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# Metabolic and behavioural risk factors for cardiovascular diseases in Southern Latin America: analysis of the Global Burden of Disease 1990–2019

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ABSTRACT

*Objectives:* Cardiovascular diseases (CVDs) are the leading causes of global mortality. Modifiable behavioural and metabolic risk factors significantly contribute to the burden of CVD. Given the vast socio-demographic and health outcome heterogeneity in Latin America, similar southern Latin American countries (Argentina, Chile, and Uruguay) were analysed as a distinct group to describe the CVD death rates related to metabolic and behavioural risk factors.
*Study design:* An ecological study was performed using data from the Global Burden of Disease Study 2019.
*Methods:* Metabolic and behavioural risk factors-related CVD death were examined by analysing age-standardised rates per 100,000 individuals in the three countries between 1990 and 2019.
*Results:* While exposure to behavioural risk is decreasing, an upwards trend was observed in metabolic risks. Among the assessed risk factors, metabolic factors emerged as the primary contributors to deaths. High fasting plasma glucose exhibited a remarkable increase in relative importance across most studied contexts. Dietary risks stood out among behavioural factors due to their complexity and substantial changes observed. Although mortality rates have declined for overall CVD, peripheral artery disease mortality is rising.
*Conclusion:* Modifiable behavioural and metabolic risk factors significantly influence CVD mortality in Southern Latin America. Despite the increasing exposure to metabolic risks, advancements in prevention and treatment are evidenced in the decline of mortality rates for most CVD. These findings emphasise the need for targeted interventions and comprehensive strategies to address their impact on cardiovascular health, advocating for healthy lifestyle behaviours to mitigate the progression and CVD development.


## Introduction

Cardiovascular disease (CVD) is a leading cause of mortality worldwide, responsible for almost one-third of all deaths.[1] Over the past 30 years, the prevalence of CVD has significantly increased.[2] In 2019, ischaemic heart disease (IHD) accounted for 49.2% of all

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cardiovascular-related deaths,[3] making it the most prevalent form of CVD.[1] Stroke is the second-leading cause of death globally, with most incident strokes being ischaemic (IS) in aetiology.[4] Between 1990 and 2019, IS-related deaths increased from 2.04 million to 3.29 million across the globe and are projected to reach 4.9 million by 2030.[5] Peripheral artery disease (PAD), while often overlooked (especially in countries with lower socioeconomic development),[6] is a crucial component of CVDs. Despite accounting for just 74,100 deaths worldwide,[6] PAD can significantly impact the quality of life due to the increased risk for limb amputation;[7] indeed, among the various forms of CVDs, PAD is associated with the most significant reduction in the quality of life.[8]

While recent studies have explored the impact of non-traditional cardiovascular risk factors, such as air pollution,[9] metabolic and behavioural risk factors remain the major contributors to CVD.[3] Additionally, socio-demographic factors have been highly associated with CVD;[2,10] for instance, the Socio-demographic Index (SDI)—as a composite indicator of income per capita, average educational attainment, and fertility rates under 25 years of age—has been used to assess its association with CVD mortality. Remarkably worse scenarios were found in countries with lower SDIs.[2] Indeed, at least three-quarters of premature mortality due to CVDs occurs in low- and middle-income countries, which is the case in most South American countries.[11]

Although South American countries are often grouped in the literature, they are heterogeneous,[12] and their health outcomes can vary among these countries due to differences in poverty levels, health education, publicly available healthcare systems, and resources.[12] Disparities are also evident in per-capita gross domestic product (GDP) and health expenditures. For instance, Bolivia reported a per-capita GDP of $USD 3,523, whereas Uruguay reported it as $USD 20,795 in 2022. Health expenditure as a percentage of GDP also varies, with Venezuela spending only 2.19% on health care compared to Argentina's 9.5%. Moreover, life expectancy at birth differs among countries, with Bolivia at 64 years and Chile at 79 years in 2021.[13]

In the context of understanding epidemiological transitions, the Global Burden of Disease (GBD) study[14] has grouped Argentina, Chile, and Uruguay to form the Southern Latin America (SLA) region, which is part of their high-income super-region. These countries exhibit similarities in various aspects, such as income levels, health expenditure (ranging from 9.33 to 9.47% of GDP),[13] high life expectancy (ranging from 75 to 79 years),[13] and the implementation of relevant health public policies, such as the food-front-labelling laws. Analysing Argentina, Chile, and Uruguay as a distinct group makes assessing their health outcomes easier and allows meaningful comparisons with other countries or regions, such as the USA or Europe. Therefore, this study aimed to describe the burden of CVD deaths attributable to metabolic and behavioural risk factors and their evolution over the years in these three South American countries: Argentina, Chile, and Uruguay.

## Methods

### *Data source*

Data for this study were obtained from the GBD 2019 edition via the online Global Health Data Exchange (GHDx) query tool (available at http://ghdx.healthdata.org/gbd-results-tool).[14] This tool enables the generation of standardised reports by applying filters such as location, time (1990–2019), age, and sex. The GBD initiative is a comprehensive effort that systematically quantifies the magnitude of major diseases, risk factors, and clinical outcomes.[15] To estimate the exposure to specific risk factors contributing to CVD, the GBD initiative utilises a diverse range of data sources, including published studies, household surveys, censuses, administrative data, ground monitor data, or remote sensing.[10] The methodology used by GBD for estimating the CVD burden due to specific risk factor exposures has been described in seven steps: 1. effect size estimation; 2. exposure estimation; 3. the theoretical minimum risk exposure level (TMREL), 4. estimate population-attributable fractions; 5. estimate summary exposure values (SEV); 6. mediation; and 7. estimate attributable burden. Each step has been previously described in detail elsewhere.[10]

### *GBD database analyses*

Countries grouped by GBD in the SLA, which is part of the "high-income" super-region: Argentina, Chile, and Uruguay were included. Data were analysed as a region and for each country separately.

Data regarding CVDs (overall), IHD (International Classification of Diseases [ICD-10] codes: I20–I25.9), stroke (ICD-10 codes: G45-G46.8, I60–I63.9, I65–I66.9, I67.0-I67.3, I67.5-I67.6, I68.1-I68.2, I69.0-I69.3), and PAD (ICD-10 codes: I70.2-I70.8, I73–I73.9) were obtained from GHDx. The study assessed various risk factors for these outcomes, including i) metabolic risks: overall, high body mass index (BMI), high fasting plasma glucose (FPG), high low-density lipoprotein (LDL) cholesterol, high systolic blood pressure (SBP) and kidney dysfunction and ii) behavioural risks: overall, alcohol use, dietary risks (overall and their derivatives), low physical activity, and tobacco use. To simplify the explanation of the results, the dietary-derived risk factors were classified into "high-in" diets (a diet high in sodium, processed meat, sugar-sweetened beverages, trans fatty acids, and red meat) and "low-in" diets (a diet low in nuts and seeds, seafood omega-3 fatty acids, poly-unsaturated fatty acids, legumes, fruits, vegetables, whole grains, and fibre). Also, even though tobacco includes primary smoking, second-hand smoke, and chewing tobacco, it was considered as an overall measure. This classification and the three-level risk factors hierarchy are shown in Supplementary Figure 1.

### *Statistical analyses*

Data are presented for both sexes, including overall categories and individual risk factors. Rates are expressed per 100,000 individuals, age-adjusted, and with 95% uncertainty intervals (UIs). Three measurements were obtained: death rate per cause, SEV per risk factor studied, and cardiovascular mortality rate attributable to each risk factor when above the TMREL, which has been extensively described elsewhere.[10]

The SEV is a standardised measure that quantifies exposure to a risk factor on a scale from 0 to 100 and compares the distribution of excess risk times' exposure level to a population where everyone is at maximum risk; 0 indicates a minimal risk for everyone, whereas 100 implies the entire population is at maximum risk.[10]

The relative percentage change in mortality over the study period was calculated by comparing the mean death rate of the 1990–1994 and 2015–2019 periods. The 95% confidence intervals (CIs) for the relative change were also calculated using the delta method. To describe changes over time in the relative importance of each risk factor for each cause of death, lines depicting ranking evolution were created for comparing risk factors every five years. R version 4.3.1 (R Core Team) was used for analyses and data visualisation, where packages "ggplot2" and "CGPfunctions" were used.

## Results

### *Overview of mortality and exposure to risk factors*

In 2019, the CVD mortality rate in the SLA region was 166.2/100,000 individuals (95% UI: 152.1–175.0). Among the countries,

Argentina (183.9 [95% UI: 168.9–194.1]) had the highest CVD mortality rate, followed by Uruguay (161.6 [95% UI: 146.4–170.6]) and Chile (126.8 [95% UI: 113.6–134.6]). Fig. 1 shows the mortality rates in 2019 per each cause of death. Regarding the relative death rate differences over time, PAD showed an overall death rate increase of 50% (95% CI: 47.6–52.3) in both sexes in Chile, reaching 1.21 (95% UI: 0.57–2.24) in 2019. Absolute and relative changes over time in mortality for overall CVDs and each disease studied are depicted in Supplementary Figure 2.

High BMI (68.2% [95% CI: 63.0–73.3]), high FPG (62.3% [95% CI: 54.1–70.5]), and overall metabolic risk (54.8% [95% CI: 49.9–59.7]) were among the top three risk factors with the highest relative increase in exposure in the region. However, the risk factors with the greatest exposure levels showed lower relative changes: a diet high in red meat with a relative change of 5.6% (95% CI: 5.2–6.1), low in whole grains (−8.1%; 95% CI: -8.8 to −7.2), and low in legumes (−6.4%; 95% CI: -7.6 to −5.3) (Fig. 2).

*CVD death rate attributed to risk factors*

Metabolic risk factors (1st level) emerged as the major mortality driver for overall CVDs (Fig. 3) and for each assessed individual disease (Supplementary Figures 3 to 5), with no variation across the years. The mortality rates for overall CVDs in 2019, attributable to first-level metabolic and behavioural risk factors, are presented in Table 1. Also, the top three metabolic and behavioural risk factors are shown in Supplementary Tables 1 and 2, respectively.

When analysing the changes from 1990 to 2019, high FPG stood out due to its increasing relative importance on overall CVD mortality rates, particularly among males (Fig. 3). In Chile, considering both sexes, it soared from the 8th to the 5th position, in Uruguay, from the 14th to the 6th position, whereas in Argentina, this trend was mainly observed among males. Similar trends were identified for each disease when assessed individually (Supplementary Figures 6 to 14 and Supplementary Table 3). Additionally, relative to overall CVD deaths attributable to third-level dietary risk factors, the SLA region experienced changes characterised by a decrease in the relative importance of several “low-in” diets and a rise in the importance of some “high-in” diets (Fig. 3). For instance, among females, the relevance of a diet low in whole grains, fibre, seafood omega-3 fatty acids, and polyunsaturated fatty acids decreased. In contrast, the relative importance of a diet high in sugar-sweetened beverages increased. Among males, diets low in whole grains, legumes, fruits, seafood omega-3 fatty acids, and polyunsaturated

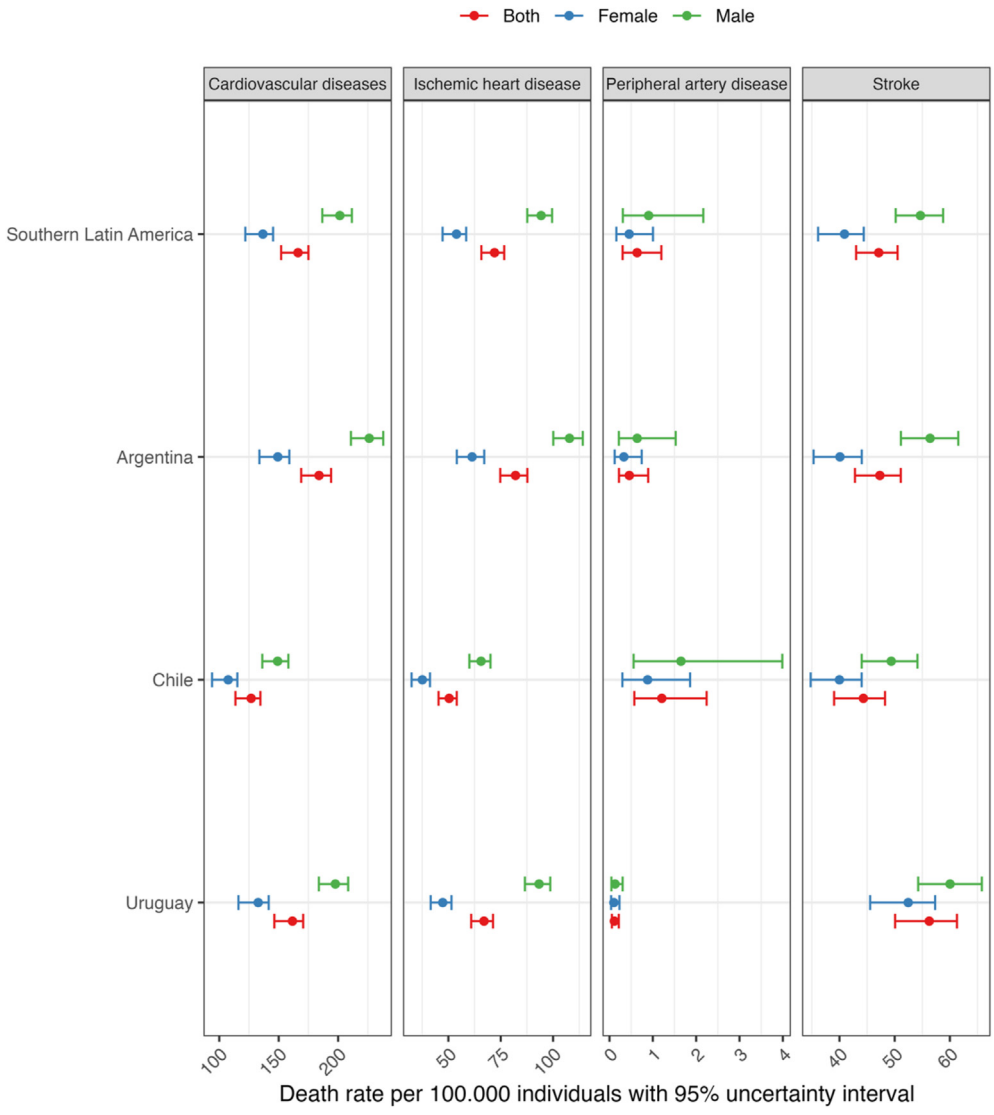


**Fig. 1.** Cardiovascular death rate per cause in 2019. Age-standardised death rate per cause in 2019 for Southern Latin America as a group and for each country studied separately.

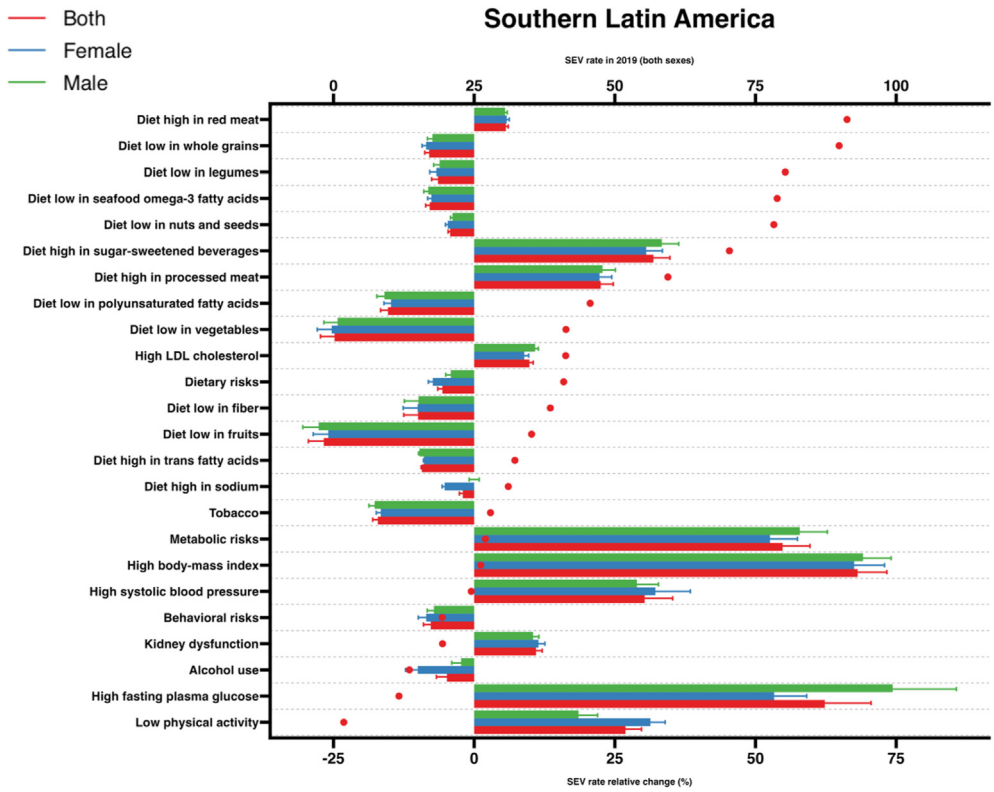


**Fig. 2.** Summary exposure value (SEV) for each risk factor. SEV rate relative change (below axis: bars): Relative change in the average SEV for each assessed risk factor over the 5-year periods 1990–1994 to 2015–2019. SEV rate in 2019 for both sexes (above axis: dots).

fatty acids decreased in importance, in contrast with the rise of diets high in sodium, trans fatty acids, and processed meat. The only diets that escaped this rule were those low in nuts and seeds and those high in red meat (both among females). Similar results were found for IHD (Supplementary Figure 3) and for each country analysed separately (overall CVD: Supplementary Figures 6 to 14; IHD: Supplementary Figures 15 to 23).

In addition, there was a notable decrease in the relative importance of tobacco consumption for overall CVD (Fig. 3), IHD (Supplementary Figure 3), stroke (Supplementary Figure 4), and PAD (Supplementary Figure 5). However, among Argentinean and Uruguayan males, tobacco consumption emerged as the most relevant 2nd-level risk factor leading to PAD-related deaths (Supplementary Figures 32 and 38). Few risk factors were associated with mortality in PAD compared to the other CVDs assessed in the present study (Supplementary Figures 5 and 33 to 41).

## Discussion

### *Main findings*

Using GBD data, we investigated the impact of several metabolic and behavioural risk factors on overall CVDs, IHD, stroke, and PAD mortality among SLA countries. Interestingly, although the SEV of metabolic risks is rising, the age-standardised mortality rates have declined. This paradoxical finding may be attributed to the improved access to healthcare services in these countries.[10] However, among the risk factors assessed, metabolic risk factors emerged as primary contributors to deaths, with high FPG standing out for its significant increase in relative importance among most studied contexts. Moreover, dietary risks were notable due to their complexity and substantial changes in associated mortality. A significant decline of over 40% in relative death rates was observed for IHD and stroke. In contrast, PAD warrants attention due to its upwards trajectory in all countries, as well as for the considerable impact of tobacco use on its burden.

### *Implications*

Recently introduced non-statin therapies for lipid-lowering and anti-obesity/anti-diabetes drugs, such as Glucagon-like Peptide 1 receptor agonists (GLP1-RA) and sodium-glucose cotransporter 2 inhibitor, represent exciting advances in preventive cardiology. These developments highlight the importance of interdisciplinary collaboration between endocrinologists, heart failure specialists, and cardiologists in improving individual and population-level health care.[11] International comparisons of CVD burdens are valuable for policymakers in developing strategies to prevent and treat CVDs.[16] Understanding the epidemiological basis of the CVD death burden is critical for prioritising, designing, and implementing preventive strategies, such as the health services technical package HEARTS in the Americas, introduced by the Pan American Health Organization. This initiative suggests a model that reorients the management of hypertension and CVD, aiming to shift the focus from a secondary or tertiary level of care to the primary care setting, where the majority of individuals with hypertension are diagnosed and receive treatment.[17]

Many traditional cardiovascular risk factors assessed in the present study are causally interlinked and associated with other variables, such as age,[18] social determinants of health,[10] multimorbidity, built environment,[18] and overall physical fitness.[19] While certain CVD-related factors, such as air pollution and green space, primarily require policy intervention,[9] the risk factors we have evaluated can also be targeted at the individual level.[3] These

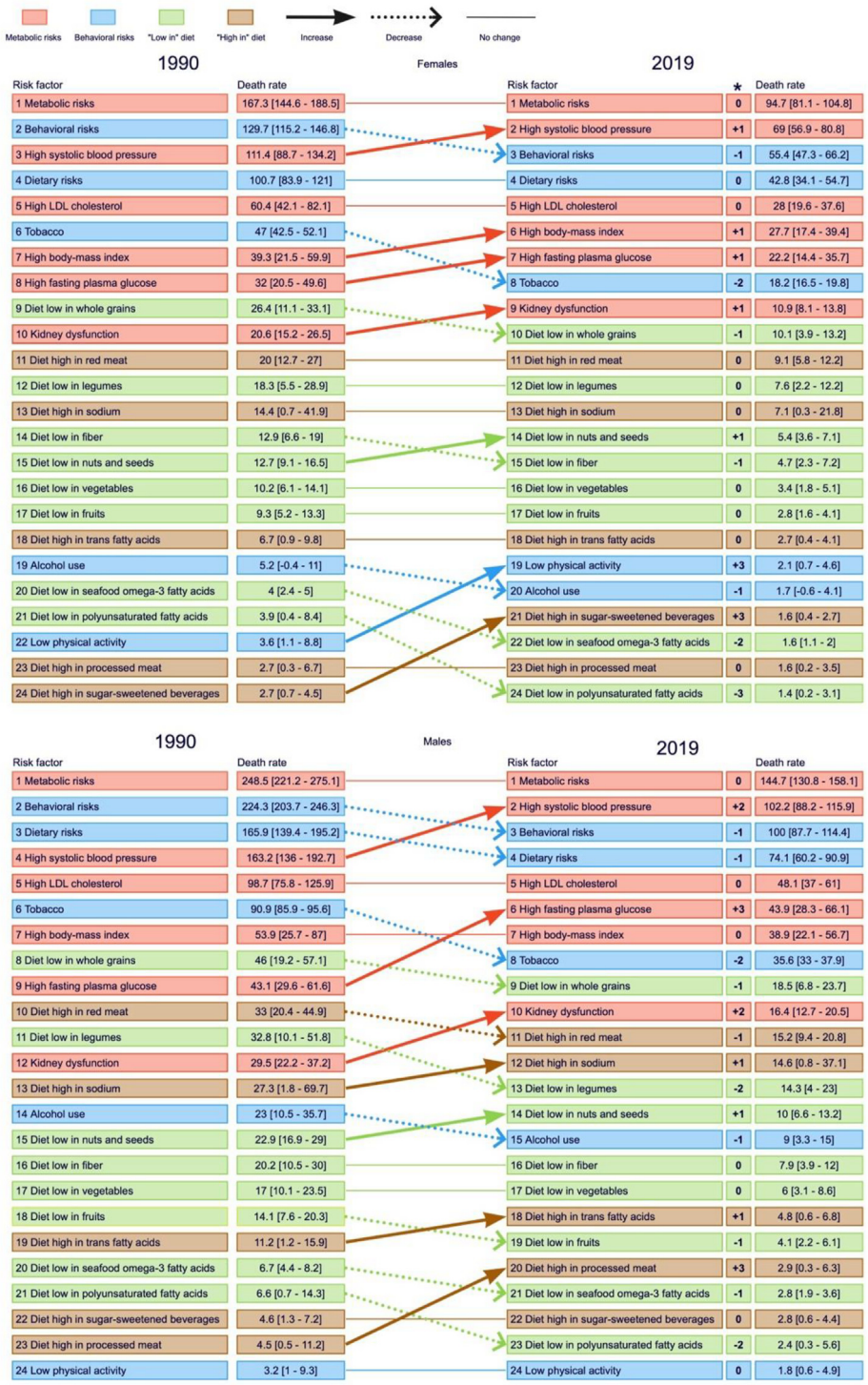


**Fig. 3.** Ranking of risk factors for cardiovascular disease mortality in SLA. Death rate (per 100,000 individuals) with 95% uncertainty interval (95% UI) (*) Change in the "ranking" of risk factor over time. SLA: Southern Latin America.

risk factors are closely interconnected, rather than having a simple additive effect, and targeting multiple risk factors might lead to a synergistic reduction in CVD incidence.

Numerous studies have examined the effectiveness of structured strategies to improve cardiovascular outcomes in patients.[20,21] For instance, some randomised controlled trials have explored non-pharmacological interventions,[20,21] though there is still a scarcity of favourable data. In contrast, the China Rural Hypertension Control Project trial, taking a different approach by assessing a village-based, doctor-led multifaceted intervention, showed promising results for further scaling in low-resource populations.[22,23] However, although lifestyle modifications through nutritional interventions and regular physical activity represent the initial approach to addressing obesity and related CVDs, their feasibility and efficacy may be limited, particularly in the long term. Thus, delaying the beginning of an appropriate pharmacological

**Table 1**
Mortality rates in 2019, per each cause of death, attributable to first-level behavioural and metabolic risk factors.

| Cause of dead | Country | Both | | Female | | Male | |
|---|---|---|---|---|---|---|---|
| | | Behavioural risk | Metabolic risk | Behavioural risk | Metabolic risk | Behavioural risk | Metabolic risk |
| IHD | SLA | 47.63 [41.55–53.44] | 60.18 [53.28–66.27] | 34.52 [29.52–39.32] | 44.53 [37.77–50.12] | 63.36 [55.61–70.49] | 79.3 [71.18–87.35] |
| | Argentina | 54.5 [47.38–61.12] | 67.58 [59.34–74.94] | 39.53 [33.68–45.18] | 50.01 [42.37–56.91] | 72.69 [64–81.17] | 89.33 [79.94–98.75] |
| | Chile | 32.4 [27.8–36.91] | 44.52 [39.33–48.81] | 23.5 [19.65–27.23] | 33.1 [27.87–37.19] | 42.78 [36.71–48.63] | 58.06 [52.09–63.34] |
| | Uruguay | 46.05 [40.49–51.14] | 55.64 [48.92–61.6] | 30.76 [26.11–34.95] | 38.34 [31.79–43.45] | 66.12 [58.65–73.19] | 78.67 [70.41–86.58] |
| Stroke | SLA | 20.78 [17.8–24.46] | 32.2 [27.32–37.3] | 16.37 [13.65–19.48] | 27.48 [22.79–32] | 26.36 [22.48–30.96] | 37.98 [32.69–43.98] |
| | Argentina | 21.76 [18.63–25.52] | 31.32 [26.55–36.3] | 16.76 [13.94–20.01] | 26.14 [21.53–30.72] | 28.19 [24.1–33.1] | 37.81 [31.92–44.31] |
| | Chile | 17.77 [14.39–21.45] | 33.27 [28.15–38.67] | 14.59 [11.64–17.93] | 29.59 [24.35–34.92] | 21.65 [17.5–26.47] | 37.51 [31.89–43.41] |
| | Uruguay | 24.08 [20.43–28.6] | 36.73 [30.21–44.06] | 20.17 [16.58–24.41] | 33.11 [26.41–40.44] | 29.21 [24.86–34.46] | 40.89 [34.53–48.46] |
| PAD | SLA | 0.15 [0.06–0.29] | 0.35 [0.17–0.66] | 0.09 [0.03–0.19] | 0.24 [0.09–0.54] | 0.23 [0.08–0.56] | 0.51 [0.17–1.21] |
| | Argentina | 0.13 [0.06–0.25] | 0.23 [0.11–0.45] | 0.07 [0.03–0.16] | 0.16 [0.06–0.37] | 0.2 [0.07–0.48] | 0.33 [0.11–0.79] |
| | Chile | 0.23 [0.1–0.46] | 0.71 [0.34–1.36] | 0.14 [0.04–0.31] | 0.51 [0.18–1.11] | 0.34 [0.11–0.85] | 0.98 [0.32–2.39] |
| | Uruguay | 0.03 [0.01–0.06] | 0.05 [0.03–0.1] | 0.02 [0.01–0.04] | 0.04 [0.02–0.1] | 0.04 [0.01–0.1] | 0.06 [0.02–0.15] |

SLA: Southern Latin America; IHD: ischaemic heart disease; PAD: eripheral artery disease.

treatment is not advisable if this may rapidly promote beneficial consequences.[24] In this vein, trials of GLP1-RA[25,26] have attracted attention by showing promising results in preventing major adverse cardiovascular events.[24]

### *Comparison with similar results*

Globally, there has been a significant increase in metabolic risks, particularly high FPG and BMI. Surprisingly, despite the expected correlation between high BMI and high LDL cholesterol, the latter has remained constant in recent years, likely due to changes in diet and pharmacological interventions. However, although high SBP is not increasing as quickly as high BMI or high FPG, it has become the foremost risk factor for the global disease burden.[10] This finding was further supported by combining GBD and local data from New Zealand, which also identified high SBP as a priority for preventing health loss associated with CVDs.[27] In this context, stricter blood pressure targets of 110–130 mmHg, compared to 130–150 mmHg, have decreased the incidence of cardiovascular events in elderly patients with hypertension.[28]

Furthermore, there has been a substantial underestimation of PAD-related burden, especially in lower-SDI regions. Indeed, in Western Europe, the age-standardised death rate in 2019 was 1.89 (95% UI: 0.89–3.49), with an increase of 11.02% when comparing 1990 with 2019.[29] This contrasts with the lower rates in the countries assessed in the current study, where Uruguay had the lowest rate of 0.11 (95% UI: 0.06–0.22), yet the leading risks for PAD-related deaths remain similar across these regions.[29]

When comparing with other regions during the same period (1990–2019), the epidemiological changes in age-standardised mortality rates of CVD were heterogeneous across the GBD regions, where high-income Asia Pacific and Australasia experienced the biggest decrease, whereas Oceania, Central Asia, and Western Sub-Saharan Africa have shown stable trends. Additionally, in 2019, Central Asia and Eastern Europe experienced the worst scenarios with rates age-standardised mortality rates of 575.23 and 464.70 (per 100,000 individuals), respectively,[2] far from the rates experienced for Argentina, Chile, and Uruguay.

### *Strengths and limitations*

This study presents an overview of the role played by major modifiable cardiovascular risk factors, enabling comparisons over time in three similar countries, considering sex-related differences and focussing on the most recent data and relevant modifiable risk factors. Nonetheless, the results of this study did not reflect the potential effects of some recent public health policies. For instance, all three countries enacted food-front-labelling laws: Chile in 2012,[30] followed by Uruguay in 2018,[31] and Argentina in 2021.[32] Although implementing these laws can impact people's behaviour and modify the composition of some processed foods,[33] this study did not capture the potential effects of these public health policies.

Furthermore, GBD estimates rely on the availability and quality of primary data. First, regarding the measurement of exposure to risk factors, it is relevant to note that patterns of data availability were non-uniform across geography and over time; in some cases, data collection was performed using less reliable methodologies, such as self-reporting.[10] Second, while high BMI was considered a risk factor, central adiposity could be more effective in predicting and discriminating CVD risk.[34,35] Third, the lack of sub-national information for the assessed countries limits the evaluation of cultural and behavioural differences within large territories, encompassing diverse climates and influences from indigenous communities; this information would be of significant interest, particularly for Argentina and Chile. Finally, new CVD risk factors such as sleep quality, recently included in the American Heart Association's Life's Essential 8, have not been considered in the GBD and may represent a substantial part of the attributable cause for developing CVD.[36] Finally, the present study did not assess the burden of morbidity of the studied pathologies.

### *Conclusion*

Behavioural and metabolic risk factors remain significant contributors to CVD in high-income countries in the SLA region. Over the past 30 years, death rates for IHD and stroke have shown a decline, reflecting advancements in prevention and treatment. However, rates of PAD have exhibited an upwards trend during the same period. High SBP, elevated FPG, and tobacco use continue to be crucial risk factors and main drivers of CVD burden in the region. The changes in exposure to these risk factors underscore the need for targeted interventions and comprehensive strategies to mitigate their impact on cardiovascular health. Efforts should focus on promoting healthy lifestyle behaviours, such as regular physical activity, adopting a balanced diet, and smoking cessation, to mitigate the progression and development of CVD in this population. By targeting these modifiable risk factors, healthcare systems and public health initiatives can work towards reducing the burden of CVD and improving the overall cardiovascular health of individuals in SLA.

## Author statements

### *Ethical approval*

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*Competing interests*

None to declare.

*Contributors*

C.B-V, S.D, and F.P-R contributed to the conception and design of the study. S.D advised on all statistical aspects. C.B-V performed the literature search, the analyses and interpreted the data with the support of S.D and F.P-R. All authors critically reviewed this and previous draughts. All authors approved the final draft for submission. S.D and F.P-R contributed equally to this work and are joint senior authors. F.P-R is the guarantor.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2024.06.039.

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