is also a global indicator for tracking non-communicable disease (NCD) trends.[17]

This study assesses LDL-c–attributable mortality and DALYs over time and geography, supporting global CVD monitoring and prevention efforts. This analysis supersedes previous GBD results[18] by incorporating new exposure data, revised outcome definitions, updated relative risks (RR), and improved counterfactual distributions.[19] This manuscript was produced as part of the GBD Collaborator Network and adheres to the GBD Protocol.

Methods (531/150-250 words)

As part of GBD 2023[20] comparative risk assessment, we quantified the relationship between LDL-c levels and IHD and ischemic stroke, as well as the total burden attributable to high LDL-c (relative to the theoretical minimum risk exposure level (TMREL) of 0.9-1.4 mmol/L), among adults 25 years and older, across 204 countries and territories by age and sex, from 1990 to 2023. LDL-c was selected over other lipid biomarkers to align with clinical guidelines, reflect causal evidence, maximize data availability, and avoid double counting. A summary of the methods specific to LDL-c burden estimation is provided below, with full details provided in the appendix and prior publications.[21]

Estimating LDL-c distributions

LDL-c population levels (in mmol/L) were derived from 705 population-based studies, covering 4.7 billion individuals from 1962 to 2023. All data sources are available at the Global Health Data Exchange (GHDx) repository.[22]

We included studies reporting LDL-c, HDL-c, total cholesterol (TC), and/or triglycerides (TG). When direct LDL-c measurements were unavailable, we imputed them using the Friedewald equation[23] or regression models (Appendix Section 5.1.1).

Mean LDL-c values were estimated using spatiotemporal Gaussian process regression (ST-GPR)[24] incorporating covariates to inform data-sparse locations (Appendix Section 6.1.1). LDL-c standard deviation was modeled using a log-linear regression (Appendix Section 6.1.2). Global sex-specific distributions were derived from a weighted ensemble of 12 parametric families based on fit to person-level data (Appendix Section 6.1.3). We also estimated the number of individuals with high LDL-c.

Relative Risks for Outcomes Related to LDL-c

We conducted a systematic review and meta-analysis of 36 randomized controlled trials (RCTs),[25] following PRISMA guidelines,[26] to estimate RR for IHD and ischemic stroke using the Burden of Proof (BoP) framework[27,25,28] (Appendix Section 6.2).

Only IHD and ischemic stroke were included as outcomes, based on evidence that LDL-c–related burden is primarily driven by atherosclerotic mechanisms. Non-ischemic strokes were excluded due to distinct pathophysiology.[29]

Theoretical Minimum Risk Exposure Level (TMREL)

The TMREL was defined as the LDL-c concentration associated with the lowest combined risk of IHD and ischemic stroke. Based on the lowest LDL-c levels observed in the RCTs from the meta-analysis, the TMREL was set as a uniform distribution from 0.9 to 1.4 mmol/L (Appendix Section 6.3).

Attributable Burden

We estimated disease-specific population attributable fractions (PAFs) and the burden attributable to high LDL-c in terms of deaths and DALYs by age, sex, location, and year, using standard equations for continuous risk factors (Appendix Section 6.4.1). Additionally, PAFs and DALYs were calculated for each 1 mmol/L increment of LDL-c using Geoffrey Rose's[30] method (Appendix Section 6.4.2). LDL-c–attributable burden was calculated by applying PAFs to corresponding outcome-specific deaths and DALYs (Appendix Section 6.4.3).

Uncertainty Intervals

Uncertainty was quantified using a Monte Carlo simulation with 250 draws. 95% uncertainty intervals (UI) were defined by the 2.5th and 97.5th percentiles of the posterior distribution.

Socio-demographic Index Analysis

Given known variation in disease burden by development level, we used the Socio-demographic Index (SDI)—a composite of income, education and fertility[31]—to compare the burden across locations.

GBD Research and Reporting Practices

GBD 2023 complies with GATHER guidelines[32] (appendix table S1). Analyses were performed using R (version 4.4.2) and Python (version 3.10.4). All statistical code and data are publicly available.

Results (words 1,161/1000-1250 words)

Trends in LDL-c Levels and Prevalence

Between 1990 and 2023, the number of adults aged 25 years or older with LDL-c levels ≥1.4 mmol/L increased from 21 (95% UI: 18–25) million to 147 (95% UI: 130–165) million (Supplementary Appendix Figure S9). The population with LDL-c ≥3.0 mmol/L grew from 85 (95% UI: 75–95) million to 280 (95% UI: 250–310) million (Supplementary Appendix Figure S10).). In 2023, 3.6% of men and 2.4% of women had LDL-c levels at or below 1.4 mmol/L, while 39.4% of men and 44.7% of women exceeded 3.0 mmol/L (Supplementary Appendix Figure S11).

Globally, mean LDL-c levels increased from 1.4±0.4 mmol/L in 1990 to 1.7±0.4 mmol/L in 2023. Throughout the study period, LDL-c levels were highest in Central and Eastern Europe and Central Asia, followed by Southeast Asia, East Asia and Oceania, Latin America, North Africa and the Middle East, and South Asia. Sub-Saharan Africa consistently had by far the lowest LDL-c levels (Supplementary Appendix Figure S12).

While global LDL-c trends were relatively stable, regional patterns diverged. The sharpest increases occurred in Southeast Asia, East Asia and Oceania (annual change: 1.5%; absolute change: 21.7%), while high-income countries like Norway and Austria experienced declines of up to 10.0% in mean LDL-c levels. Low-SDI countries, with lower baseline levels, including Cameroon, Bangladesh and Tanzania, showed upward trends (Appendix Figure S12).

Attributable Burden of Disease Due to High LDL-c

Since 1990, the estimated number of deaths and DALYs attributable to high LDL-c increased by ~40%, reaching 3.6 (95% UI: 2.6–6.2) million deaths and 90.7 (95% UI: 61.3–122) million DALYs in 2023 (Table 1). In 2023, high LDL-c ranked as the 7th and 8th contributor of all-cause deaths and DALYs and was the 3rd and 2nd largest contributor to CVD deaths and DALYs, respectively. It accounted for 6.1% (95% UI: 3.7%–8.9%) of all-cause deaths, 8.1% (95% UI: 5.0%–11.9%) of NCDs deaths and 18.9% (95% UI: 12.4%–27.6%) of CVD deaths. High LDL-c contributed to nearly one-third of IHD deaths (2.7 million [95% UI: 1.8–3.8]) and approximately one-fifth of ischemic stroke deaths (0.87 million [95% UI: 0.29–1.5]). It accounted for 3.3% (95% UI: 2.1%–4.5%) of all-cause DALYs, 5.0% (95% UI: 3.2%–6.9%) of NCD DALYs, and 20.8% (95% UI: 13.6%–29.0%) of CVD DALYs.

In 2023, 27.3% of LDL-c-attributable DALYs occurred in individuals with LDL-c levels between 1.4 and 3.0 mmol/L. The remaining LDL-c attributable DALYs occurred in individuals with LDL-c 3.0 mmol/L or higher (Figure 1). IHD accounted for 72% of total LDL-c related DALYs globally and consistently exceeded ischemic stroke across regions, sexes, and locations (Appendix Figure S13).

Over the study period, global all-age rates for deaths and DALYs attributable to high LDL- decreased by ~8%, reaching 45.0 (UI 95%: 27.6–66.5) deaths and 1,124.9 (95% UI: 731.2–1,529) DALYs per 100,000 in 2023, respectively. However, age-standardized CVD global deaths and DALY rates due to high LDL-c declined by 45.6% and 39.5%, respectively, with an annual decrease of 0.45%. Specifically, age-standardized global CVD death rates due to high LDL-c decreased from 74.3 (95% UI: 42.7–109.0) in 1990 to 40.5 (95% UI: 24.9–59.9) deaths per 100,000 in 2023. Age-standardized CVD DALY rates declined from 1,656.7 (95% UI: 1,018.0–2,368) in 1990 to 1,002.6 (95% UI: 653.6–1,363.9) DALYs per 100,000 in 2023.

Age and Sex Differences

From 1990 to 2023, age-specific DALY rates for CVD due to high LDL-c declined across all ages and both sexes. In 2023, rates were higher in males under 75 and higher in females at older ages (Appendix Figure S14). In 2023, the number of DALYs due to elevated LDL-c was higher in men than women (55.0 million (95% UI: 37.3–75.3) vs. 35.7 million (95% UI: 22.4–51.8)). Age-standardized DALY rates declined annually by 0.92% (95% UI: 0.80%–1.03%) in men and

1.37% (95% UI: 1.26%–1.50%) in women. DALYs rates increased steadily with age (Appendix figure S14).

Regional and Country-Level LDL-c Attributable Burden

In 2023, age-standardized DALYs rates varied substantially from 2,252.6 (95% UI 1507.4–3,038.2) per 100,000 in Eastern Europe to 322.0 (95% UI 208.7–446.6) per 100,000 in high-income Asia Pacific. Age-standardized DALYs rates were higher in Eastern Europe, Oceania, Central Asia and North Africa and the middle East with more than 1,500 DALYs per 100,000 and lower in Hi-income Asia Pacific, Australasia and Western Europe with less than 500 DALYs per 100,000. The variation of LDL-c age-standardized DALYs rates was greater across countries, ranging from 4,333.8 (95% UI: 2,758.1–6,174.8) DALYs per 100,000 in Nauru to 265.3 (95% UI: 153.2–379.2) in the Republic of Korea. (Figure 2A).

From 1990 to 2023, high-income countries experienced pronounced declines in age-standardized DALY rates attributable to high LDL-c, with an average reduction of 64% reduction over the 30-year period. Australasia (-76%), Western Europe (70%) and Central Europe (61%), Southern (58.9%) and Tropical (58.1%) Latin America and high-income Asia Pacific (57.8%) and high-income North America (56.3%), all more than halved their rates, representing the larger reductions observed. In contrast, while Sub-Saharan Africa had some one of the lowest age-standardized DALY rates in 2023, trends varied markedly across subregions: Eastern Sub-Saharan Africa increased by 23%, Western Sub-Saharan Africa by 7.2% and Central Sub-Saharan by 6.2%, while Southern Sub-Saharan Africa achieve a 17.7% reduction (Figure 2B).

Global DALYs peaked around LDL-c levels between 3.0 and 4.0 mmol/L, with a sharp decline beyond 5.5 mmol/L (Figure 4). However, 20% of DALYs occurred at LDL-c levels below 3.0 mmol/L. Regions contributing most substantially to the global burden included South Asia, East Asia, and high-income regions, as reflected by the wider area under the curve in those strata. Of the total burden attributable to high LDL-c, 34% of DALYs occurred in India and China.

The lower panel presents the population distribution of LDL-c by region, illustrating substantial variation in exposure levels across regions. For example, while South Asia and sub-Saharan Africa had lower mean LDL-c levels, regions such as Central and Eastern Europe showed higher average values and wider distributions. This juxtaposition underscores the differences in both exposure and attributable burden by region.

Socio-demographic Index Analysis

The burden of CVD attributable to high LDL-c varied by SDI level (Figure 4). Age-standardized DALY rates attributable to high LDL-c increased from low to middle SDI levels and then declined steadily at higher SDI values, forming an inverted U-shaped pattern. Countries with intermediate development experienced the highest LDL-c-related burden compared to those at either end of the development spectrum. Sub-Saharan African countries had lower attributable DALY rates and clustered toward the lower SDI end, while countries in Central and Eastern Europe, as well as parts of the Middle East and South Asia, show higher burden despite heterogeneous SDI levels.

In high-SDI countries, the all-age DALY rate per 100,000 declined from 1,879 (95% UI: 1,182–2,635) in 1990 to 1,392 (95% UI 911–1,925) in 2023. The age-standardized DALY rate showed a more pronounced reduction, declining by 55% from 1,840 (95% UI: 1,182–2,635) to 827.3 (95% UI: 556–1,228) per 100,000 over the same period. In contrast, low-SDI countries experienced increases in both all-age and age-standardized DALY rates. The all-age rate increased from 33.5 (95% UI 12.3–74.8) to 38.9 (95% UI 15.2–82.7) per 100,000 in 2023 while the age-standardized DALY rate increased from 1,001 (95% UI 573–1,550) to 1,107 (95% UI 718–1,592) per 100,000.

Discussion (words 1,069/1000)

Our findings reveal a persistent and uneven disease burden attributable to elevated LDL-c. Despite progress in the development and delivery of effective lipid-lowering therapies, the number of individuals at risk of adverse cardiovascular outcomes due to elevated LDL-c has increased substantially since 1990, with a corresponding increase in the number of associated deaths and DALYs. In 2023, high LDL-c was responsible for 6.0% of global deaths and 3.3% of all DALYs, including 11.7% of deaths and 5.0% of DALYs from NCD-related deaths and nearly one-fifth of CVD deaths (18.9%) and DALYs (20.8%).

Diverging trends between the absolute burden and all-age and age-standardized rates, as well as across regions and SDI levels, reflect the influence of aging and population growth and underscore the need for age- and context-specific interventions to address the rising LDL-c-attributable burden. As the world population continues to age, an increasing burden of LDL-c is

expected due to age-associated metabolic changes and cumulative risk exposure over time, especially in the absence of improvements in diagnosis, access to care, and treatment.

While age-standardized CVD DALY rates due to high LDL-c declined in many high-SDI countries—particularly in Western Europe and North America—gains were uneven. Rates increased in South Asia, while most other regions have seen stagnation. Between 1990 and 2023, 107 countries experienced declines in LDL-c–related CVD burden, with the greatest reductions observed in Australasia and Western Europe, whereas the burden increased in 26 countries. These patterns align with findings from other studies, for instance, analyses in India report rising hypercholesterolemia prevalence across several states over the past decade, particularly in northern and southern states, indicating worsening LDL-c control in South Asia.[33] Moreover, multiple studies have shown that meaningful improvements in cholesterol profiles and reductions in the disease burden attributable to high LDL-c have occurred primarily in high-income countries.[34,35] In contrast, low- and middle-income countries continue to exhibit rising hypercholesterolemia prevalence[36], persistently high exposure[37], and minimal progress in access to care and treatment.[34] Key challenges include limited availability and affordability of lipid-lowering therapies, particularly access to statins[38] and the laboratory capacity for lipid profiling, both of which restrict early detection and long-term risk reduction. Addressing these structural inequities, alongside advocating for lifestyle interventions and ensuring equitable access to pharmaceutical therapies for high-risk individuals, will be essential to reversing current trends.

While statins remain the cornerstone of LDL-c management, fixed-dose combination therapies or "polypills" with statins represent a promising strategy to simplify CVD treatment regimens, improve adherence, lower costs and expand access, particularly in resource-limited settings.[39,40] Beyond polypills, novel lipid-lowering therapies using advanced technology such as PCSK9 inhibitors and siRNA-based approaches, have broadened the therapeutic landscape by offering opportunities for more intensified LDL-c reduction and introducing alternative delivery mechanisms, such as injectable formulations.[41,42] However, the widespread adoption of these novel therapies requires careful evaluation of the healthcare infrastructure, cost-effectiveness, and appropriate patient selection thought individual risk stratification.

Even statins—despite being safe—remain underused due to the asymptomatic nature of hypercholesterolemia, low awareness, testing and medication costs, limited public-sector availability, health-system gaps, and perceived side effects.[43–46] Addressing these barriers through improved diagnostic access, affordable medicines, and standardized treatment protocols is essential to increase uptake and adherence.

Building on these priorities, efforts to effectively tackle the global LDL-c-related burden must extend beyond pharmacological solutions alone and adopt a strategic, multifaceted, and comprehensive approach that strengthens all stages of the care cascade. This includes: 1) early detection through targeted screening of high-risk individuals; 2) public education to raise awareness of risks associated with elevated LDL-c; 3) the implementation of novel population-level strategies to strengthen health systems and policies to ensure equitable access to affordable treatment; 4) promotion of sustainable lifestyle modifications, and 5) investment in research and surveillance to inform resource allocation and monitor progress.

Crucially, these efforts must be tailored to demographic and epidemiological contexts. Strengthening community-based interventions and integrating cardiovascular care into primary health systems can further enhance long-term impact. Universal health coverage to support primary care access will be essential.

This study provides a comprehensive and current global assessment of the burden attributable to high LDL-c, using updated data sources and methodological improvements.[21,47–49] By systematically quantifying the population-level impact of elevated LDL-c on cardiovascular disease mortality and disability across countries, ages, and sexes, these findings offer robust evidence to inform policy and guide prevention strategies worldwide.

Our manuscript aims to address the limitations of previous analyses and explores new avenues for assessing the burden of disease attributable to high LDL-c cholesterol. By adopting a comprehensive approach and accounting for the complex relationships between LDL-c exposure and disease outcomes, we hope to inform evidence-based strategies for reducing the global burden of CVD associated with high cholesterol levels.

Unlike previous comparative analyses, which were often based on limited or non-representative data sources and focused solely on total cholesterol exposure trends, our estimates account for

subnational variation, include LDL-c-specific measurements, and integrate location-specific corrections for data gaps.

While our analysis provides a comprehensive overview of the global burden attributable to high LDL-c, several limitations inherent to the GBD comparative risk assessment framework must be acknowledged. First, the estimation of attributable burden depends on the availability and quality of exposure and outcome data, which can be limited or inconsistent across countries, particularly in low- and middle-income regions. Although statistical modeling techniques are used to address data gaps, these may introduce additional uncertainty and may not fully capture local context. Measurement and estimation error must be considered when interpreting trends, especially in settings with sparse data. Second, RR are predominantly derived from meta-analyses of high-income country RCTs, which may not be generalize to all locations. The GBD methodology does not fully account for the synergistic effects of multiple co-occurring risk factors but accounts for mediation.

Importantly, this study focuses only on two cardiovascular outcomes—ischemic heart disease and ischemic stroke—which capture the largest share of LDL-c–related burden but do not represent the full spectrum of possible clinical outcomes. Future research should explore the contribution of elevated LDL-c to other diseases such as peripheral arterial disease, vascular dementia, and other lipid-associated conditions.[50,51] Broadening the scope of analysis will help to design more comprehensive prevention strategies.

Future research should incorporate life-course approaches to assess cumulative LDL-c exposure and clarify mediation pathways and interactions with other modifiable risk factors, such as smoking, alcohol use, and obesity. This evidence is critical to design effective prevention strategies that account for individual risk profiles and population-level disparities in burden and access to care.

Global LDL-c prevention and control could reduce a substantial share of CVD deaths and extend health span for millions. With less than five years to meet the Sustainable Development Goals, urgent action is needed to scale interventions and accelerate progress.

Conclusion

Despite progress in LDL-c management options, the burden attributable to high LDL-c has remained largely unchanged since 1990. In 2023, one-fifth of CVD deaths and DALYs were

linked to high LDL-c, with the absolute number of affected individuals increasing substantially over the past three decades. Our findings underscore the critical need for intensified, equitable, and context-specific strategies to reduce LDL-c exposure and mitigate its contribution to atherosclerotic CVD. This includes ensuring access to diagnostic and treatment tools, promoting sustainable lifestyle changes, and investing in innovative, population-level interventions that support lifelong cardiovascular health.

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List of Figures and Tables

Figures

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Figure 2. Age-standardized rate per 100,000 population of DALYs attributable to high LDL-c, both sexes, 2023 (A) and annualized percentage change in age-standardized DALYs rate attributable to high LDL-c, both sexes, 1990–2023 (B).

Figure 3. All-cause disability-adjusted life years (DALYs) by LDL-c level and region, 2023.

Figure 4. Age-standardized disability-adjusted life years (DALYs) rate per 100,000 attributable to high LDL-c in 2023 by Socio-demographic Index.

Tables

Table 1. Deaths and age-standardized death rates of high LDL-c in 1990 and 2023 and the temporal trend of age-standardized death rates from 1990 to 2023.

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