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RESEARCH

Global, regional, and national trends in peripheral arterial disease among older adults: findings from the global burden of disease study 2021

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Abstract

Importance Lower extremity peripheral arterial disease (PAD) is a significant health concern among older adults globally, affecting both mortality and quality of life.

Objective To evaluate the temporospatial trends and its risk factors in lower extremity PAD-related burden among adults aged 60 years and older from 1990 to 2021.

Design, setting, and participants This repeated cross-sectional study utilized data from the Global Burden of Disease Study 2021, encompassing 204 countries and territories. The study population included adults aged 60 years and older.

Exposure Lower extremity PAD among older adults from January 1990 to December 2021.

Main outcomes and measures Primary outcomes included age-standardized prevalence rates (ASPR), mortality rates (ASMR), disability-adjusted life-years (DALYs), and average annual percentage changes (AAPCs). Trends were analyzed by age, sex, and sociodemographic index (SDI). Joinpoint regression analysis was used to identify significant trend changes.

Results From 1990 to 2021, global trends showed decreases in lower extremity PAD-related prevalence, mortality, and DALYs. Significant geographical disparities were observed: high-SDI regions had the highest prevalence (11,171.66 per 100,000 in 2021) but showed declining trends (AAPC, -0.74; 95% CI, -0.80 to -0.68), while low-SDI regions had the lowest prevalence (4,842.40 per 100,000) but demonstrated increasing trends (AAPC, 0.22; 95% CI, 0.21 to 0.24). Regionally, although lower extremity PAD-related prevalence showed a decreasing trend in most regions from 1990 to 2021, there were still some regions with an increasing trend (North Africa and Middle East AAPC, 0.57; 95% CI, 0.55 to 0.59). Temporal analysis showed sex-specific divergent trends in recent years, with males exhibiting an upward trend since 2015 (APC, 0.15; 95% CI, 0.07 to 0.24), while females showed a slowed decline since 2014 (APC, -0.06; 95% CI, -0.12 to -0.01). Decomposition analysis identified population growth as the primary driver of PAD burden increase, with epidemiological changes showing contrasting effects across SDI regions. Among risk factors, high fasting glucose emerged as the leading contributor, while smoking's contribution decreased.

Conclusions and relevance This study revealed significant disparities in lower extremity PAD burden across different SDI levels and regions, with low-SDI countries facing an increasing burden. The contrasting trends between high- and low-SDI regions, coupled with varying risk factor patterns (particularly the rise in high fasting glucose and decline in smoking), suggest the need for targeted interventions in resource-limited settings to address this growing health challenge among older adults.

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Key points

Question What are the trends in the burden of lower extremity PAD among older adults at the global, regional, and sociodemographic index subgroup levels from 1990 to 2021?

Finding In this cross-sectional study among older adults, although lower extremity PAD prevalence (measured per 100000 population) decreased from 9525.09 to 8220.21 from 1990 to 2021, divergent trends were observed with high-SDI countries showing decline while low-SDI countries demonstrated increases. Population growth was the primary driver of PAD burden globally, while risk factor patterns varied significantly, with high fasting glucose emerging as the leading risk factor and smoking showing substantial decline.

Meaning The lower extremity PAD burden among older adults shows significant disparities across SDI regions, highlighting the need to address healthcare inequities and strengthen preventive measures in low-SDI countries. The changing patterns of risk factors underscore the importance of targeted interventions and comprehensive disease management strategies across different socioeconomic settings.

Keywords Peripheral arterial disease · Disability-adjusted life-years · Time trends · Health inequalities

Introduction

Lower extremity peripheral artery disease (PAD) is the third leading cause of atherosclerotic cardiovascular morbidity, following coronary artery disease and stroke [1–3]. PAD has emerged as a critical global health challenge in the 21st century, particularly affecting older adults who bear the greatest disease burden. According to the Global Burden of Disease Study 2019, the number of people aged 40 years and older with PAD reached 113 million in 2019, with a global prevalence of 1.52% [4]. PAD demonstrates a strong age-disease correlation, being relatively uncommon before age 60 years but affecting approximately 20% of people aged 80 years and older [5]. The age-specific prevalence peaks at ages 70–74 years, making older adults the most clinically relevant population for understanding disease burden and developing targeted interventions [6]. World Health Organization have highlighted that without timely intervention, aging populations worldwide face increasingly high risks of PAD-related complications and mortality, with estimates suggesting significant healthcare burden by 2030. Aging demographics and cardiovascular health are intricately linked [7, 8]. PAD disproportionately affects not only through direct vascular complications but also indirectly through reduced mobility, falls risk, and quality of life impairment [9, 10]. Older adults are particularly vulnerable to PAD complications due to their reduced physiological reserve and higher prevalence of comorbidities compared to younger populations [11–13]. In this population, PAD presents with distinctive clinical characteristics and progression patterns, with research indicating that while approximately 75% of people with PAD report no change in leg symptoms over time [3], those with PAD have significantly greater annual declines in functional performance. This disconnect between subjective symptoms and objective functional decline is particularly pronounced in older adults, further complicating clinical management [4]. Despite their vulnerabilities, older adults' specific PAD management needs often receive insufficient attention in healthcare planning and resource allocation [7].

Global populations are aging at unprecedented rates, prompting widespread societal changes. The UN General Assembly's declaration of 2021–2030 as the Decade of Healthy Ageing underscores the urgent need for policymakers to enhance older adults' quality of life, both present and future [14, 15]. The inclusion of older adults in WHO's Global Strategy for Healthy Ageing and numerous national healthcare initiatives demonstrates the critical importance of monitoring their health [14, 16, 17]. However, many studies lack age-standardized processes, which limits the ability to make cross-regional and cross-national comparisons. Global estimates of age-standardized prevalence rates (ASPR), age-standardized death rates (ASMR), and the age-standardized disability-adjusted life years rates (ASDR) for lower extremity peripheral arterial disease in older adults over the past decades could address gaps in disease statistics. These estimates would enhance understanding of the burden of lower extremity peripheral arterial disease both globally and in specific regions. Policymakers could use this data to provide evidence-based healthcare, prevention strategies, and resource allocation for lower extremity peripheral arterial disease in older adults, potentially improving personal well-being and socioeconomic productivity.

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021 is a critical resource in epidemiological research [18]. In this study, we extracted data from the GBD Study 2021 and calculated ASPR, ASMR, and ASDR of lower extremity peripheral arterial disease in older adults from 1990 to 2021, further analyzing their temporal trends and progress in health management, at global, regional, and national levels.

Method

Data sources

GBD 2021 project, supported by over 11,500 collaborators from 164 countries, provides a comprehensive assessment of global health status and disease burden [19]. This monumental effort involves extensive data collection, review, and analysis. Detailed information on data sources can be accessed through the GBD 2021 Data Input Sources tool on the Institute for Health Metrics and Evaluation website (https://ghdx.healthdata.org/gbd-2021/sources) [19, 20]. The methodological details of the GBD Study 2021 have been previously published [18]. These studies comprehensively detail health burdens associated with 371 diseases and injuries and 88 risk factors across 204 countries and territories [21]. We retrieved estimates of prevalence, death, and disability-adjusted life years rates rate for lower extremity peripheral arterial disease, along with their 95% uncertainty intervals (UI), for 8 age groups (60–64, 65–69, 70–74, 75–79, 80–84, 85–89, 90–94, 95 + years) from 1990 to 2021 using the Global Health Data Exchange (GHDx) query tool (https://vizhub.healthdata.org/gbd-results/). Regarding lower extremity peripheral arterial disease, details on definitions, input data and modelling strategies are available in Supplemental Method. This study follows the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) [22].

Patient and public involvement

The patients and the public were not involved in the design, conduct, reporting or dissemination of our study, so informed consent and institutional review board approval were waived. For GBD studies, the Institutional Review Board of the University of Washington waived the requirement for informed consent to access the GBD data (https://www.healthdata.org/research-analysis/gbd).

Definition of socio-demographic index (SDI)

The SDI is a metric that evaluates a country or region's level of development based on fertility rates, educational attainment, and per capita income, on a scale from 0 to 1 and was categorized into high (0.805129-1), high-middle (0.689504–0.805129), middle (0.607679–0.689504), low-middle (0.454743–0.607679), and low (0-0.454743) levels [23]. Higher SDI values denote greater socioeconomic development. Research has shown that SDI correlates with variations in disease prevalence and mortality rates, highlighting the interplay between socioeconomic factors and health outcomes [23, 24].

Risk factors

Our analysis specifically examined key risk factors identified in the GBD 2021 study: smoking, high fasting glucose, diet high in sodium, lead exposure, kidney dysfunction, and high blood pressure. We incorporated data on attributable PAD-related ASDR associated with these risk factors, stratified by region to elucidate geographical disparities. To quantify the impact of these risk factors, we employed advanced methodological approaches including DisMod-MR 2.1 and spatiotemporal Gaussian process regression. These methodologies enabled systematic modeling of exposure distributions across demographic groups and geographical locations. For each risk factor, we established a theoretical minimum risk exposure level (TMREL) based on epidemiological evidence, representing the exposure threshold associated with minimal PAD risk. Through integration of exposure data, relative risk estimates, and TMRELs, we computed population attributable fractions (PAFs) for each risk factor. To translate these fractions into meaningful health outcomes, we multiplied the PAFs by the ASDR, thereby generating estimates of risk-attributable burden. This analytical framework provides critical insights into the contributions of modifiable risk factors to PAD pathogenesis [25, 26].

Statistical analysis

To estimate ASPR, ASMR, and ASDR of lower extremity peripheral arterial disease in older adults, direct age standardization was employed [24, 27]. Joinpoint regression analysis was used to assess trends in ASPR, ASMR, and ASDR. Each segment's epidemiological trend is evaluated by calculating the annual percentage change (APC) and 95% confidence interval (CI). The average annual percentage change (AAPC) was also calculated for an overall assessment, encompassing the entire study period from 1990 to 2021 [28, 29]. In addition, to derive an in-depth understanding of explanatory factors driving changes in lower extremity peripheral arterial disease in older adults (prevalence, death, and DALYs) from 1990 to 2021, we conducted decomposition analyses by (i) disease subgroups and sexes, and (ii) population size, age structure, and epidemiologic changes (details in Supplementary Methods). All analyses were conducted using R software (v.4.3.0) (http://www.r-project.org).

Results

Global trends

Globally, the lower extremity PAD-related prevalence among older adults decreased from 9525.09 to 8220.21 per 100,000 population from 1990 to 2021 (AAPC, -0.48; 95% CI, -0.49 to -0.46). The lower extremity PAD-related mortality rate showed a more substantial decline from 10.05 to 6.41 per 100,000 population (AAPC, -1.51; 95% CI, -1.64 to -1.39). Similarly, lower extremity PAD-related DALYs decreased from 190.72 to 132.31 per 100,000 population (AAPC, -1.25; 95% CI, -1.41 to -1.10). Overall, a decreasing trend was observed across all three metrics globally during the study period, with mortality rates showing the most significant reduction (Table 1). During the period 1990 to 2021, joinpoints were present in the lower extremity PAD-related prevalence for older adults in 2006 and 2015, with APCs of -0.68 (95% CI, -0.69 to -0.67), -0.45 (95% CI, -0.48 to -0.42), and 0.01 (95% CI, -0.04 to 0.06), respectively. The initial significant decline in prevalence ($P<0.001$) gradually decelerated and ultimately stabilized in the most recent period ($P=0.678$). For mortality rates, a joinpoint was identified in 1999, after which there was a significant decline (APC, -2.08; 95% CI, -2.19 to -1.97). The DALYs showed joinpoints in 2000 and 2006, with varying rates of decline across periods, with the most pronounced improvement occurring during 2000–2006 (APC, -2.31; 95% CI, -2.95 to -1.66; $P<0.001$) (Fig. 1 and Supplementary Table 1, Figs. 1 and 2).

From 1990 to 2021, the lower extremity PAD-related prevalence decreased globally for both males and females (Table 1). Specifically, the lower extremity PAD-related prevalence decreased from 6743.07 in 1990 to 5958.16 in 2021 per 100,000 population among males, with an AAPC of -0.40 (95% CI, -0.42 to -0.38), and from 11517.01 in 1990 to 10040.24 in 2021 per 100,000 population among females, with an AAPC of -0.45 (95% CI, -0.47 to -0.43). During the same period, the lower extremity PAD-related mortality rates also showed notable improvement, decreasing from 11.52 to 7.38 per 100,000 population among males, with an AAPC of -1.49 (95% CI, -1.68 to -1.30), and from 8.88 to 5.56 per 100,000 population among females, with an AAPC of -1.54 (95% CI, -1.67 to -1.41). When examining temporal patterns of mortality, joinpoint regression analysis revealed important differences between sexes: males exhibited a more complex trend with three distinct periods (1990–2000, 2000–2007, and 2007–2021), with the most substantial decline occurring during 2000–2007 (APC, -2.47; 95% CI, -3.11 to -1.83), whereas females demonstrated a simpler pattern with only one joinpoint in 1999, after which mortality declined consistently and significantly (APC, -2.19; 95% CI, -2.30 to -2.07). Similarly, the disease burden measured by lower extremity PAD-related DALYs decreased from 206.22 to 139.95 per 100,000 population among males, with an AAPC of -1.33 (95% CI, -1.51 to -1.15), and from 176.69 to 124.70 per 100,000 population among females, with an AAPC of -1.18 (95% CI, -1.31 to -1.06). Consistent with mortality trends, joinpoint analysis of DALYs revealed temporal variations with the most pronounced improvements occurring during similar middle periods for both sexes—males experienced the steepest decline during 2000–2007 (APC, -2.41; 95% CI, -3.02 to -1.80), while females showed their most significant reduction during 1999–2006 (APC, -1.94; 95% CI, -2.37 to -1.51). Despite these overall improvements, the joinpoint regression model highlighted divergent trends in global prevalence between sexes in recent years, with males exhibiting an upward trend (APC, 0.15; 95% CI, 0.07 to 0.24) since 2015, while females showed a significantly slowed decline (APC, -0.06; 95% CI, -0.12 to -0.01) since 2014 (Supplementary Table 2).Globally, the prevalence of lower extremity PAD in older adults showed varying trends across different age groups between 1990 and 2021. The most notable changes were observed in the 70–74 age group, where the prevalence decreased from 1990 to 2015 (APCs, -0.75 and −0.29) but showed an upward trend from 2015 to 2021 (APC, 0.26; 95% CI, 0.03 to 0.49; $P=0.031$). The prevalence in the oldest age group (95 plus) showed a strong decline from 1990 to 2005 (APC, -1.08; 95% CI, -1.13 to -1.04), followed by a moderate decrease from 2005 to 2013 (APC, -0.80; 95% CI, -0.94 to -0.67), and finally stabilized from 2013 to 2021 (APC, 0.06; 95% CI, -0.05 to 0.17 $P=0.026$) (Supplementary Table 3). Overall, the lower extremity PAD-related prevalence decreased with the magnitude of change higher in high-SDI countries (AAPC, -0.74; 95% CI, -0.80 to -0.68) than in low-SDI countries where it actually increased (AAPC, 0.22; 95% CI, 0.21 to 0.24) (Table 1; Fig. 2). Notably, although high-SDI regions had the highest burden of lower extremity PAD with a prevalence of 11171.66 (95% UI, 9262.86 to 13431.02) per 100,000 in 2021, they showed a declining trend, while low-SDI regions, despite having a lowest prevalence of 4842.40 (95% UI, 3880.91 to 6010.23) per 100,000, demonstrated an increasing trend. The results of the joinpoint regression analyses showed that in high-SDI countries, prevalence declined steadily from 1990 to 2014 (APCs, -1.16 and −0.47) before showing a slight increase (APC, 0.22; 95% CI, 0.08 to 0.36), while low-SDI countries experienced a continuous increase throughout the study period (Fig. 1 and Supplementary Table 4). Further analysis by sex revealed that in high-SDI regions, males showed a more pronounced recent increase in prevalence (APC, 0.68; 95% CI, 0.52 to 0.85) from 2015 to 2021 compared to females (APC, 0.06; 95% CI, -0.07 to 0.19)

Table 1 ASPR, ASMR and ASDR of lower extremity peripheral arterial disease in older adults in 1990 and 2021, and change from 1990 to 2021 at the global and regional level. Abbreviations: ASPR, age-standardized prevalence rate; ASMR, age-standardized death rate; ASDR, age-standardized disability-adjusted life years rates; SDI, sociodemographic index; UI, uncertainty interval; AAPC, average annual percent change; CI, confidence interval

Characteristic	ASPR, per 100,000 (95% UI)		AAPC (95% CI)	ASMR, per 100,000 (95% UI)		AAPC (95% CI)	ASDR, per 100,000 (95% UI)		AAPC (95% CI)
	1990	2021		1990	2021		1990	2021	
Global	9525.09 (7740.3 to 11623.72)	8220.21 (6717.35 to 9995.68)	-0.48 (-0.49 to -0.46)	10.05 (8.85 to 11)	6.41 (5.47 to 7.12)	-1.51 (-1.64 to -1.39)	190.72 (153.79 to 246.97)	132.31 (102.89 to 177.17)	-1.25 (-1.41 to -1.1)
Sex									
Female	11517.01 (9370.63 to 14049.72)	10040.24 (8187.47 to 12205.46)	-0.45 (-0.47 to -0.43)	8.88 (7.63 to 9.77)	5.56 (4.54 to 6.27)	-1.54 (-1.67 to -1.41)	176.69 (134.7 to 242.26)	124.7 (89.87 to 178.29)	-1.18 (-1.31 to -1.06)
Male	6743.07 (5468.09 to 8274.73)	5958.16 (4863.54 to 7249.08)	-0.4 (-0.42 to -0.38)	11.52 (10.36 to 12.62)	7.38 (6.54 to 8.36)	-1.49 (-1.68 to -1.3)	206.22 (175.3 to 250.3)	139.95 (116.86 to 175)	-1.33 (-1.51 to -1.15)
SDI									
High SDI region	14087.42 (11504.23 to 17155.46)	11171.66 (9262.86 to 13431.02)	-0.74 (-0.8 to -0.68)	12.92 (11.45 to 13.82)	9.59 (8.15 to 10.5)	-1.01 (-1.23 to -0.79)	246.44 (202.31 to 315.32)	185.46 (150.23 to 236.75)	-0.92 (-1.03 to -0.81)
High-middle SDI region	8977.99 (7284.35 to 10970.22)	8411.88 (6806.38 to 10289.66)	-0.26 (-0.34 to -0.18)	16.04 (14.17 to 17.78)	7.96 (6.89 to 8.81)	-2.42 (-2.97 to -1.87)	279.56 (235.08 to 338.98)	159.41 (129.16 to 206.15)	-1.92 (-2.21 to -1.64)
Middle SDI region	6807.28 (5482.05 to 8386.93)	7006.94 (5657.95 to 8617.49)	0.07 (0.04 to 0.1)	2.8 (2.45 to 3.1)	2.62 (2.26 to 2.91)	-0.17 (-0.4 to 0.06)	86.45 (58.7 to 133.52)	80.35 (55.5 to 122.16)	-0.26 (-0.42 to -0.11)
Low-middle SDI region	5372.81 (4308.93 to 6646.7)	5803.07 (4659.47 to 7178.84)	0.24 (0.23 to 0.26)	1.88 (1.23 to 2.84)	2.99 (2.25 to 3.94)	1.49 (1.32 to 1.66)	64.69 (38.54 to 104.29)	80.2 (54.37 to 119.3)	0.68 (0.59 to 0.78)
Low SDI region	4514.94 (3612.3 to 5621.44)	4842.4 (3880.91 to 6010.23)	0.22 (0.21 to 0.24)	3.76 (1.6 to 7.72)	5.52 (2.9 to 10.4)	1.26 (1.1 to 1.41)	88.9 (44.08 to 154.77)	113.19 (62.5 to 191.41)	0.77 (0.66 to 0.87)
Regional Level									
Andean Latin America	4185.58 (3347.55 to 5224.68)	4578.39 (3657.6 to 5679.81)	0.29 (0.27 to 0.31)	0.55 (0.36 to 0.82)	1.08 (0.8 to 1.47)	2.26 (1.5 to 3.02)	35.47 (19.18 to 63)	41.04 (25.53 to 67.88)	0.49 (0.28 to 0.7)
Australasia	10250.99 (8295.74 to 12552.51)	7301.23 (5886.32 to 8986.48)	-1.11 (-1.13 to -1.09)	25.87 (22.22 to 29.02)	12.42 (9.92 to 14.37)	-2.31 (-2.85 to -1.77)	383.2 (327.16 to 445.8)	181.82 (145.05 to 223.41)	-2.39 (-2.57 to -2.22)
Caribbean	5591.14 (4461.47 to 6936.57)	5906.67 (4729.02 to 7323.44)	0.17 (0.16 to 0.18)	12.59 (11.08 to 14.05)	14.42 (12.21 to 16.47)	0.47 (0.33 to 0.6)	208.21 (178.58 to 247.44)	241.26 (203.9 to 286.92)	0.54 (0.43 to 0.64)
Central Asia	5564.57 (4457.11 to 6893.18)	6077.42 (4883.61 to 7517.78)	0.29 (0.26 to 0.32)	1.68 (1.31 to 2.14)	3.56 (2.99 to 4.19)	2.46 (0.95 to 4)	59.97 (38.96 to 94.03)	87.22 (64.24 to 123.29)	1.21 (0.39 to 2.03)
Central Europe	6882.19 (5516.1 to 8478.25)	6842.26 (5514.64 to 8425.25)	-0.01 (-0.04 to 0.02)	19.8 (17.88 to 21.6)	20.28 (17.53 to 22.64)	-0.04 (-0.83 to 0.75)	333 (294.58 to 380.42)	329.79 (283.05 to 383.05)	0.05 (-0.42 to 0.53)
Central Latin America	6239.1 (4995.9 to 7738.41)	5974.37 (4779.45 to 7389.36)	-0.14 (-0.18 to -0.1)	5.75 (5.2 to 6.22)	3.17 (2.71 to 3.58)	-1.97 (-2.41 to -1.53)	116.93 (92 to 156.57)	78.24 (57.39 to 113.28)	-1.33 (-1.6 to -1.07)
Central Sub-Saharan Africa	4738.99 (3780.08 to 5915.37)	4878.86 (3900.97 to 6092.94)	0.1 (0.07 to 0.13)	9.05 (3.92 to 18.12)	13.22 (6.81 to 24.88)	1.23 (1.04 to 1.42)	176.44 (87.45 to 321.85)	239.86 (134.19 to 422.78)	0.99 (0.85 to 1.14)
East Asia	7419.34 (5989.84 to 9092.91)	7857.42 (6361.87 to 9610.32)	0.15 (0.1 to 0.2)	0.74 (0.53 to 0.94)	0.95 (0.74 to 1.21)	0.74 (0.49 to 0.99)	64.71 (34.02 to 117.44)	60.48 (33.65 to 106.82)	-0.26 (-0.36 to -0.16)
Eastern Europe	7075.7 (5682.95 to 8721.65)	7805.4 (6278.91 to 9591.59)	0.32 (0.3 to 0.34)	31.5 (27.22 to 36.33)	20.19 (17.36 to 23.26)	-1.45 (-2.16 to -0.74)	514.9 (442.58 to 597.34)	363.84 (314.1 to 424.28)	-1.02 (-1.57 to -0.47)

Table 1 (continued)

Characteristic	ASPR, per 100,000 (95% UI)		AAPC (95% CI)	ASMR, per 100,000 (95% UI)		AAPC (95% CI)	ASDR, per 100,000 (95% UI)		AAPC (95% CI)
	1990	2021		1990	2021		1990	2021	
Eastern Sub-Saharan Africa	4283.64 (3424.83 to 5337.43)	4528 (3613.15 to 5637.58)	0.18 (0.17 to 0.19)	5.98 (2.74 to 12.29)	8.79 (4.99 to 16.63)	1.25 (1.17 to 1.34)	120.15 (61.3 to 217.14)	160.95 (95.51 to 286.57)	0.94 (0.89 to 0.99)
High-income Asia Pacific	11925.52 (9757.39 to 14548.68)	7798.66 (6317.01 to 9569.26)	-1.39 (-1.42 to -1.35)	2.97 (2.53 to 3.25)	2.68 (2.1 to 3.08)	-0.26 (-1.33 to 0.82)	96.95 (63.62 to 154.22)	69.05 (46.88 to 104.15)	-1.17 (-1.4 to -0.93)
High-income North America	16461.03 (13318.23 to 20167.83)	15192.2 (12855.23 to 17819.9)	-0.31 (-0.48 to -0.15)	13.11 (11.37 to 14.13)	12.39 (10.49 to 13.64)	-0.29 (-0.53 to -0.05)	256.19 (210.16 to 325.91)	241.38 (197.54 to 303.53)	-0.26 (-0.43 to -0.08)
North Africa and Middle East	5377.95 (4322.47 to 6681.58)	6409.08 (5154.28 to 7914.94)	0.57 (0.55 to 0.59)	1.31 (0.78 to 2.06)	2.13 (1.54 to 2.87)	1.49 (1.24 to 1.75)	55.11 (32.27 to 91.28)	66.29 (43.6 to 102.76)	0.56 (0.45 to 0.67)
Oceania	6616.56 (5348.43 to 8185.55)	7185.37 (5840.67 to 8839.53)	0.26 (0.24 to 0.28)	0.64 (0.35 to 1.05)	0.76 (0.42 to 1.26)	0.59 (0.42 to 0.75)	57.6 (29.03 to 106.69)	62.03 (31.99 to 113.8)	0.26 (0.22 to 0.31)
South Asia	4989.75 (3996.08 to 6182.87)	5409.58 (4338.19 to 6688.47)	0.25 (0.22 to 0.28)	0.99 (0.51 to 1.58)	1.97 (1.29 to 3.22)	2.53 (1.88 to 3.19)	49.39 (26.73 to 86.06)	61.63 (37.91 to 98.26)	0.7 (0.55 to 0.85)
Southeast Asia	7728.63 (6226.07 to 9493.63)	8315.83 (6695.08 to 10190.63)	0.23 (0.2 to 0.26)	0.57 (0.44 to 0.72)	0.91 (0.69 to 1.2)	1.6 (1.48 to 1.72)	65.21 (33.93 to 119.58)	69.01 (37.77 to 122.77)	0.21 (0.17 to 0.25)
Southern Latin America	10161.8 (8202.58 to 12568.67)	9126.84 (7412.96 to 11255.46)	-0.36 (-0.41 to -0.32)	4.26 (3.71 to 4.75)	3.77 (3.18 to 4.24)	-0.42 (-1 to 0.16)	117.52 (84.17 to 175.09)	98.28 (70.8 to 145.01)	-0.62 (-0.99 to -0.25)
Southern Sub-Saharan Africa	7347.38 (5893.62 to 9046.06)	6645.84 (5344.64 to 8217.53)	-0.34 (-0.35 to -0.32)	8.67 (6.29 to 11.23)	13.53 (11.44 to 15.9)	1.47 (1.27 to 1.67)	182.22 (130.74 to 245.76)	258.31 (214.53 to 311.79)	1.16 (1 to 1.32)
Tropical Latin America	6659.38 (5350.25 to 8226.6)	5804.63 (4658.69 to 7185.95)	-0.45 (-0.48 to -0.43)	10.85 (9.67 to 11.73)	9.54 (8.13 to 10.5)	-0.18 (-0.63 to 0.28)	203.54 (173.52 to 246.31)	179.24 (151.53 to 215.14)	-0.25 (-0.59 to 0.09)
Western Europe	15140.45 (12442.59 to 18411.69)	11351.19 (9257.21 to 13908.23)	-0.93 (-0.96 to -0.89)	16.2 (14.38 to 17.36)	10.93 (9.14 to 12.13)	-1.32 (-1.6 to -1.04)	299.06 (245.63 to 380.81)	200.64 (160.1 to 257.01)	-1.29 (-1.55 to -1.02)
Western Sub-Saharan Africa	4274 (3420.27 to 5324.84)	4708.12 (3773.79 to 5843.46)	0.32 (0.31 to 0.33)	7.24 (3.72 to 14.66)	10.64 (5.71 to 21.3)	1.27 (1.17 to 1.37)	132.69 (71.96 to 240.45)	182.1 (104.65 to 334.06)	1.06 (0.97 to 1.14)

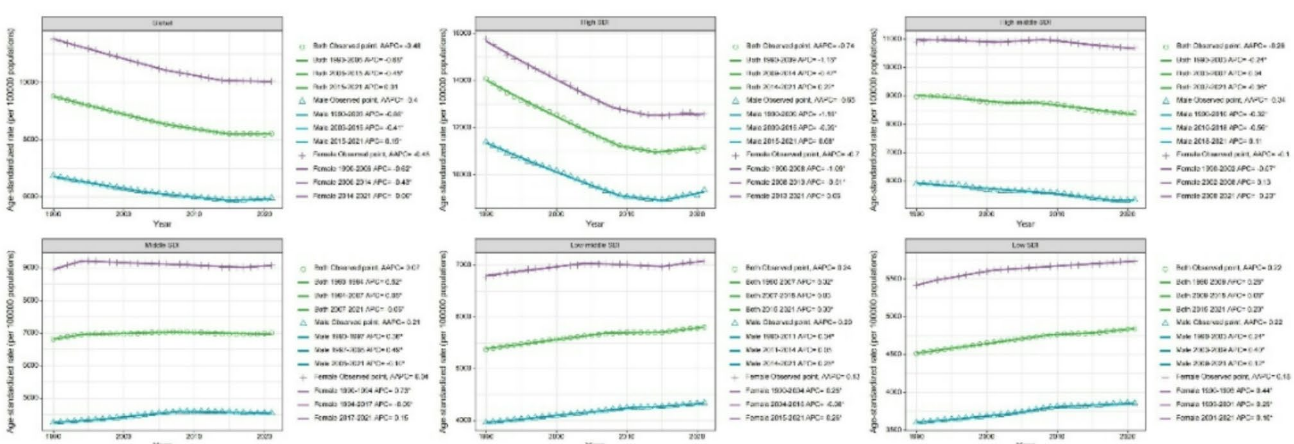

Fig. 1 Joinpoint Regression Analysis of Age-standardized Prevalence Rate of Lower Extremity Peripheral Arterial Disease In Older Adults at the Global and 5 SDI Regions From 1990 to 2021. P-value $*P<0.05$

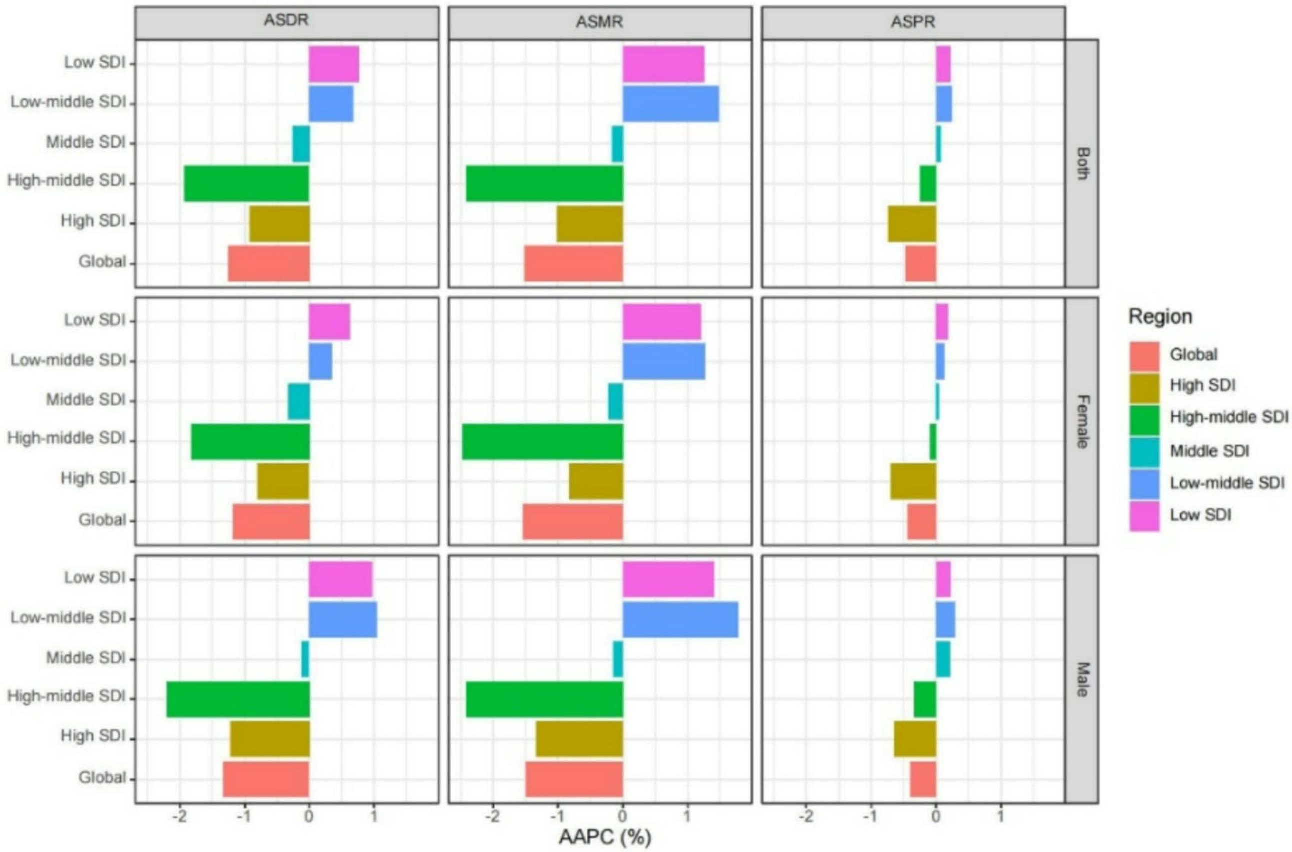

Fig. 2 Average Annual Percent Change of Age-standardized Prevalence, Death, and DALYs Rate From 1990 to 2021 in SDI Regions

from 2013 to 2021. In low-SDI regions, both males and females showed consistent increases throughout the study period, with males showing slightly higher rates of increase in recent years (Supplementary Table 5). The results of the joinpoint regression analyses of the mortality and DALYs of lower extremity PAD at the global level from 1990 to 2021 according to the SDI regions among older adults are shown in Supplementary Table 4 and Figs. 1 and 2.

Regional trends

Regionally, the largest decreases in prevalence of lower extremity PAD from 1990 to 2021 were experienced in High-income Asia Pacific (from 11925.52 to 7798.66 per 100000 population; AAPC, -1.39; 95% CI, -1.42 to -1.35) and Australasia (from 10250.99 to 7301.23 per 100000 population; AAPC, -1.11; 95% CI, -1.13 to -1.09). Although the lower extremity PAD-related prevalence showed a downward trend in many regions from 1990 to 2021, there was still an upward trend in some regions (Supplementary Fig. 3). The largest increase was observed in North Africa and Middle East (from 5377.95 to 6409.08 per 100000 population; AAPC, 0.57; 95% CI, 0.55 to 0.59), followed by Eastern Europe (from 7075.7 to 7805.4 per 100000 population; AAPC, 0.32; 95% CI, 0.3 to 0.34) (Table 1). Significant correlations (all $P<0.01$) were observed between SDI and PAD burden metrics, with prevalence showing strong correlation with SDI($R=0.72$) (Supplementary Fig. 4). The regional mortality and lower extremity PAD-related AAPCs between 1990 and 2021 are shown in Table 1.

At the regional level, the lower extremity PAD-related DALYs showed varying trends from 1990 to 2021, with the most pronounced decline in Australasia (from 383.20 to 181.82 per 100000 population; AAPC, -2.39; 95% CI, -2.57 to -2.22). In 2021, Eastern Europe had the region with the highest DALYs due to lower extremity PAD (363.84 per 100000 population), while Andean Latin America had the lowest (41.04 per 100000 population) (Table 1). The joinpoint regression analysis of lower extremity PAD for the 21 regions is presented in Supplementary Table 6.

National trends

At the national level, the sharpest decline in the lower extremity PAD-related prevalence from 1990 to 2021 was in Japan (from 12245.19 to 8052.29 per 100000 population;

AAPC, -1.38; 95% CI, -1.42 to -1.34) (Figs. 3 and 4). Japan also had one of the lowest lower extremity PAD-related prevalence rates in 2021 among high-income countries. Lebanon showed the most pronounced increase in lower extremity PAD prevalence, rising from 5949.61 to 8000.00 per 100,000 population, with an AAPC of 0.99 (95% CI, 0.96 to 1.02) (Supplementary Table 7). For the lower extremity PAD-related DALYs and mortality from 1990 to 2021, a decreasing trend was observed in most high-income nations, with Sweden showing the fastest pace of decline in mortality (AAPC, -3.91; 95% CI, -4.52 to -3.30). Contrastingly, Georgia showed a markedly increasing trend in mortality (AAPC, 14.45; 95% CI, 6.48 to 23.02) (Supplementary Table 7). The joinpoint regression results for the

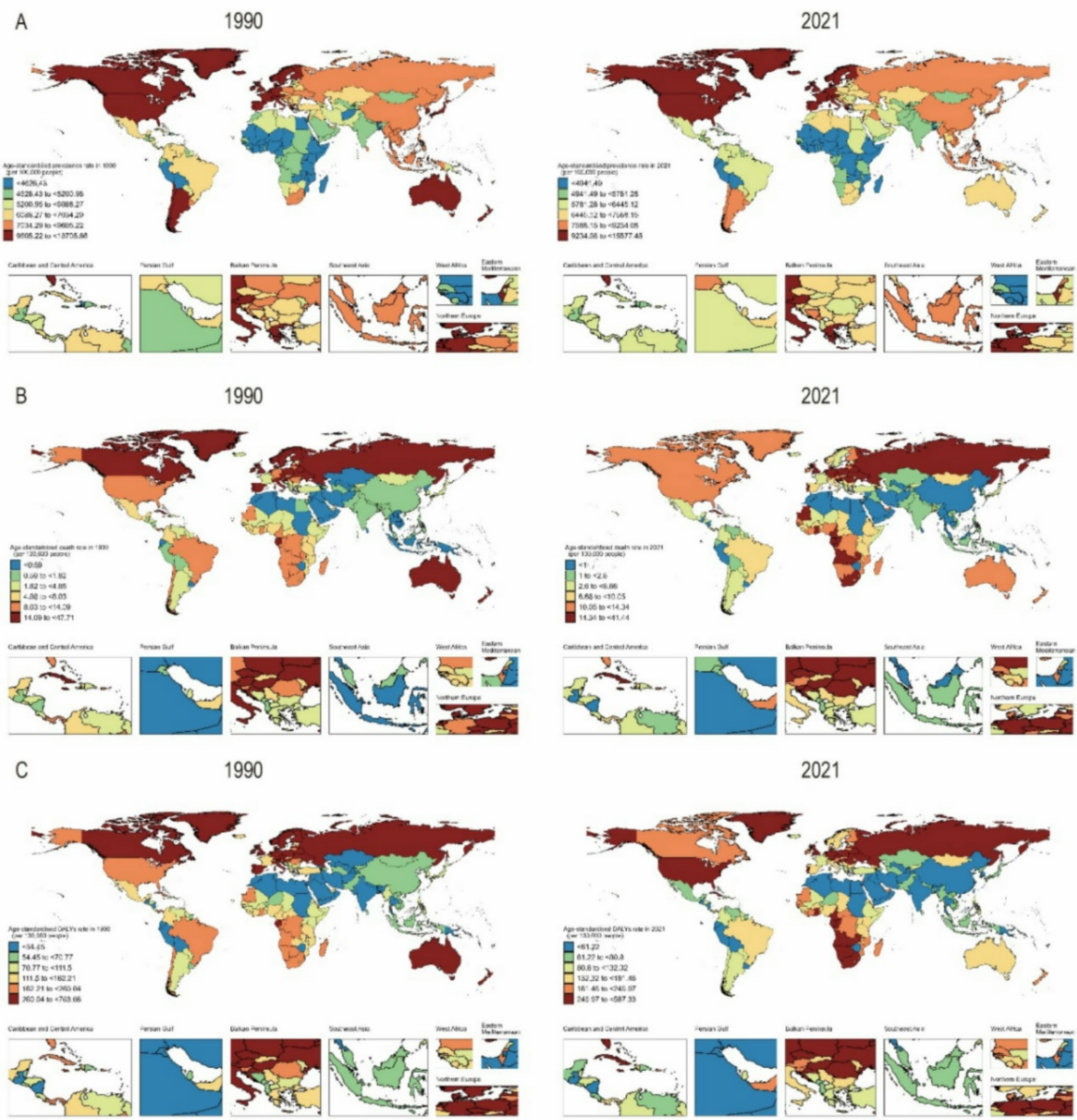

Fig. 3 Maps Showing (**A**) Age-standardized Prevalence, (**B**) death, and (**C**) DALYs Rate of Lower Extremity Peripheral Arterial Disease In Older Adults, in 204 Countries and Territories, Between 1990 and 2021

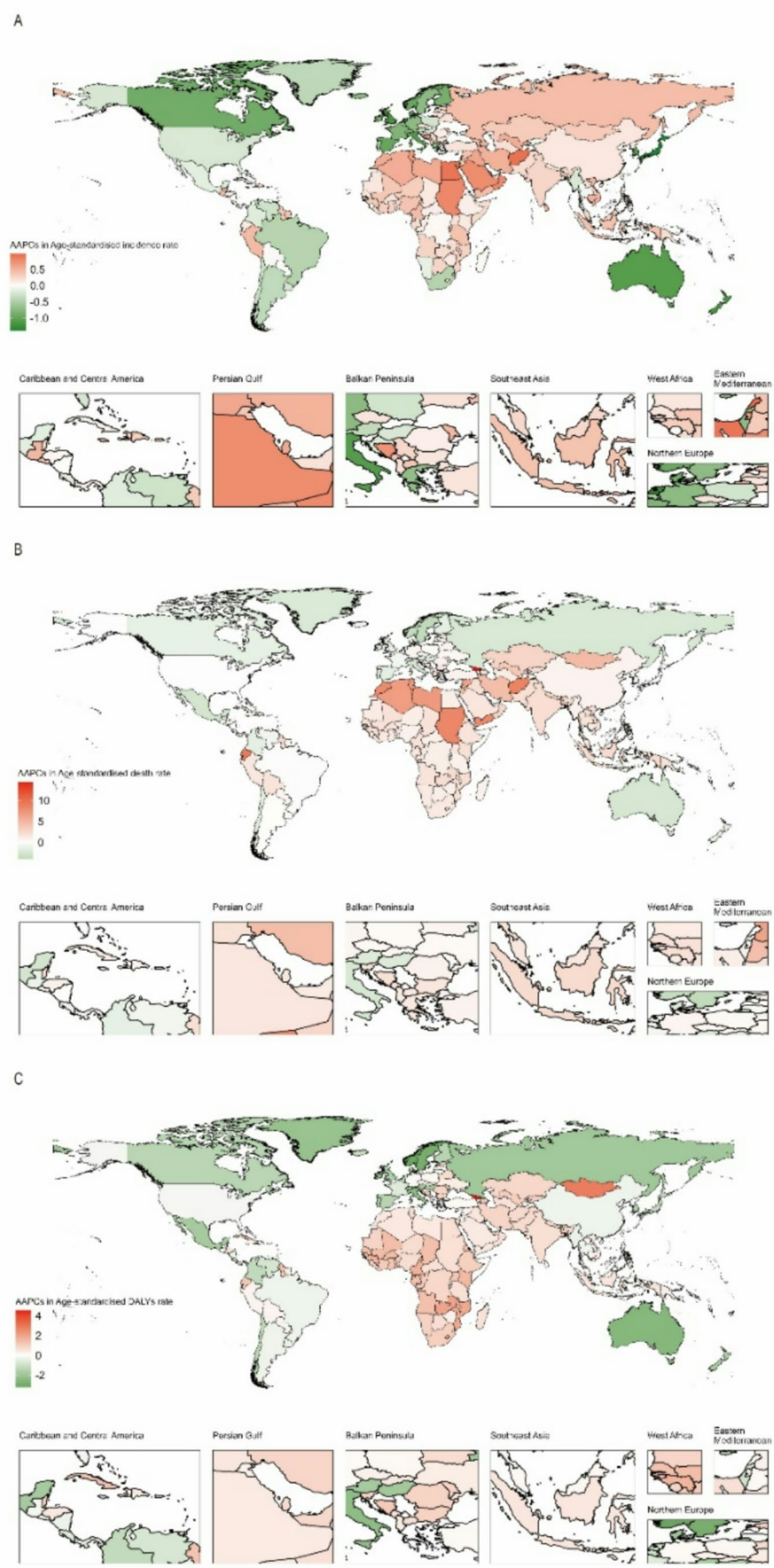

Fig. 4 World Map of AAPCs in (**A**) Age-standardized Prevalence, (**B**) Deaths, and (**C**) DALYs Rate of Lower Extremity Peripheral Arterial Disease In Older Adults From 1990 to 2021. AAPC, average annual percentage change

national lower extremity PAD prevalence, mortality, and DALYs are shown in Supplementary Table 8.

Decomposition analysis

From 1990 to 2021, a substantial increase in PAD burden was observed globally, with the highest increase detected in low-middle SDI regions. Population growth was the primary driver, accounting for 110.75% of the global change in DALYs, while aging and epidemiological changes contributed 14.03% and −51.82%, respectively. Notably, negative epidemiological effects were observed in high, high-middle, and middle SDI regions, while positive epidemiological changes were seen in low and low-middle SDI regions, suggesting disparities in disease prevention and management across development levels. This pattern highlights significant global health inequities in PAD management, where higher SDI regions have successfully implemented interventions to offset demographic pressures, while lower SDI regions face the combined challenge of growing populations, progressive aging, and deteriorating disease control mechanisms (Fig. 5 and Supplementary Table 9).

Risk factors

The age-standardized DALYs rate of peripheral artery disease attributable to all risk factors in 2021 varied across SDI regions globally (Fig. 6). Smoking remained a significant risk factor, with global DALYs of 21.2% in 2021, showing a decrease from 27.3% in 1990. High fasting glucose emerged as the leading risk factor, with global DALYs reaching 38.4% in 2021, markedly increased from 22.3% in 1990. High blood pressure contributed to 13.2% of global DALYs in 2021, slightly decreased from 14.1% in 1990. Kidney dysfunction accounted for 29.9% of global DALYs in 2021, comparable to 29.8% in 1990. Diet high in sodium and lead exposure showed relatively low contributions, with global DALYs of 0.7% and 0.6% respectively in 2021. Across SDI regions, high SDI areas demonstrated the most substantial changes, particularly in smoking (decreased from 32.4 to 23.3%) and high fasting glucose (increased from 22.6 to 42.8%). Low SDI regions showed persistent challenges with high fasting glucose (increased from 23.1 to 36.8%) and kidney dysfunction (slight increase from 28 to 28.6%) (Fig. 6).

Discussion

To our knowledge, this study presents the first systematic analysis examining the global burden of lower extremity PAD among older adults across diverse sociodemographic contexts from 1990 to 2021. While our analysis demonstrates an overall decline in global PAD burden, the findings highlight critical variations in disease distribution and impact across different regions and SDI levels, suggesting complex underlying patterns that warrant targeted interventions. These trends indicate that PAD burden may remain

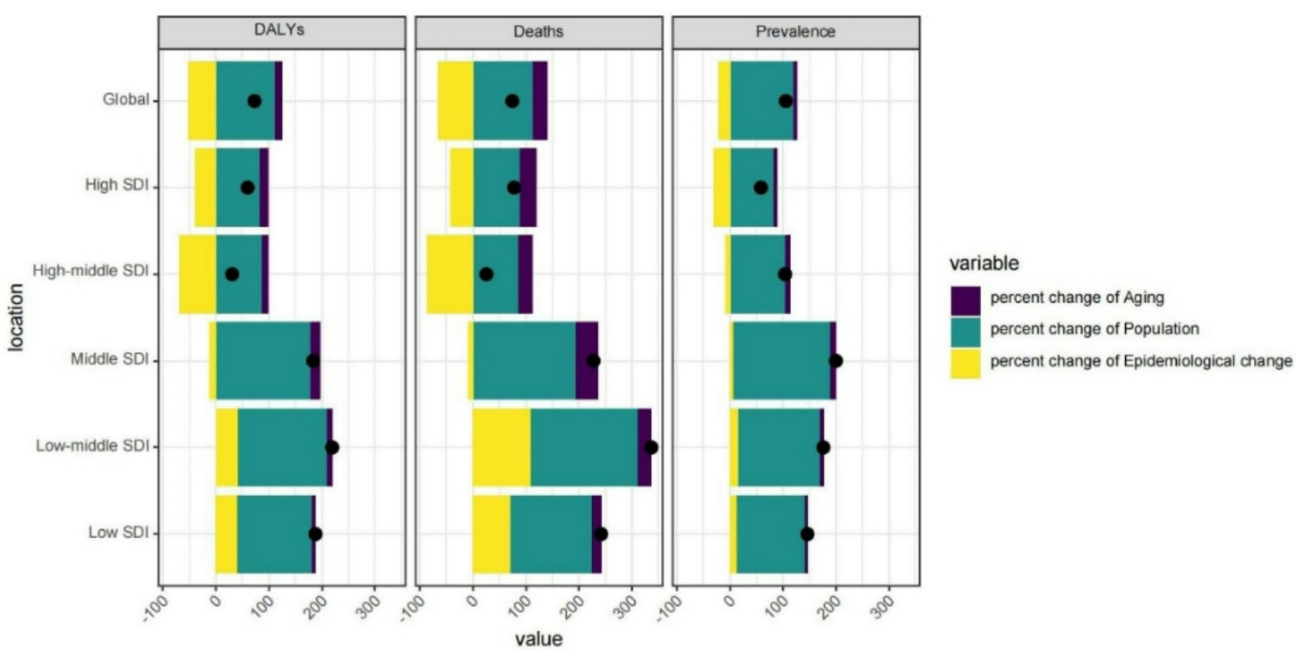

Fig. 5 Changes in Prevalence, Deaths, and DALYs Percentage Change of Lower Extremity Peripheral Arterial Disease In Older Adults According to Population-level Determinants of Population Growth, Aging, and Epidemiological Change From 1990 to 2021 Globally and 5 SDI regions

Fig. 6 Age-standardized DALYs Rate of Lower Extremity Peripheral Arterial Disease In Older Adults Attributed to Risk factors Between 1990 and 2021

a substantial challenge, particularly in low-SDI regions, emphasizing the urgent need for developing tailored prevention strategies and strengthening healthcare systems to address this growing public health concern [1, 30–32].

Notably, our findings reveal a striking disparity in elderly PAD burden across different socioeconomic contexts, highlighting significant global health inequities that demand immediate attention, particularly as UN projections indicate that one in six people globally will be over age 65 by 2050, amid unprecedented global economic challenges of inflation and monetary tightening that strain healthcare budgets [33, 34]. Most concerning is the divergent trend between high- and low-SDI countries, where high-SDI regions, despite having the highest burden with a prevalence of 11,171.66 per 100,000 in 2021, demonstrated a consistent decline (AAPC, -0.74). This apparently high burden in high-SDI regions can be attributed to increased metabolic stress (i.e., hypertension and hyperglycemia) and enhanced disease detection capabilities in their elderly populations [35], while the declining trend reflects the success of comprehensive geriatric care systems and age-friendly healthcare policies, though increasingly challenged by healthcare worker shortages and burnout in the post-pandemic era [36, 37]. The analysis of risk factors further illuminates these patterns, with high-SDI regions showing notable success in reducing smoking-attributable DALYs (from 32.4 to 23.3%) while facing growing challenges from high fasting glucose (increased from 22.6 to 42.8%).

In stark contrast, low-SDI regions, while showing the lowest prevalence, experienced a troubling upward trend (AAPC, 0.22), coupled with persistent challenges in managing key risk factors, particularly high fasting glucose and kidney dysfunction. This seemingly low burden likely masks significant underdiagnosis of mild or asymptomatic PAD in elderly populations, particularly concerning as developing nations face difficult trade-offs between healthcare investment and debt management amid rising interest rates and currency depreciation affecting medical equipment and pharmaceutical import costs. The decomposition analysis reveals that this trend is primarily driven by population growth and aging, particularly pronounced in low-middle SDI regions (contributing 201.12% to death increases), coupled with positive epidemiological changes, suggesting inadequate adaptation of healthcare systems to aging populations [38]. This disparity becomes even more pronounced when examining mortality rates, where high-middle SDI countries achieved substantial improvements (AAPC, -2.42) through robust elderly care infrastructure, while low-middle SDI countries faced increasing mortality (AAPC, 1.49) amid struggles to establish comprehensive geriatric care systems and maintain healthcare workforce stability [39]. Factors associated with lower socioeconomic development, such as insufficient access to elderly-specific care, inadequate long-term care facilities [39], and suboptimal conditions for healthy aging, may contribute to this increased disease burden and mortality, exacerbated by the current global economic headwinds affecting healthcare system investments.

The temporal analysis further reveals a statistically significant pattern in high-SDI countries, where the initial steady decline in prevalence from 1990 to 2014 has recently shifted towards a slight but meaningful increase (APC, 0.22; 95% CI, 0.18 to 0.26; $P<0.001$), particularly among elderly males (APC, 0.68; 95% CI, 0.59 to 0.77; $P<0.001$), reflecting the emergence of "super-aged societies" amid intensifying healthcare budget pressures [40]. This increase translates to approximately 15,000 additional PAD cases annually in the elderly population of high-SDI countries, potentially increasing the clinical burden of complications and interventional procedures by 8–12%. While aging contributed significantly to PAD burden (attributable risk ratio 2.34, 95% CI, 2.11 to 2.57), these patterns reflect not only the complex interplay of healthcare access and preventive strategies but also the unprecedented demographic transition occurring globally. This transition, characterized by rapid population aging alongside industrialization and urbanization, particularly challenges developing nations facing the dual burden of establishing elderly care infrastructure while managing increasing metabolic risk factors, a situation complicated by current inflationary pressures on healthcare delivery costs [41, 42]. Our regression models demonstrate that each 5-year increase in population age corresponds to a clinically significant 18.7% (95% CI, 16.2–21.3%; $P<0.001$) higher risk of PAD-related complications requiring intervention. Collectively, these findings suggest that while the global burden of elderly PAD is increasingly shifting toward resource-limited settings, with population aging and growth being primary drivers, new challenges are emerging even in developed regions' elderly care systems, necessitating healthcare system resilience building in the post-pandemic era. The clinical significance of these trends is substantial, as our analysis indicates that implementation of targeted screening programs could prevent an estimated 22.4% (95% CI, 18.7–26.1%) of major adverse limb events in high-risk elderly populations. This necessitates tailored, age-specific interventions that address both the resource disparities and the evolving disease patterns across different socioeconomic contexts, particularly crucial as nations worldwide navigate economic uncertainties while implementing aging-related sustainable development goals and healthcare system strengthening initiatives.

Building upon these socioeconomic patterns, particularly the challenges faced by low-middle SDI countries, our regional analysis reveals concerning geographic disparities in elderly PAD burden, particularly in North Africa and Middle East where prevalence increased significantly, followed by Eastern Europe, regions currently facing heightened economic pressures from global inflation and regional geopolitical tensions affecting healthcare investments [43–45]. Several potential mechanisms may explain the increasing trends in PAD burden in North Africa and Middle East. First, these regions are experiencing rapid epidemiological transitions characterized by increasing prevalence of metabolic risk factors, particularly diabetes mellitus and obesity, driven by urbanization and adoption of Western dietary patterns high in refined carbohydrates and saturated fats [46, 47]. Second, tobacco consumption, including traditional water pipe smoking, remains highly prevalent in many countries across this region, contributing to accelerated atherosclerotic disease progression [48, 49]. Finally, regional healthcare systems face structural challenges in implementing comprehensive vascular screening programs for aging populations, particularly in countries experiencing economic instability or conflict [50–52]. In contrast, High-income Asia Pacific demonstrated remarkable progress, achieving the largest reduction in PAD prevalence, followed by Australasia. These improvements, particularly noteworthy given these regions' status as "super-aged societies" and recent challenges with post-pandemic healthcare system recovery and workforce shortages, exemplify how robust healthcare infrastructure and systematic preventive strategies can effectively mitigate the impact of population aging on chronic disease burden. The strong correlation between SDI and PAD burden ($R=0.72$) provides crucial context for these regional patterns, suggesting that while higher SDI regions may show elevated prevalence partly due to enhanced detection capabilities, they are better equipped to manage and reduce disease burden amid ongoing global economic headwinds. This interpretation requires careful consideration when examining regional extremes - from Eastern Europe's highest DALYs to Andean Latin America's notably low burden in 2021 - as these disparities likely reflect not only true differences in disease burden but also variations in diagnostic capabilities and healthcare access, particularly in regions struggling to establish comprehensive geriatric care systems amid rising medical equipment costs and currency depreciation pressures. Australasia's substantial improvement in DALYs (AAPC, -2.39) further validates the effectiveness of comprehensive elderly care approaches, though even successful regions face emerging challenges in maintaining healthcare workforce stability and system resilience in the post-pandemic landscape. These regional disparities ultimately highlight how the effective implementation of elderly PAD management remains heavily influenced by healthcare system maturity and socioeconomic resources, suggesting the need for targeted, region-specific interventions that account for varying levels of healthcare system development and economic constraints in an increasingly challenging global economic environment.

At the national level, detailed analysis reveals notable country-specific patterns that reflect complex interactions between healthcare systems, demographics, and socioeconomic factors. Japan demonstrated the most significant decline in PAD prevalence [53], attributable to its comprehensive universal healthcare coverage, systematic screening programs, and strong primary care infrastructure, despite having one of the world's most aged populations [40]. In contrast, Lebanon's marked increase in prevalence reflects the combined impact of rapid population aging, regional economic instability affecting healthcare investments, and disrupted healthcare delivery systems. The stark contrast in mortality trends between Sweden further illustrates how healthcare system maturity influences outcomes [54]. Sweden's success can be attributed to its well-established elderly care infrastructure, comprehensive vascular screening programs, and sustained healthcare workforce stability [54, 55]. Georgia's increasing trend, conversely, reflects the challenges of healthcare system transition, limited specialized vascular care access, and economic constraints affecting medical technology adoption and preventive care implementation. These national variations underscore how differences in healthcare policy prioritization, system resilience, and economic resources shape PAD outcomes in aging populations.

Limitations

Several limitations should be noted. First, data availability constraints meant some regions relied heavily on GBD 2021 statistical modeling techniques rather than raw data. While modeling methods continue to improve, better raw data collection remains essential for accurate estimation. Second, healthcare system limitations in resource-constrained regions may have led to misdiagnosis and underdiagnosis of PAD, potentially underestimating the true disease burden. Third, variations in diagnostic capabilities and access to vascular specialists across different regions could affect the consistency of PAD diagnosis and reporting. Fourth, despite analyzing trends in adults aged 60 years and older, our study could not account for the impact of specific healthcare infrastructure and treatment accessibility on outcomes. Additionally, the GBD 2021 database limitations prevented analysis of certain socioeconomic factors that might influence PAD development and progression, and sensitivity analysis are needed to validate their utility in the future.

Conclusions

Our analysis revealed marked disparities in lower extremity PAD burden, with low-SDI regions experiencing increasing trends despite lower prevalence rates. This pattern highlights critical healthcare inequities that require urgent attention. The shift in risk factor patterns, particularly the rise of high fasting glucose and decline in smoking, suggests evolving challenges in disease prevention and management. Moving forward, it is essential to incorporate these findings into global health strategies and sustainable development frameworks. Countries must collaborate to implement targeted interventions in resource-limited settings, focusing on strengthening preventive measures and improving healthcare accessibility for older adults. Additionally, addressing modifiable risk factors through comprehensive disease management strategies will be crucial in reducing the growing burden of lower extremity PAD across different socioeconomic settings.

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Author contributions All authors have made substantial contributions to this study. Xiaohan Qiu Conceptualization, Supervision, Funding acquisition, Writing-review & editing; Xiaohan Qiu and Ben Hu Data Curation, Writing-original draft preparation, Writing-review & editing, Visualization, Software; Jiahan Ke, Min Wang.and Huasu Zeng. Writing-review & editing.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Ethical approval This study utilized secondary data from the Global Burden of Disease (GBD) database, which is publicly available and contains aggregated, anonymized data. The GBD database is maintained by the Institute for Health Metrics and Evaluation (IHME) and adheres to international ethical standards for data collection and reporting.

Consent declaration The data used in this study were obtained from the Global Burden of Disease (GBD) database, which contains aggregated population-level information. No individual patient data were accessed or analyzed in this research. The GBD data are collected by the Institute for Health Metrics and Evaluation (IHME) through multiple sources following appropriate consent procedures where applicable. As this study involved secondary analysis of anonymized, publicly available data, individual informed consent was not required.

Competing interests The authors declare no competing interests.

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