International Journal of Women's Health

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Global Burden, Attributable Risk Factors, and Future Projections of Lower Extremity Peripheral Arterial Disease Among Postmenopausal Women

Jie Yuan[1], Baolei Guo[2,3], Zhirong Li[1], Qianchuan Yi[1], Likuan Tu[1], Bo Tang[1], Fan Li[4]

[1]Department of General Surgery, University-Town Hospital of Chongqing Medical University, Chongqing, 400000, People's Republic of China; [2]Department of Vascular Surgery, Zhongshan Hospital, Fudan University, Shanghai, 200032, People's Republic of China; [3]Institute of Vascular Surgery, Fudan University, Shanghai, 200032, People's Republic of China; [4]Department of Surgery and Anesthesiology, University-Town Hospital of Chongqing Medical University, Chongqing, 400000, People's Republic of China

Correspondence: Fan Li, Department of Surgery and Anesthesiology, University-Town Hospital of Chongqing Medical University, No. 55, University-Town Middle Road, Shapingba District, Chongqing, 400000, People's Republic of China, Email dcxyylf@hospital.cqmu.edu.cn

Purpose: This study aimed to conduct a comprehensive analysis of the global burden and attributable risk factors for lower extremity peripheral arterial disease (LEPAD) among postmenopausal women, and project future trends.

Methods: All data were obtained from the Global Burden of Disease Study 2021, stratified by age, sex, and region to evaluate disparities. We performed decomposition analysis to quantify the contributions of population growth, aging, and epidemiological changes, and comparative risk assessment to evaluate attributable risk factors. The Bayesian age-period-cohort (BAPC) model was applied to project future trends by 2035.

Results: In 2021, there were 66,392,811 prevalent cases, 33,854 deaths, and 777,299 DALYs of LEPAD among postmenopausal women globally. Due to population growth and aging, these figures increased by 99.84%, 72.93%, and 73.06%, respectively, compared to 1990. High fasting plasma glucose was the leading attributable risk factor. Projections indicate a continued increase in the global burden by 2035.

Conclusion: Our findings reveal a substantial and persistently increasing burden of LEPAD among postmenopausal women globally. Targeted strategies are urgently needed to ensure healthier aging among this vulnerable population.

Keywords: lower extremity peripheral arterial disease, postmenopausal women, global burden, risk factors, future trends

Introduction

Lower extremity peripheral arterial disease (LEPAD) is a prevalent cardiovascular disease primarily characterized by atherosclerosis, associated with increased risks of amputation, myocardial infarction, stroke, impaired quality of life, and mortality.[1–3] In 2021, LEPAD affects over 113 million population globally, with incidence increasing progressively with advancing age.[4–6] The global prevalent cases of LEPAD were projected to increase by 220% and reach 360 million population by 2050.[7] Chronic limb-threatening ischemia, a severe form of LEPAD, is characterized by 1-year amputation rate of 15–20% and 1-year mortality rate of 15–40%. Within a period of 4–5 years, the mortality rate typically exceeds 50%.[8] High fasting plasma glucose, kidney dysfunction, high body-mass index (BMI), high systolic blood pressure, and smoking were the main attributable risk factors for LEPAD.[5,6]

Notably, postmenopausal women constitute a distinct high-risk population for LEPAD, attributable to aging, estrogen decline, and the high prevalence of metabolic syndrome.[9] Vascular senescence and cellular senescence are key drivers of atherosclerosis, an irreversible process that accumulates with advancing age.[10–12] Estrogen confers protective cardiovascular benefits, and its postmenopausal reduction significantly elevates cardiovascular risk.[13,14] Metabolic syndrome, as a common risk factor for LEPAD, demonstrates higher prevalence among postmenopausal women.[15,16] The combination of aging, menopause, and metabolic syndrome substantially amplifies LEPAD susceptibility in this population. Compared

https://doi.org/10.2147/IJWH.S589009
Received: 15 December 2025
Accepted: 25 April 2026
Published: 5 May 2026

to men, women with LEPAD characteristically exhibit leg symptoms at more advanced ages and disease stages, encounter elevated quality-of-life impairment, and face elevated risks of cardiovascular and cerebrovascular events.[2,17]

As early as 2012, the American Heart Association highlighted the need for greater awareness of LEPAD in women.[18] Nevertheless, the condition remains underrecognized and understudied in women, with a substantially underestimated risk and reduced healthcare access compared to men, particularly in socioeconomically disadvantaged regions.[17,19] With global aging accelerating, LEPAD burden is escalating, posing growing challenges to public health systems worldwide. A comprehensive assessment of the epidemiology and burden trends of LEPAD among postmenopausal women is imperative for developing effective prevention strategies, optimizing healthcare resource allocation, and advancing clinical management.

The Global Burden of Disease Study (GBD) 2021 provides updated estimates of health loss across diseases, injuries, and risk factors over time and by sociodemographic groups.[20,21] Although prior studies have examined LEPAD epidemiology and burden, systematic analyses focusing on postmenopausal women remain limited.[22–24] To address this gap, we aim to systematically assess the global burden of LEPAD among postmenopausal women, quantify key modifiable risk factors for LEPAD, and project future burden trends using the GBD 2021 data. Our study is expected to enhance understanding of LEPAD epidemiology among this vulnerable population globally, support evidence-based prevention and intervention strategies for policymakers and clinicians, and ultimately reduce the substantial public health burden imposed by LEPAD.

Materials and Methods

Date Sources

The GBD database provides systematically collated epidemiological data from 204 countries and territories, grouped into 21 predefined GBD regions based on geographic and epidemiological similarity.[20] In GBD 2021, LEPAD was defined as an ankle-brachial index (ABI) $\leq$ 0.90, mapped to ICD-10 codes I70.2–I70.8 and I73–I73.9. Menopause is clinically defined as permanent cessation of ovarian function, diagnosed after 12 consecutive months of amenorrhea, typically occurring between ages 45–55 years.[16,25] Accordingly, we defined postmenopausal status as age $\geq$ 55 years, consistent with previous epidemiological criteria.[26,27] Using GBD 2021 data, we extracted data on prevalence, deaths, and disability-adjusted life years (DALYs) of LEPAD across nine age groups (55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, 90–94, and $\geq$95 years) from 1990 to 2021, along with the corresponding uncertainty intervals (UIs). All the data were retrieved using the GBD Results tool (https://gbd2021.healthdata.org/gbd-results/). This investigation is in accordance with the guidelines for Accurate and Transparent Health Estimates Reporting (GATHER).[28] As GBD utilizes de-identified data, the University of Washington Institutional Review Board granted a waiver of informed consent.[22]

Burden Metrics

The primary burden metrics included prevalence, deaths, DALYs, age-standardized prevalence rate (ASPR), age-standardized mortality rate (ASMR), age-standardized DALYs rate (ASDR), and average annual percentage change (AAPC). DALY is a comprehensive metric for evaluating the overall burden of disease, injury, or health condition. The metric is designed to quantify the population's health status at a given point in time by aggregating the loss of health from both fatal and non-fatal outcomes.

Age-standardized rate (ASR) is defined as the weighted average of age-specific rates and is calculated according to the GBD standard population structure, thus eliminating the confounding effect of differences in age distribution between populations. It is computed by the following formula:

$$\mathrm{ASR} = \frac{\sum_{i=1}^{N} a_i w_i}{\sum_{i=1}^{N} w_i}$$

Where a_i represents the age-specific rate in the ith age group, w_i represents the number of individuals in the corresponding age group of the GBD standard population, and N represents its total number of individuals. The standard population structure used in this study was obtained directly from the official Institute for Health Metrics and Evaluation (IHME) GBD resources, which have been previously validated and widely applied.[29,30]

AAPC is a summary measure of the trend over a prespecified fixed interval. It is computed as a weighted average of the annual percentage changes from the joinpoint model, with the weights equal to the length of the annual percentage change interval, and is commonly employed to analyze health trends across time periods.[31] The formula for ASR is:

$$\text{AAPC} = \left\{ \exp\left(\frac{\sum^{w_i} b_i}{\sum^{w_i}} \right) - 1 \right\} \times 100$$

Where b_i represents the slope coefficient for the ith segment with i indexing the segments in the desired range of years, and w_i represents the length of each segment in the range of years. When the 95% confidence interval (CI) for AAPC is entirely above zero, it is indicative of an overall average annual increase during the study period and vice versa. When the 95% CI contains zero, it is indicative of a stable trend during the study period.

Socio-Demographic Index (SDI)

The SDI is a composite metric of regional development based on its lag-distributed income per capita, mean years of education, and fertility rates among females younger than 25 years. Ranging from 0 to 1, higher values reflect greater socioeconomic development. Studies have shown that SDI correlates with disease burden patterns, supporting its relevance in health disparity research.[32,33] In GBD 2021, all 204 countries and territories are classified into five distinct SDI subgroups (high, high-middle, middle, low-middle, and low SDI quintile) based on the SDI quintile.

Decomposition Analysis

This study performed a decomposition analysis to quantify the drivers of changes in prevalence, deaths, and DALYs of LEPAD among postmenopausal women. This method attributes changes in the absolute burden between two time points to three factors: population growth, aging, and epidemiological changes. The detailed specifications of the decomposition methodology are described in Supplementary Material 1 and have been well established in prior research.[32,34]

Risk Factors

GBD 2021 provides comprehensive estimates of exposure levels, relative health risks, and attributable burden for 88 risk factors.[21] We analyzed the impact of attributable risk factors on the DALYs of LEPAD among postmenopausal women, stratified by SDI to identify disparities. All analyses were based on the GBD comparative risk assessment framework, and employed sophisticated analytical approaches including two Bayesian statistical models (disease model meta-regression and spatiotemporal Gaussian process regression).[21] Population-attributable fraction (PAF) was used to quantify the contribution of risk factors, which is the proportional change in health risk that would occur if exposure to a risk factor were reduced to the theoretical minimum risk exposure level.

Statistical Analyses and Data Visualizations

Previous studies have explained the methodology of the GBD 2021 in detail.[20,32] In this study, LEPAD burden among postmenopausal women was stratified by age, sex, and SDI. Future burden trends by 2035 were projected using a Bayesian age-period-cohort (BAPC) model, which dynamically integrates age, period, and cohort effects within a traditional generalized linear modeling framework. Supplementary Material 2 provides more information on the fundamental principles and fit process of BPAC. All statistical analyses and data visualizations were performed using R (version 4.4.2) and JD_GBDR (V2.6.2, Jingding Medical Technology Co., Ltd).

Results

Global Burden of LEPAD Among Postmenopausal Women in 2021

In 2021, there were 66,392,811 prevalent cases, 33,854 deaths, and 777,299 DALYs of LEPAD among postmenopausal women globally, accounting for 58.39%, 49.97%, and 49.88% of the total individuals, respectively (Table 1). At the GBD

Table 1 Number and Age-Standardized Rate (ASR) of Prevalence, Deaths, and Disability-Adjusted Life years (DALYs) for Lower Extremity Peripheral Arterial Disease Among Postmenopausal Women in 1990/2021, and Their Average Annual Percentage Change (AAPC) From 1990 to 2021

Location	1990		2021		1990–2021 AAPC (95% CI)
	Number (95% UI)	ASR per 100,000 (95% UI)	Number (95% UI)	ASR per 100,000 (95% UI)	
Prevalence					
Global	33,223,176 (28,592,718, 38,764,628)	9230.14 (7943.70, 10,769.68)	66,392,811 (57,438,568, 77,161,304)	8441.89 (7303.35, 9811.11)	−0.29 (−0.31, −0.27)
High SDI	15,107,051 (13,057,291, 17,561,800)	14,309.09 (12,367.60, 16,634.18)	22,096,593 (19,387,451, 25,339,472)	11,982.28 (10,513.20, 13,740.79)	−0.57 (−0.63, −0.51)
High-middle SDI	8,700,653 (7,517,806, 10,128,520)	8943.09 (7727.28, 10,410.74)	17,439,183 (15,036,063, 20,359,645)	9280.97 (8002.05, 10,835.21)	0.11 (0.09, 0.13)
Middle SDI	6,204,011 (5,255,929, 7,341,250)	6971.51 (5906.14, 8249.44)	18,128,569 (15,545,195, 21,212,929)	7365.75 (6316.11, 8618.94)	0.17 (0.16, 0.19)
Low-middle SDI	2,477,929 (2,106,263, 2,935,846)	5004.65 (4254.00, 5929.50)	6,910,892 (5,904,303, 8,153,917)	5506.89 (4704.80, 6497.38)	0.32 (0.30, 0.33)
Low SDI	702,271 (591,934, 842,098)	3869.12 (3261.22, 4639.49)	1,765,433 (1,498,565, 2,091,802)	4219.61 (3581.76, 4999.67)	0.28 (0.27, 0.29)
Andean Latin America	65,102 (55,797, 76,751)	3780.28 (3239.94, 4456.71)	216,135 (183,977, 255,778)	4178.35 (3556.68, 4944.73)	0.32 (0.31, 0.34)
Australasia	233,585 (198,613, 274,428)	10,954.17 (9314.12, 12,869.55)	393,641 (337,341, 461,604)	8496.60 (7281.37, 9963.54)	−0.82 (−0.86, −0.78)
Caribbean	115,915 (98,534, 136,811)	5210.60 (4429.31, 6149.89)	281,491 (240,704, 330,581)	5733.49 (4902.72, 6733.38)	0.31 (0.30, 0.32)
Central Asia	244,213 (209,770, 287,183)	5132.85 (4408.92, 6035.98)	423,644 (363,358, 498,285)	5189.95 (4451.41, 6104.36)	0.04 (−0.00, 0.07)
Central Europe	1,008,209 (865,865, 1,183,486)	6692.48 (5747.60, 7855.96)	1,529,944 (1,314,130, 1,800,954)	7339.39 (6304.10, 8639.47)	0.30 (0.28, 0.32)
Central Latin America	405,866 (347,160, 477,050)	5771.09 (4936.34, 6783.26)	1,282,701 (1,101,409, 1,504,080)	5550.70 (4766.18, 6508.68)	−0.11 (−0.13, −0.10)
Central Sub-Saharan Africa	728,62 (60,990, 87,915)	3625.77 (3035.01, 4374.87)	186,904 (157,978, 222,276)	3813.45 (3223.28, 4535.15)	0.17 (0.16, 0.19)
East Asia	6,155,660 (5,191,797, 7,289,290)	8121.21 (6849.57, 9616.81)	18,415,727 (15,788,702, 21,553,096)	9097.39 (7799.63, 10,647.25)	0.35 (0.31, 0.40)
Eastern Europe	2,269,249 (1,959,974, 2,661,021)	7190.18 (6210.24, 8431.52)	3,345,381 (2,881,017, 3,895,611)	8766.75 (7549.86, 10,208.65)	0.64 (0.60, 0.68)
Eastern Sub-Saharan Africa	217,287 (184,177, 259,145)	3589.06 (3042.16, 4280.44)	541,911 (460,716, 646,479)	3827.46 (3253.99, 4566.02)	0.21 (0.19, 0.23)
High-income Asia Pacific	2,606,389 (2,254,666, 3,033,961)	13,318.38 (11,521.11, 15,503.23)	4,311,919 (3,721,273, 5,008,519)	11,303.82 (9755.43, 13,129.98)	−0.52 (−0.57, −0.47)
High-income North America	5,171,125 (4,429,069, 6,026,542)	15,743.17 (13,484.03, 18,347.43)	8,249,599 (7,346,922, 9,259,127)	13,693.70 (12,195.32, 15,369.43)	−0.44 (−0.50, −0.38)
North Africa and Middle East	649,018 (552,043, 772,664)	4678.56 (3979.50, 5569.89)	2,118,723 (1,826,555, 2,499,643)	5627.55 (4851.53, 6639.32)	0.61 (0.59, 0.63)
Oceania	13,038 (10,893, 15,766)	5640.96 (4712.82, 6821.28)	36,506 (31,114, 43,682)	6210.38 (5293.11, 7431.16)	0.30 (0.28, 0.33)
South Asia	2,079,829 (1,763,025, 2,474,247)	4617.46 (3914.12, 5493.11)	6,615,750 (5,657,908, 7,785,739)	5225.25 (4468.72, 6149.33)	0.41 (0.38, 0.43)
Southeast Asia	168,7564 (1,433,546, 1,989,568)	7490.76 (6363.23, 8831.30)	4,997,075 (4,272,500, 5,877,657)	8149.01 (6967.41, 9585.03)	0.28 (0.25, 0.31)
Southern Latin America	424,430 (362,644, 499,040)	9678.59 (8269.63, 11,379.96)	776,854 (669,122, 903,693)	9546.70 (8222.79, 11,105.42)	−0.05 (−0.10, −0.00)
Southern Sub-Saharan Africa	182,615 (156,690, 214,769)	7248.91 (6219.83, 8525.24)	341,523 (291,261, 401,314)	5997.49 (5114.84, 7047.49)	−0.60 (−0.62, −0.59)
Tropical Latin America	509,016 (438,468, 599,044)	6310.31 (5435.72, 7426.40)	1,355,036 (1,169,050, 1,591,499)	5569.64 (4805.18, 6541.58)	−0.40 (−0.42, −0.38)
Western Europe	886,1751 (7,691,037, 10,259,847)	15,948.07 (13,841.19, 18,464.15)	10,346,201 (8,971,191, 12,019,891)	12,903.30 (11,188.45, 14,990.65)	−0.69 (−0.73, −0.65)
Western Sub-Saharan Africa	250,451 (213,964, 297,123)	3599.61 (3075.19, 4270.39)	626,146 (535,594, 742,362)	3664.83 (3134.83, 4345.04)	0.06 (0.04, 0.08)
Deaths					
Global	19,577 (17,249, 21,333)	5.44 (4.79, 5.93)	33,854 (28,536, 37,915)	4.30 (3.63, 4.82)	−0.77 (−0.99, −0.54)
High SDI	9700 (8446, 10,453)	9.19 (8.00, 9.90)	17,651 (14,211, 19,628)	9.57 (7.71, 10.64)	0.15 (−0.08, 0.38)
High-middle SDI	8151 (7093, 9040)	8.38 (7.29, 9.29)	9941 (8393, 11,198)	5.29 (4.47, 5.96)	−1.49 (−1.84, −1.14)
Middle SDI	1055 (935, 1166)	1.19 (1.05, 1.31)	3530 (2988, 4097)	1.43 (1.21, 1.66)	0.72 (0.57, 0.86)
Low-middle SDI	391 (301, 577)	0.79 (0.61, 1.16)	1757 (1285, 2470)	1.40 (1.02, 1.97)	1.86 (1.68, 2.04)

https://doi.org/10.2147/IJWH.S589009

Low SDI	247 (102, 514)	1.36 (0.56, 2.83)	896 (566, 1649)	2.14 (1.35, 3.94)	1.50 (1.36, 1.65)
Andean Latin America	6 (4, 8)	0.34 (0.26, 0.45)	41 (32, 52)	0.80 (0.62, 1.01)	2.96 (2.06, 3.87)
Australasia	370 (316, 405)	17.36 (14.83, 18.98)	552 (431, 633)	11.91 (9.31, 13.66)	−1.19 (−1.52, −0.86)
Caribbean	162 (145, 178)	7.27 (6.50, 7.99)	526 (454, 593)	10.71 (9.24, 12.08)	1.27 (1.05, 1.48)
Central Asia	45 (34, 57)	0.95 (0.72, 1.21)	147 (126, 169)	1.80 (1.54, 2.07)	2.01 (1.23, 2.78)
Central Europe	1369 (1249, 1471)	9.09 (8.29, 9.76)	3491 (2947, 3934)	16.75 (14.14, 18.87)	2.22 (1.57, 2.87)
Central Latin America	242 (219, 261)	3.45 (3.11, 3.71)	520 (447, 589)	2.25 (1.94, 2.55)	−1.26 (−1.66, −0.86)
Central Sub-Saharan Africa	45 (12, 98)	2.23 (0.59, 4.86)	207 (75, 427)	4.22 (1.53, 8.72)	2.08 (1.99, 2.16)
East Asia	237 (171, 314)	0.31 (0.23, 0.41)	947 (710, 1192)	0.47 (0.35, 0.59)	1.34 (1.04, 1.65)
Eastern Europe	5621 (4782, 6373)	17.81 (15.15, 20.19)	4978 (4249, 5839)	13.05 (11.14, 15.30)	−0.94 (−1.38, −0.51)
Eastern Sub-Saharan Africa	119 (54, 238)	1.97 (0.89, 3.92)	462 (246, 867)	3.26 (1.74, 6.12)	1.66 (1.59, 1.72)
High-income Asia Pacific	276 (229, 302)	1.41 (1.17, 1.54)	1492 (1048, 1785)	3.91 (2.75, 4.68)	3.16 (2.53, 3.79)
High-income North America	3508 (2986, 3808)	10.68 (9.09, 11.59)	6458 (5270, 7179)	10.72 (8.75, 11.92)	0.11 (−0.08, 0.30)
North Africa and Middle East	69 (48, 96)	0.49 (0.35, 0.69)	372 (292, 471)	0.99 (0.78, 1.25)	2.46 (2.21, 2.70)
Oceania	0 (0, 1)	0.18 (0.13, 0.26)	2 (1, 2)	0.27 (0.19, 0.40)	1.27 (1.04, 1.51)
South Asia	173 (112, 298)	0.38 (0.25, 0.66)	1176 (627, 2695)	0.93 (0.49, 2.13)	3.02 (2.63, 3.42)
Southeast Asia	39 (31, 49)	0.17 (0.14, 0.22)	216 (177, 256)	0.35 (0.29, 0.42)	2.38 (2.19, 2.56)
Southern Latin America	92 (81, 100)	2.09 (1.84, 2.27)	227 (187, 253)	2.79 (2.30, 3.10)	1.10 (0.60, 1.60)
Southern Sub-Saharan Africa	101 (69, 138)	3.99 (2.72, 5.46)	368 (314, 429)	6.46 (5.51, 7.53)	1.65 (1.54, 1.76)
Tropical Latin America	441 (399, 473)	5.47 (4.94, 5.87)	1556 (1304, 1729)	6.40 (5.36, 7.11)	0.61 (0.22, 0.99)
Western Europe	6424 (5632, 6922)	11.56 (10.14, 12.46)	9493 (7445, 10,711)	11.84 (9.28, 13.36)	0.11 (−0.21, 0.44)
Western Sub-Saharan Africa	238 (75, 479)	3.43 (1.08, 6.89)	622 (211, 1148)	3.64 (1.24, 6.72)	0.17 (0.01, 0.33)
DALYs					
Global	449,141 (352,024, 627,374)	124.78 (97.80, 174.30)	777,299 (584,993, 1,107,794)	98.83 (74.38, 140.86)	−0.76 (−0.89, −0.63)
High SDI	196,186 (157,449, 257,361)	185.82 (149.13, 243.77)	310,102 (248,022, 396,354)	168.16 (134.49, 214.93)	−0.32 (−0.45, −0.19)
High-middle SDI	166,065 (133,280, 213,694)	170.69 (136.99, 219.65)	219,348 (169,717, 312,086)	116.73 (90.32, 166.09)	−1.20 (−1.57, −0.84)
Middle SDI	55,818 (34,865, 92,724)	62.72 (39.18, 104.19)	154,337 (99,186, 253,164)	62.71 (40.30, 102.86)	0.01 (−0.04, 0.05)
Low-middle SDI	21,673 (12,946, 37,022)	43.77 (26.15, 74.77)	66,947 (42,715, 105,503)	53.35 (34.04, 84.07)	0.65 (0.58, 0.72)
Low SDI	8762 (4862, 14,329)	48.28 (26.79, 78.95)	25,283 (15,981, 40,672)	60.43 (38.20, 97.21)	0.73 (0.68, 0.78)
Andean Latin America	482 (274, 889)	27.96 (15.90, 51.64)	1724 (1119, 2811)	33.33 (21.63, 54.35)	0.57 (0.39, 0.74)
Australasia	5627 (4827, 6632)	263.88 (226.35, 311.00)	7575 (6078, 9175)	163.50 (131.18, 198.04)	−1.52 (−1.77, −1.27)
Caribbean	3049 (2631, 3673)	137.08 (118.28, 165.10)	8703 (7469, 10,392)	177.27 (152.12, 211.66)	0.89 (0.71, 1.07)
Central Asia	2057 (1300, 3429)	43.23 (27.33, 72.07)	4358 (3095, 6476)	53.38 (37.91, 79.34)	0.64 (0.21, 1.07)
Central Europe	24,990 (21,609, 29,905)	165.88 (143.44, 198.51)	52,700 (44,425, 62,675)	252.81 (213.12, 300.66)	1.47 (1.00, 1.94)
Central Latin America	5880 (4599, 8222)	83.61 (65.40, 116.91)	14,136 (10,353, 20,987)	61.17 (44.80, 90.82)	−0.95 (−1.18, −0.72)
Central Sub-Saharan Africa	1339 (554, 2408)	66.64 (27.57, 119.81)	4810 (2140, 9133)	98.14 (43.66, 186.35)	1.27 (1.21, 1.33)
East Asia	43,798 (22,627, 81,873)	57.78 (29.85, 108.02)	115,792 (60,716, 219,447)	57.20 (29.99, 108.41)	−0.04 (−0.11, 0.02)
Eastern Europe	96,441 (80,029, 112,244)	305.58 (253.58, 355.65)	87,183 (73,439, 104,194)	228.47 (192.45, 273.05)	−1.01 (−1.38, −0.63)

(*Continued*)

https://doi.org/10.2147/IJWH.S589009

https://doi.org/10.2147/IJWH.S589009

Table 1 (Continued).

Location	1990		2021		1990–2021 AAPC (95% CI)
	Number (95% UI)	ASR per 100,000 (95% UI)	Number (95% UI)	ASR per 100,000 (95% UI)	
Eastern Sub-Saharan Africa	3464 (1871, 5602)	57.22 (30.90, 92.53)	10,848 (6273, 17,477)	76.62 (44.30, 123.44)	0.93 (0.88, 0.97)
High-income Asia Pacific	15,420 (9170, 26,698)	78.80 (46.86, 136.42)	33,922 (23,052, 50,062)	88.93 (60.43, 131.24)	0.36 (0.22, 0.50)
High-income North America	67,128 (55,593, 85,642)	204.37 (169.25, 260.73)	117,172 (97,561, 144,878)	194.50 (161.94, 240.49)	−0.15 (−0.32, 0.02)
North Africa and Middle East	4815 (2836, 8540)	34.71 (20.45, 61.56)	16,032 (10,272, 26,274)	42.58 (27.28, 69.79)	0.68 (0.63, 0.73)
Oceania	92 (48, 172)	39.83 (20.97, 74.57)	258 (140, 477)	43.91 (23.79, 81.21)	0.30 (0.25, 0.35)
South Asia	15,512 (8466, 27,990)	34.44 (18.80, 62.14)	55,374 (31,233, 95,359)	43.74 (24.67, 75.32)	0.78 (0.71, 0.85)
Southeast Asia	11,523 (5812, 22,151)	51.15 (25.80, 98.32)	32,660 (16,969, 61,995)	53.26 (27.67, 101.10)	0.14 (0.10, 0.18)
Southern Latin America	3492 (2332, 5574)	79.62 (53.17, 127.11)	6542 (4557, 9903)	80.39 (56.00, 121.70)	0.06 (−0.17, 0.30)
Southern Sub-Saharan Africa	2699 (1763, 3898)	107.13 (69.98, 154.72)	8294 (6900, 10,285)	145.65 (121.17, 180.61)	1.05 (0.98, 1.13)
Tropical Latin America	10,055 (8385, 12,833)	124.66 (103.95, 159.09)	30,766 (25,571, 37,589)	126.46 (105.10, 154.50)	0.10 (−0.21, 0.41)
Western Europe	125,958 (100,883, 165,831)	226.68 (181.55, 298.44)	154,908 (122,232, 198,485)	193.19 (152.44, 247.54)	−0.49 (−0.70, −0.29)
Western Sub-Saharan Africa	5319 (2193, 8908)	76.45 (31.51, 128.03)	13,542 (5976, 22,074)	79.26 (34.98, 129.20)	0.12 (0.03, 0.20)

regional level, East Asia recorded the highest prevalence cases (18,415,727), and Western Europe recorded the highest deaths (9493) and DALYs (154 908) (Table 1).

Following age standardization, the global ASPR, ASMR, and ASDR were 8441.89, 4.30, and 98.83 per 100,000 population, respectively (Table 1). At the GBD regional level, the region with the highest ASPR was High-income North America (13,693.70 per 100,000population). Meanwhile, Central Europe recorded both the highest ASMR (16.75 per 100,000 population) and ASDR (252.81 per 100,000 population) (Table 1).

Burden Trends of LEPAD Among Postmenopausal Women From 1990 to 2021

From 1990 to 2021, the global prevalent cases, deaths, and DALYs of LEPAD among postmenopausal women demonstrated a marked increasing trend, with increases of 99.84%, 72.93%, and 73.06%, respectively (Table 1 and Figure 1). In contrast, the global ASPR, ASMR, and ASDR showed an overall declining trend, with declines of 8.54% (AAPC: −0.29), 20.96% (AAPC: −0.77), and 20.8% (AAPC: −0.78), respectively (Table 1 and Figure 1).

At the GBD regional level, the most significant increases in ASPR, ASMR, and ASDR were observed in North Africa and Middle East (AAPC: 0.61), High-income Asia Pacific (AAPC: 3.36), and Central Europe (AAPC: 1.50), respectively, while the most substantial declines occurred in Australasia (AAPC: −0.83), Eastern Europe (AAPC: −1.29), and Australasia (AAPC: −1.51), respectively (Table 1).

Comparative Analysis Between Postmenopausal Women and Age-Matched Men

From 1990 to 2021, postmenopausal women consistently demonstrated greater prevalence cases and ASPR of LEPAD than age-matched men. Despite maintaining lower ASMR and ASDR than age-matched men, postmenopausal women exhibited greater absolute deaths and DALYs (Figure 1 and Supplementary Table 1).

Analysis stratified by age revealed that ASPR, ASMR, and ASDR showed a consistent upward trend with advancing age in both sexes. Postmenopausal women exhibited higher prevalence cases and ASPR across all age groups. Regarding deaths and DALYs, postmenopausal women progressively surpassed age-matched men with advancing age (Figure 1 and Supplementary Table 2).

Decomposition Analysis of LEPAD Burden Among Postmenopausal Women

At the global level, population growth constituted the primary driver of increased prevalent cases, deaths, and DALYs of LEPAD among postmenopausal women from 1990 to 2021, followed by aging. However, epidemiological changes partially offset these increases. At the regional level, the proportional contribution of these factors varied across SDI quintiles, though population growth remained the dominant driver. Aging demonstrated its most substantial absolute contribution in the high SDI quintile. Notably, epidemiological changes had a protective effect in the high and high-middle SDI quintiles, whereas a detrimental effect was observed in the low and low-middle SDI quintiles (Figure 2 and Supplementary Table 3).

Burden of LEPAD Among Postmenopausal Women by SDI

In 2021, the highest prevalent cases, deaths, and DALYs of LEPAD among postmenopausal women were observed in the high SDI quintile, while the lowest were observed in the low SDI quintile. Following age standardization, the high SDI quintile maintained the highest ASPR, ASMR, and ASDR. The low SDI quintile recorded the lowest ASPR, while the low-middle SDI quintile recorded the lowest ASMR and ASDR (Table 1).

Spearman correlation analysis revealed significant positive associations between both ASPR ($R = 0.78$, $P < 0.001$) and ASDR ($R = 0.56$, $P < 0.001$) with SDI, while significant negative correlations were observed between their AAPC and SDI ($R = -0.25$, $P < 0.001$) and ASDR ($R = -0.26$, $P < 0.001$) (Figure 3). High SDI regions generally demonstrated elevated ASPR and ASDR compared to low SDI regions. Notably, most high SDI regions demonstrated significant declining trends over time, while most low SDI regions showed divergent increasing trends (Figure 3).

https://doi.org/10.2147/IJWH.S589009

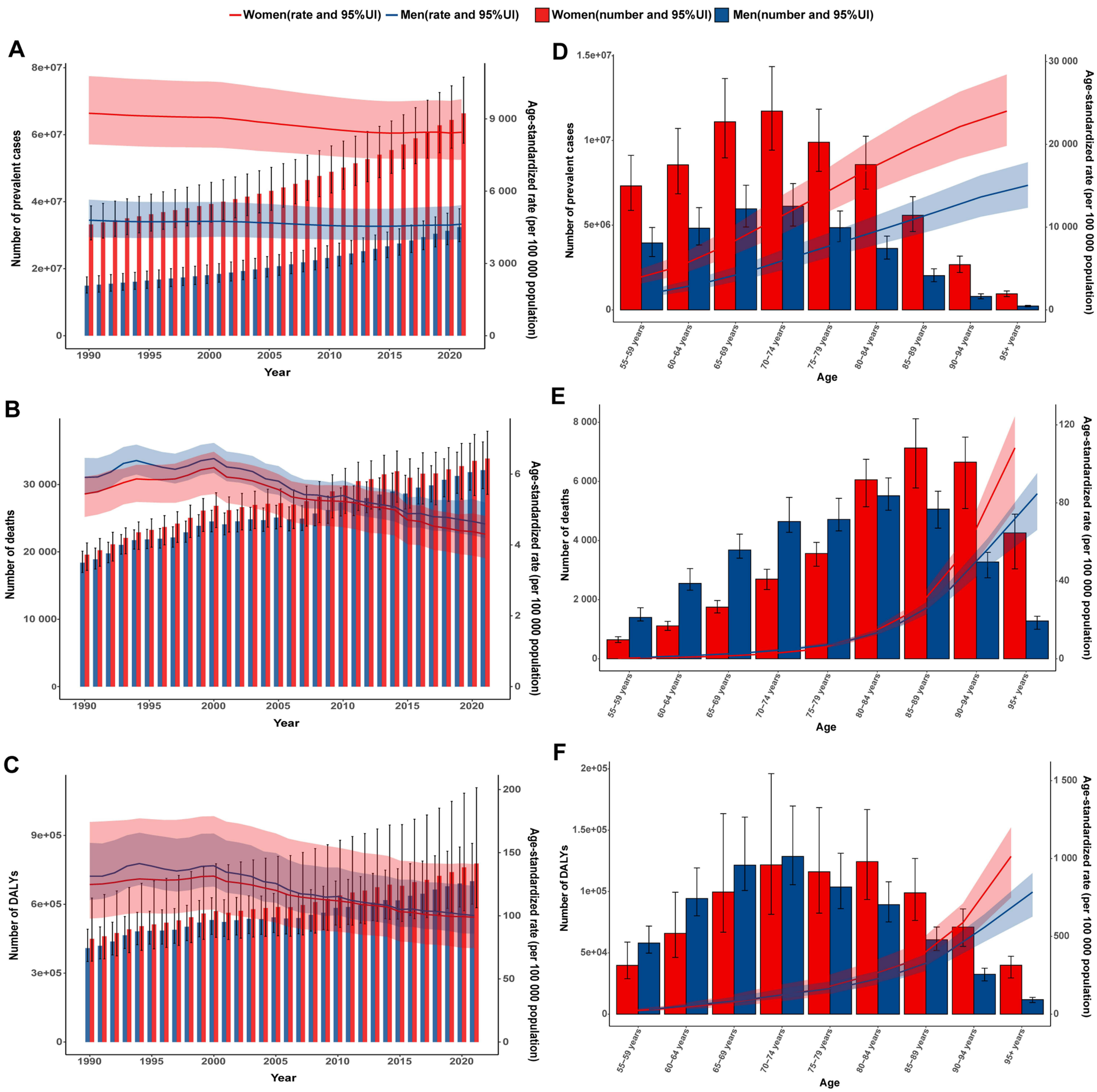

Figure 1 Number and age-standardized rate of prevalence, deaths, and disability-adjusted life years (DALYs) for lower extremity peripheral arterial disease among postmenopausal women globally by year and sex (**A–C**), and by age group and sex in 2021 (**D–F**).

Risk Factors of LEPAD Burden Among Postmenopausal Women

In GBD 2021, high fasting plasma glucose, high systolic blood pressure, high body-mass index, kidney dysfunction, smoking, and low physical activity were identified as major attributable risk factors for LEPAD. Globally, high fasting plasma glucose was the leading attributable risk factor for DALYs of LEPAD among postmenopausal women (contributing 35.39%), followed by kidney dysfunction (contributing 29.83%), high body-mass index (contributing 20.26%), and high systolic blood pressure (contributing 13.21%). Smoking and low physical activity demonstrated minor contributions (12.31% and 2.91%). Similar patterns were observed across all SDI quintiles. Notably, smoking showed a greater attributable burden in the high SDI quintile (contributing 16.55%) (Figure 4).

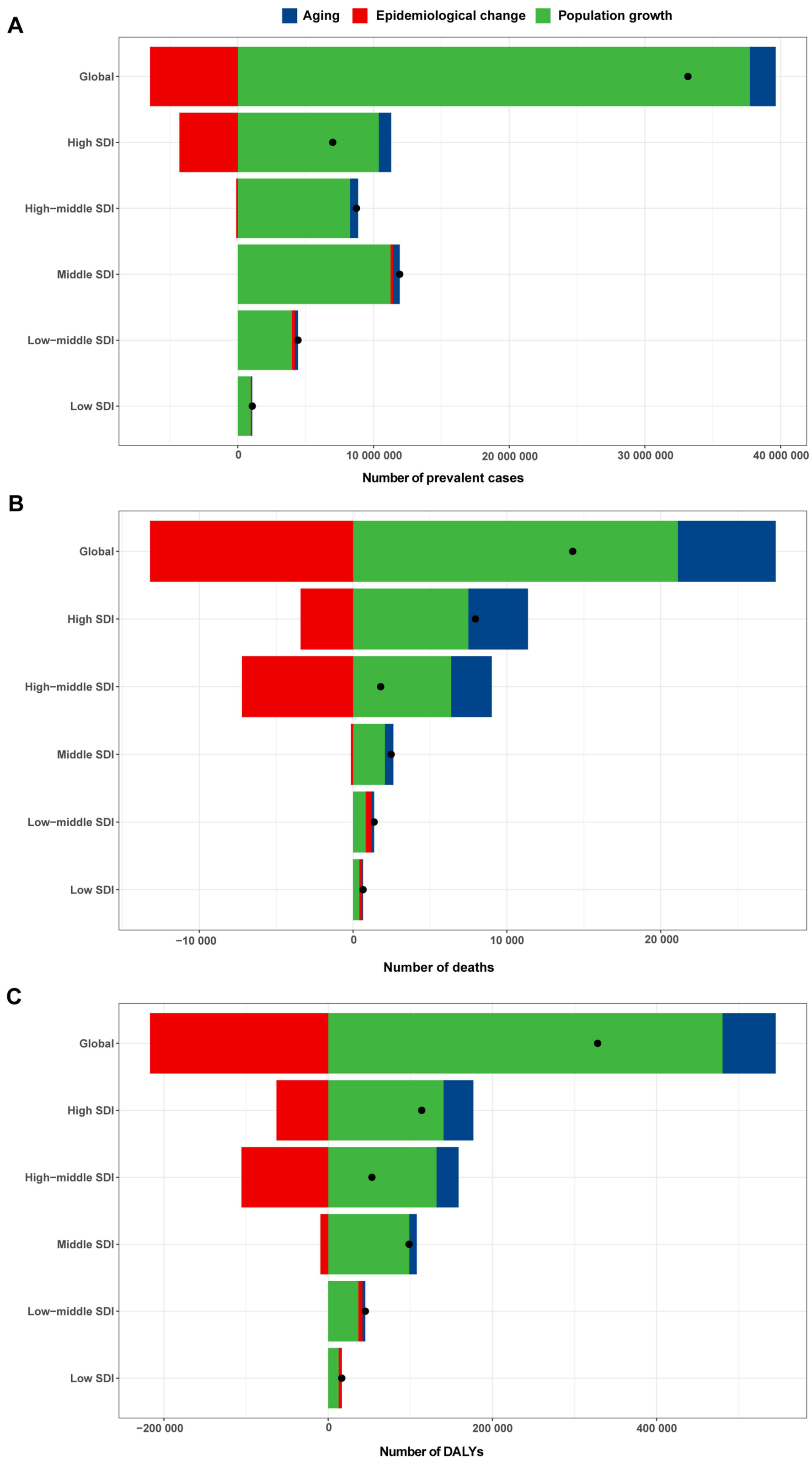

Figure 2 Changes in prevalent cases (**A**), deaths (**B**), and disability-adjusted life years (DALYs) (**C**) of lower extremity peripheral arterial disease among postmenopausal women according to population growth, aging, and epidemiological change from 1990 to 2021 at 5 socio-demographic Index (SDI) quintiles and globally.

https://doi.org/10.2147/IJWH.S589009

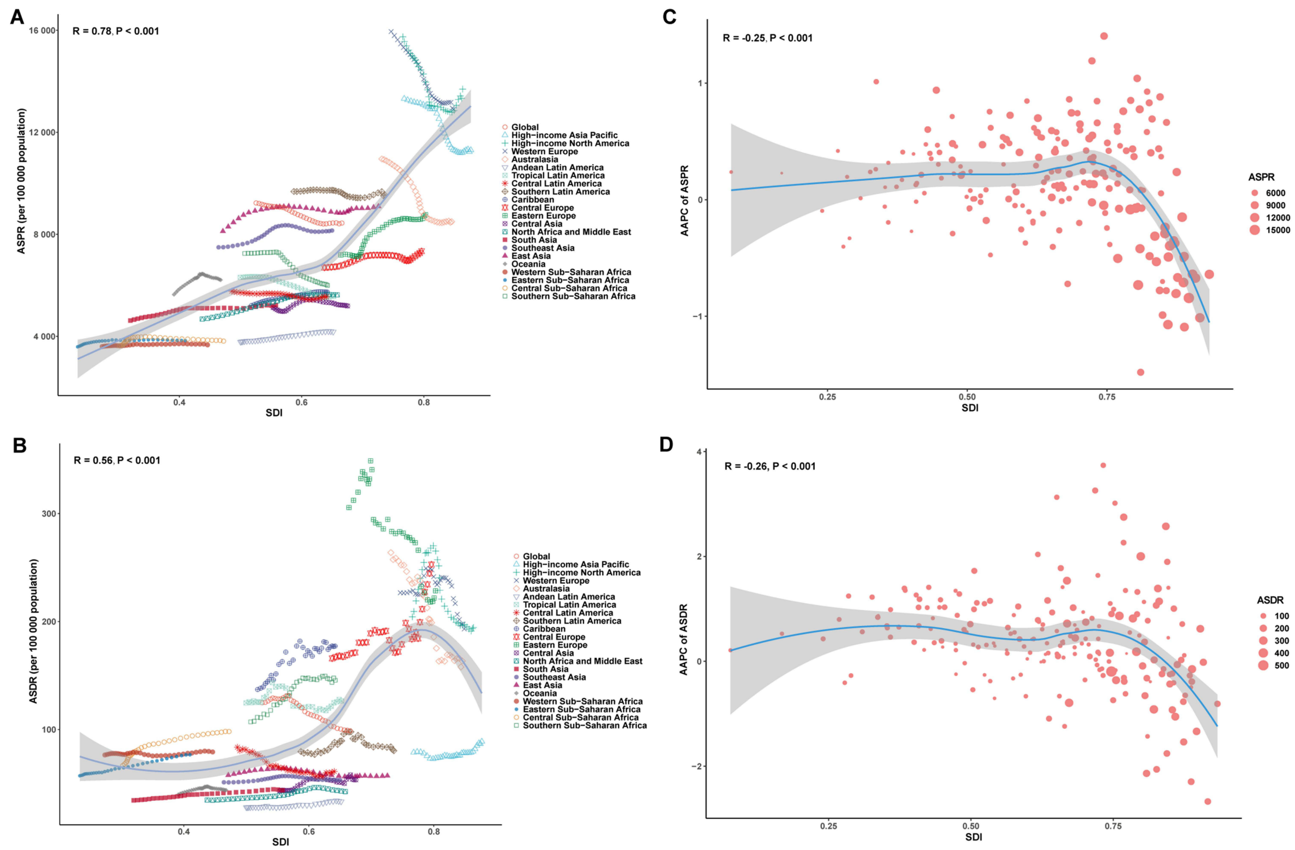

Figure 3 Age-standardized prevalence rate (ASPR) (**A**) and age-standardized disability-adjusted life years rate (ASDR) (**B**) of lower extremity peripheral arterial disease among postmenopausal women at the global and regional levels by socio-demographic Index (SDI) from 1990 to 2021, and their average annual percentage change (AAPC) (**C** and **D**) at the national levels by socio-demographic Index (SDI) in 2021. The blue line and shaded area represent the expected value and 95% CI based on the SDI, disease rates, and AAPC across all locations.

From 1990 to 2021, high fasting plasma glucose and high body-mass index exhibited a significantly increasing contribution. In contrast, the burden attributable to smoking demonstrated a decline, particularly in the high SDI quintile (Figure 4).

Projections of LEPAD Burden Among Postmenopausal Women

The BAPC model indicates that the absolute prevalence cases, deaths, and DALYs of LEPAD among postmenopausal women will continue to increase. In 2035, there will be 91,669,132 prevalent cases, 41,370 deaths, and 1,011,323 DALYs, with increases of 38.07%, 22.2%, and 30.11%, respectively, compared to 2021. Conversely, the ASPR, ASMR, and ASDR are projected to maintain a continued decline, reaching 8289.05, 3.74, and 91.45 per 100,000 population in 2035, with a decline of 1.81%, 13.02%, and 7.47% compared to 2021, respectively (Figure 5).

Discussion

LEPAD poses a significant clinical and public health challenge. Our study focuses on postmenopausal women and provides a comprehensive analysis of the global burden and attributable risk factors of LEPAD in this particular population from 1990 to 2021, which simultaneously accounts for demographic characteristics, regional disparities, risk factor profiles, and aging dynamics. Additionally, we project their future trends by 2035.

Our findings indicate that the global ASPR, ASMR, and ASDR of LEPAD among postmenopausal women generally exhibited a fluctuating decline from 1990 to 2021, reflecting improvements in disease prevention and medical technology. However, there was a significant increase in the absolute prevalence cases, deaths, and DALYs globally. This persistent absolute burden aligns with trends observed in the general population but is notably higher among postmenopausal women,[4,35,36] mainly due to the decline in estrogen levels. The effects of estrogen on cardiovascular function are

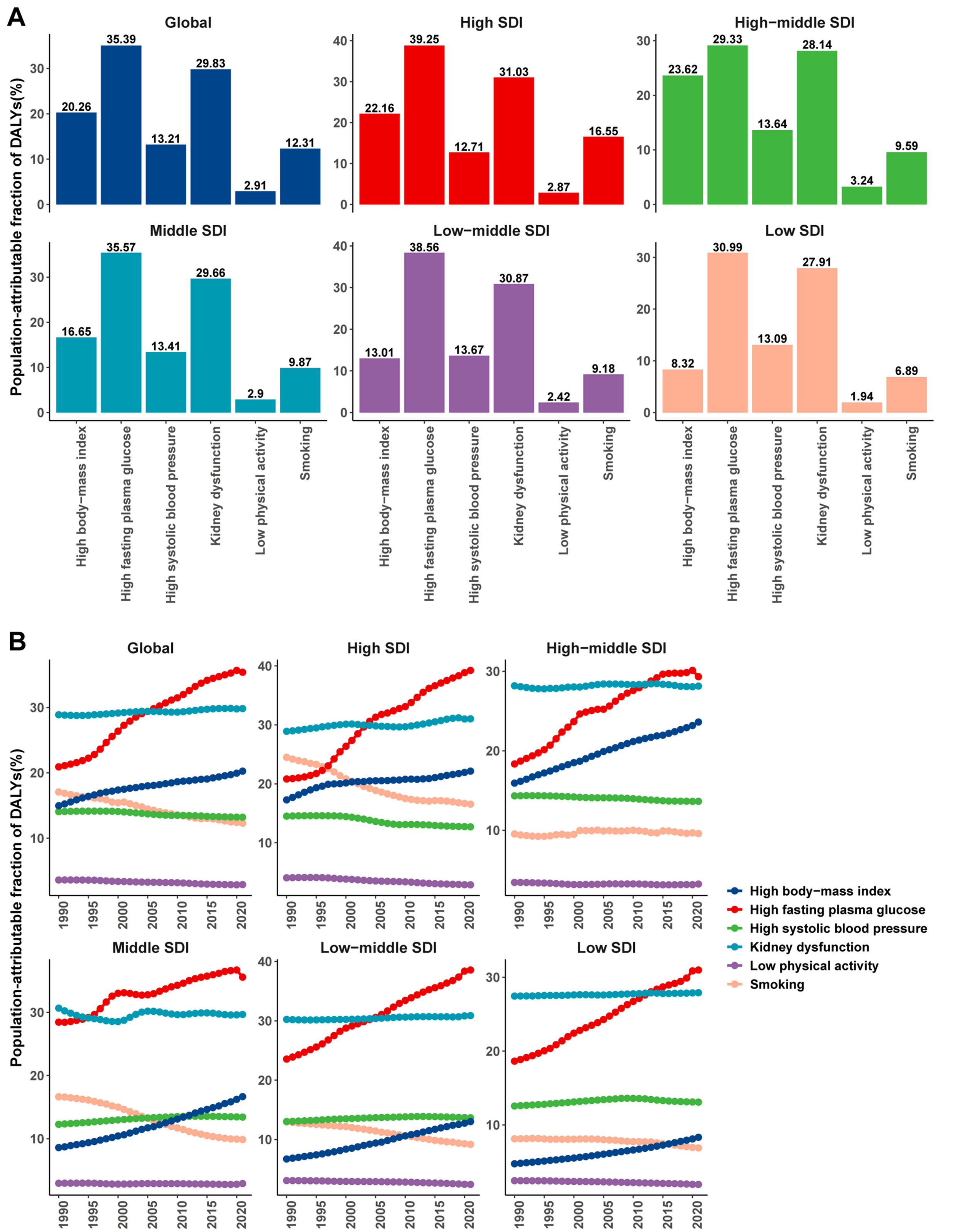

Figure 4 Population-attributable fraction of disability-adjusted life years (DALYs) (**A**) for lower extremity peripheral arterial disease among postmenopausal women in 2021, and their trends (**B**) from 1990 to 2021 at 5 socio-demographic Index (SDI) quintiles and globally.

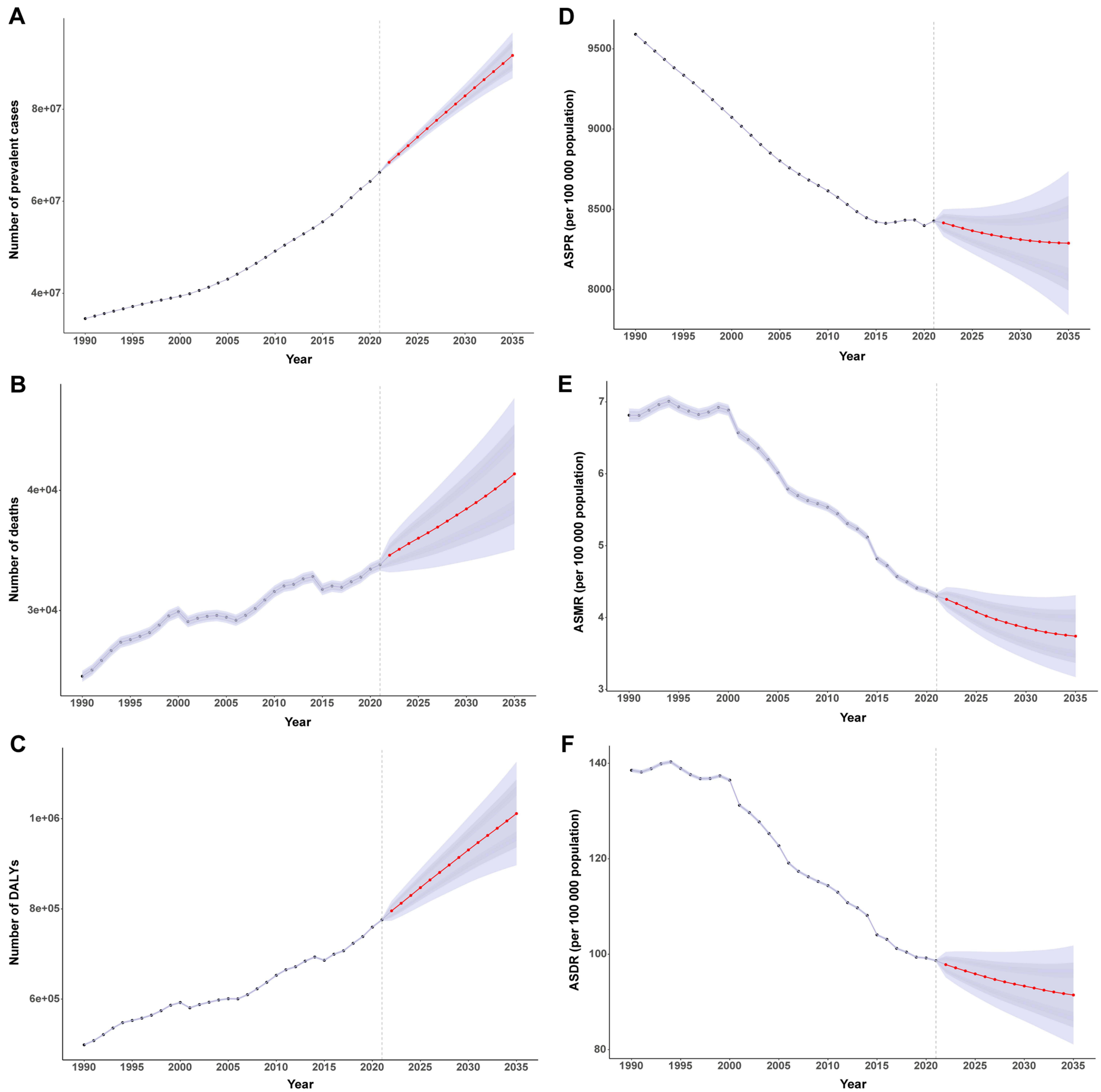

Figure 5 The future trends in global prevalent cases (**A**), deaths (**B**), disability-adjusted life years (DALYs) (**C**), age-standardized prevalence rate (ASPR) (**D**), age-standardized mortality rate (ASMR) (**E**), and age-standardized DALYs rate (ASDR) (**F**) of lower extremity peripheral arterial disease among postmenopausal women are predicted by the Bayesian age-period-cohort (BAPC) model.

mediated by nuclear and membrane estrogen receptors (ERs), including estrogen receptor alpha, beta and G protein-coupled ER.[37] Estrogen exerts vascular protective effects by regulating oxidative stress, anti-inflammation, and inhibiting leukocyte and platelet adhesion, which can reduce the incidence of atherosclerosis in young women.[38,39]

Consistent with previous reports, significant age and sex disparities were observed in our study.[4,35] Among postmenopausal women, age-standardized rates of prevalence, deaths, and DALYs progressively increased with advancing age, with the burden being particularly pronounced in the elderly population. Postmenopausal women had a higher absolute burden than age-matched men, and the age-standardized rates of deaths and DALYs of women surpassed those of age-matched men with advancing age, likely due to women's longevity and the cumulative impact of metabolic disorders.[15,16] These disparities suggest the need for population-specific interventions tailored to demographic characteristics, with particular emphasis on enhancing early screening and health management for elderly women.

Significant disparities in LEPAD burden were observed across SDI regions. This highlights the significant impact of socioeconomic factors on cardiovascular health. Overall, high SDI regions generally exhibited a greater LEPAD burden, potentially due to pronounced population growth and aging, as well as a higher metabolic syndrome prevalence.[40,41] Nevertheless, most high SDI regions demonstrated declining trends from 1990 to 2021, likely attributable to robust healthcare systems and advanced medical technology. In contrast, the increasing burden in low SDI regions may stem from limited healthcare access and insufficient medical resources. Socioeconomic disparities in LEPAD burden have been well documented.[2,42] These findings highlight systemic health inequities and call for region-specific responses: high SDI regions should enhance metabolic risk management, while low SDI regions require strengthened basic health infrastructure and improved service availability.

Our study identified high fasting plasma glucose, kidney dysfunction, high BMI, high systolic blood pressure, smoking, and low physical activity as the primary risk factors for LEPAD among postmenopausal women, aligning with previous studies.[43–47] Compared with the general population, postmenopausal women exhibited a similar pattern of risk factor contributions, with the exception of smoking.[48] The global burden attributable to smoking among postmenopausal women was significantly lower than that observed in the general population (12.31% vs 24.17%). Meanwhile, the smoking-attributable burden gradually declined from 1990 to 2021, particularly in the high SDI quintile, likely benefiting from smoking management. Notably, the continuously rising attributable burden of high fasting plasma glucose and high body-mass index may be associated with an unhealthy lifestyle and higher metabolic syndrome prevalence. Kidney dysfunction has continued to have a significant impact on LEPAD globally over the past three decades. This shifting risk profile underscores the importance of promoting healthy lifestyles and prioritizing metabolic health in current prevention frameworks.

Although global age-standardized rates of LEPAD burden among postmenopausal women declined over the past three decades, the absolute burden continued to increase, driven predominantly by population growth and aging. Epidemiological changes partially offset this increase in high SDI regions, illustrating the impact of strong health systems. Given the accelerating population aging and the rising metabolic syndrome prevalence, the absolute burden of LEPAD is projected to continue increasing, necessitating targeted strategies that address both metabolic risk management and demographic change.

It is important to acknowledge the potential limitations of this study. First, GBD data are derived from compiled national reports and publications, which raises concerns about their accuracy and completeness. Second, unreliable epidemiological data in some low-income countries may lead to underreporting or misclassification, which could result in an underestimation of the true burden. Third, mathematical modeling was required for countries with poor-quality data, which introduces possible estimation biases. Despite these limitations, our findings align with prior epidemiological evidence, which affirms the validity and robustness of our conclusions.

Conclusions

This study reveals a substantial and persistently increasing LEPAD burden globally, characterized by significant demographic and regional disparities. Given the accelerated aging and the rising metabolic syndrome prevalence, the absolute burden is projected to continue increasing. Our findings provide valuable insights and a global perspective for policymakers and clinicians. They emphasize the necessity of developing targeted strategies that account for demographic characteristics, regional disparities, and attributable risk factors to effectively reduce LEPAD burden among postmenopausal women and promote healthier aging.

AI Statement

Generative AI and AI-assisted technologies were not used in the preparation of this work.

Abbreviations

LEPAD, Lower extremity peripheral arterial disease; GBD, Global Burden of Disease; UI, Uncertainty interval; CI, Confidence interval; ASR, Age-standardized rate; DALYs, Disability-adjusted life years; ASPR, Age-standardized prevalence rate; ASMR, Age-standardized mortality rate; ASDR, Age-standardized DALYs rate; SDI, Socio-demographic Index; AAPC, Average annual percentage change; BAPC, Bayesian age-period-cohort.

Data Sharing Statement

The datasets supporting the findings of this study are available in the https://vizhub.healthdata.org/gbd-results/. Custom analysis code is available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

Based on items 1 and 2 of Article 32 of the Measures for Ethical Review of Life Science and Medical Research Involving Human Subjects dated February 18, 2023, China, this study uses publicly available, anonymized data and therefore does not require approval from the local Institutional Review Board. The requirement for informed consent was waived by the University of Washington Institutional Review Board due to deidentified and aggregated data used in GBD study.

Acknowledgments

We appreciate the excellent works by the Global Burden of Diseases Study (GBD) 2023 collaborators. This study was generously supported by Jingding Medical Tech, to whom we extend our sincere gratitude. We especially thank them for providing authorization and technical support for the JD_GBDR software.

Author Contributions

Jie Yuan: Conceptualization, Data curation, Visualization, Writing–original draft. Baolei Guo: Conceptualization, Methodology, Funding acquisition. Zhirong Li: Data curation, Formal analysis. Qianchuan Yi: Methodology, Visualization. Likuan Tu: Methodology, Visualization. Bo Tang: Supervision, Writing–review & editing. Fan Li: Conceptualization, Project administration, Writing–review & editing. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was supported by the Shanghai Municipal Science and Technology Commission Project (No. 25SF1909000) and the Shanghai Municipal Health Commission's Health Youth Talent Training Program (No. 2022YQ13).

Disclosure

The authors declare no competing interests in this work.

References

1. Bates KJ, Moore MM, Cibotti-Sun M. 2024 Lower Extremity Peripheral Artery Disease Guideline-at-a-Glance. *J Am Coll Cardiol*. 2024;83(24):2605–2609. doi:10.1016/j.jacc.2024.04.003
2. Gornik HL, Aronow HD, Goodney PP, et al. 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease: a Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2024;149(24):e1313–e1410. doi:10.1161/CIR.0000000000001251
3. Athavale A, Fukaya E, Leeper NJ. Peripheral Artery Disease: molecular Mechanisms and Novel Therapies. *Arterioscler Thromb Vasc Biol*. 2024;44(6):1165–1170. doi:10.1161/ATVBAHA.124.320195
4. Li J, Weng C, Wang T, et al. Trends in lower extremity peripheral arterial disease incidence since 1990 and forecasting future statistics using Global Burden of Disease 2021: a time-series analysis. *Front Public Health*. 2025;13:1521927. doi:10.3389/fpubh.2025.1521927
5. Zhang B, Zhang H, Gong H, Ge J. Trends and Potential Risk Factors of Lower Extremity Peripheral Arterial Disease: results from the Global Burden of Disease Study 2021. *Pulse*. 2025;13(1):140–156. doi:10.1159/000547795
6. Guo J, Li L, Wu S, et al. Global, regional, and national burden of lower extremities peripheral artery disease from 1990 to 2021 and forecast for 2050: a cross-sectional analysis from the 2021 global burden of disease study. *Int J Surg*. 2026;112(2):3042–3054. doi:10.1097/JS9.0000000000003843
7. Deng W, Deng L, Du C, et al. Forecasting the Global Burden of Peripheral Artery Disease from 2021 to 2050: a Population-Based Study. *Research*. 2025;8:0702. doi:10.34133/research.0702
8. Duff S, Mafilios MS, Bhounsule P, Hasegawa JT. The burden of critical limb ischemia: a review of recent literature. *Vasc Health Risk Manag*. 2019;15:187–208. doi:10.2147/VHRM.S209241

9. Anagnostis P, Mikhailidis DP, Blinc A, et al. Peripheral Arterial Disease: an Underestimated Aspect of Menopause-related Cardiovascular Disease. *Curr Vasc Pharmacol*. 2024;22(2):153–154. doi:10.2174/0115701611295374231212110458
10. González LDM, Romero-Orjuela SP, Rabeya FJ, Del Castillo V, Echeverri D. Age and vascular aging: an unexplored frontier. *Front Cardiovasc Med*. 2023;10:1278795. doi:10.3389/fcvm.2023.1278795
11. Xu T, Zhang Y, Zhou Y, et al. Association of Vascular Aging Phenotypes with Adverse Clinical Outcomes in the Chinese Population: a Multicentre Study. *Clin Interv Aging*. 2025;20:403–414. doi:10.2147/CIA.S485597
12. Camacho-Encina M, Booth LK, Redgrave RE, Folaranmi O, Spyridopoulos I, Richardson GD. Cellular Senescence, Mitochondrial Dysfunction, and Their Link to Cardiovascular Disease. *Cells*. 2024;13(4):353. doi:10.3390/cells13040353
13. Anagnostis P, Mikhailidis DP, Blinc A, et al. The Effect of Menopause and Menopausal Hormone Therapy on the Risk of Peripheral Artery Disease. *Curr Vasc Pharmacol*. 2023;21(5):293–296. doi:10.2174/0115701611263345230919122907
14. Nicholson CJ, Sweeney M, Robson SC, Taggart MJ. Estrogenic vascular effects are diminished by chronological aging. *Sci Rep*. 2017;7(1):12153. doi:10.1038/s41598-017-12153-5
15. Meegaswatte H, McKune AJ, Panagiotakos DB, et al. The Association Between the American Heart Association Life's Essential 8 and Metabolic Syndrome Among Postmenopausal Women: findings from NHANES 2011–2020. *Nutrients*. 2025;17(10):1688. doi:10.3390/nu17101688
16. Cho YH, Lee SY. Effect of Postmenopausal Hormone Therapy on Metabolic Syndrome and Its Components. *J Clin Med*. 2024;13(14):4043. doi:10.3390/jcm13144043
17. Pouncey AL, Woodward M. Sex-Specific Differences in Cardiovascular Risk, Risk Factors and Risk Management in the Peripheral Arterial Disease Population. *Diagnostics*. 2022;12(4):808. doi:10.3390/diagnostics12040808
18. Hirsch AT, Allison MA, Gomes AS, et al. A Call to Action: women and Peripheral Artery Disease: a Scientific Statement From the American Heart Association. *Circulation*. 2012;125(11):1449–1472. doi:10.1161/CIR.0b013e31824c39ba
19. Kavurma MM, Boccanfuso L, Cutmore C, et al. A hidden problem: peripheral artery disease in women. *Eur Heart J Qual Care Clin Outcomes*. 2023;9(4):342–350. doi:10.1093/ehjqcco/qcad011
20. GBD 2021 Diseases and Injuries Collaborators. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 2024;403(10440):2133–2161. doi:10.1016/S0140-6736(24)00757-8.
21. GBD 2021 Risk Factors Collaborators. Global burden and strength of evidence for 88 risk factors in 204 countries and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 2024;403(10440):2162–2203. doi:10.1016/S0140-6736(24)00933-4.
22. Qiu X, Hu B, Ke J, Wang M, Zeng H, Gu J. Global, regional, and national trends in peripheral arterial disease among older adults: findings from the global burden of disease study 2021. *Aging Clin Exp Res*. 2025;37(1):150. doi:10.1007/s40520-025-03037-0
23. Qu J, Zeng Z, Huo W, et al. Global Burden of Lower Extremity Peripheral Arterial Disease Associated with High Fasting Plasma Glucose: an Analysis of the Global Burden of Disease study 2021. *Eur J Vasc Endovasc Surg*. 2025:S1078. doi:10.1016/j.ejvs.2025.05.043.
24. Yan C, Chen J, Xu X, Wei H, Li J. Global burden of peripheral arterial disease (1990–2021), global burden trends and the impact of blood lead on peripheral arterial disease: a multidimensional analysis based on NHANES, GBD, and Mendelian randomization. *J Transl Med*. 2025;23(1):463. doi:10.1186/s12967-025-06408-3
25. Jeong HG, Park H. Metabolic Disorders in Menopause. *Metabolites*. 2022;12(10):954. doi:10.3390/metabo12100954
26. Xu H, Xiao W, Ding C, et al. Global burden of osteoarthritis among postmenopausal women in 204 countries and territories: a systematic analysis for the Global Burden of Disease Study 2021. *BMJ Glob Health*. 2025;10(3):e017198. doi:10.1136/bmjgh-2024-017198
27. Tan J, Zhu Z, Wang X, et al. Global burden and trends of musculoskeletal disorders in postmenopausal elderly women: a 1990–2021 analysis with projections to 2045. *Arthritis Res Ther*. 2025;27(1):127. doi:10.1186/s13075-025-03587-8
28. Stevens GA, Alkema L, Black RE, et al. Guidelines for Accurate and Transparent Health Estimates Reporting: the GATHER statement. *Lancet*. 2016;388(10062):e19–e23. doi:10.1016/S0140-6736(16)30388-9
29. Jiang Z, Zeng G, Dai H, et al. Global, regional and national burden of liver cancer 1990–2021: a systematic analysis of the global burden of disease study 2021. *BMC Public Health*. 2025;25(1):931. doi:10.1186/s12889-025-22026-6
30. Lin L, Chen P, Zhang Y, et al. Burden of type 2 diabetes mellitus and risk factor attribution among older adults: a global, regional, and national analysis from 1990 to 2021, with projections up to 2040. *Diabetes Obes Metab*. 2025;27(8):4330–4343. doi:10.1111/dom.16471
31. Clegg LX, Hankey BF, Tiwari R, Feuer EJ, Edwards BK. Estimating average annual per cent change in trend analysis. *Stat Med*. 2009;28(29):3670–3682. doi:10.1002/sim.3733
32. Wang R, Chen Y, Shao X, et al. Burden of Skin Cancer in Older Adults From 1990 to 2021 and Modelled Projection to 2050. *JAMA Dermatol*. 2025;21:e251276. doi:10.1001/jamadermatol.2025.1276
33. Liu Q, Wang H, Chen Z, et al. Global, regional, and national epidemiology of nasopharyngeal carcinoma in middle-aged and elderly patients from 1990 to 2021. *Ageing Res Rev*. 2025;104:102613. doi:10.1016/j.arr.2024.102613
34. Zhang J, Pan L, Guo Q, et al. The impact of global, regional, and national population ageing on disability-adjusted life years and deaths associated with diabetes during 1990–2019: a global decomposition analysis. *Diabetes Metab Syndr*. 2023;17(6):102791. doi:10.1016/j.dsx.2023.102791
35. Kim MS, Hwang J, Yon DK, et al. Global burden of peripheral artery disease and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Glob Health*. 2023;11(10):e1553–e1565. doi:10.1016/S2214-109X(23)00355-8
36. Tan SCW, Zheng -B-B, Tang M-L, Chu H, Zhao Y-T, Weng C. Global Burden of Cardiovascular Diseases and its Risk Factors, 1990–2021: a Systematic Analysis for the Global Burden of Disease Study 2021. *QJM*. 2025;hcaf022. doi:10.1093/qjmed/hcaf022
37. Aryan L, Younessi D, Zargari M, et al. The Role of Estrogen Receptors in Cardiovascular Disease. *Int J Mol Sci*. 2020;21(12):4314. doi:10.3390/ijms21124314
38. Kozak M, Poredoš P, Blinc A, Kaja Ježovnik M, Poredoš P. Peripheral arterial disease in women. *Vasa*. 2024;53(6):366–370. doi:10.1024/0301-1526/a001137
39. Novella S, Pérez-Cremades D, Mompeón A, Hermenegildo C. Mechanisms underlying the influence of oestrogen on cardiovascular physiology in women. *J Physiol*. 2019;597(19):4873–4886. doi:10.1113/JP278063

40. Gruber J, Lin M, Yang H, Yi J. China's Social Health Insurance in the Era of Rapid Population Aging. *JAMA Health Forum*. 2025;6(4):e251105. doi:10.1001/jamahealthforum.2025.1105
41. Zhang H, Zhou X-D, Shapiro MD, et al. Global burden of metabolic diseases, 1990–2021. *Metabolism*. 2024;160:155999. doi:10.1016/j.metabol.2024.155999
42. Hughes K, Olufajo OA, White K, et al. The Relationship Between Peripheral Arterial Disease Severity and Socioeconomic Status. *Ann Vasc Surg*. 2023;92:33–41. doi:10.1016/j.avsg.2023.01.015
43. Bai W, Li S, Liang T, Dong J, Zhou J, He J. The Relationship Between Body Mass Index and Peripheral Artery Disease: insights from the National Health and Nutrition Examination Survey and Mendelian Randomization Analysis. *J Surg Res*. 2025;306:407–416. doi:10.1016/j.jss.2024.12.038
44. Haile KE, Asgedom YS, Azeze GA, Amsalu AA, Kassie GA, Gebrekidan AY. Burden of peripheral artery disease and risk factors among patients with diabetes mellitus in sub-Saharan Africa: a systematic review and meta-analysis. *BMC Endocr Disord*. 2025;25(1):42. doi:10.1186/s12902-025-01866-8
45. Huish S, Nawaz S, Bellasi A, Diaz-Tocados JM, Haarhaus M, Sinha S. Clinical management of peripheral arterial disease in chronic kidney disease—a comprehensive review from the European Renal Association CKD-MBD Working Group. *Clin Kidney J*. 2025;18(5):sfaf089. doi:10.1093/ckj/sfaf089
46. Buso G, Darioli R, Calanca L, et al. In postmenopausal women, lower limb peripheral arterial disease, assessed by ankle-brachial index, may be a strong predictor of cardiovascular risk. *Eur J Intern Med*. 2022;99:63–69. doi:10.1016/j.ejim.2022.02.002
47. Poredoš P, Mikhailidis DP, Paraskevas KI, et al. Management of arterial hypertension in patients with peripheral arterial disease. *Int Angiol*. 2024;43(5):541–547. doi:10.23736/S0392-9590.24.05242-8
48. Fu M, Zhang H. Global burden of peripheral arterial disease and its risk factors, 1990–2021. *BMC Cardiovasc Disord*. 2025;25(1):631. doi:10.1186/s12872-025-05055-2