**The burden of high fasting plasma glucose in South American countries, 1990–2019: a systematic analysis for the Global Burden of Disease Study**

Running head: The burden of high fasting plasma glucose in South American

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**Abstract (Max 250; 250 words)**

**Objective:** To describe the burden of hyperglycemia, characterized by the Global Burden of Disease (GBD) Study as high fasting plasma glucose (HFPG), in South American countries from 1990 to 2019.

**Study design:** A descriptive epidemiological study.

**Methods:** We investigated the burden attributable to HFPG in adults >25 years in 12 South American countries from 1990 to 2019. The GBD performed a systematic analysis of gathered data to estimate the HFPG summary exposure value (SEV) and mortality, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life years (DALYs) lost due to HFPG. We evaluated these metics and their variation across the Socio-Demographic Index (SDI) in South America using age-standardized estimates.

**Results:** Between 1990 and 2019, in most countries deaths (median -xxx%), YLLs (median -xxx%), and DALYs (median -xxx%) decreased, while the SEV (median xxx%) and YLDs (median xxx%) increased. In 2019, Guyana had the highest exposure (SEV=23.2; 95% UI 21.1-25.2) and overall burden (DALYs=6,632.1; 95% UI 5,237.1-8,243.3/100.000 population). Peru had the lowest exposure (SEV=7.7; 95% UI 6.6-8.9) and burden (DALYs=1,143.1; 95% UI 889.2-1,445.9/100.000). Guyana also had the highest (YLDs=1,212.5; 95% UI 838-1,649.2/100.000) and Uruguay the lowest (YLDs=357.9; 95% UI 242.4-485.6/100.000) disability burdens.

**Conclusions:** South America´s HFPG burden is large and heterogeneous. While age-standardized premature mortality has generally decreased, hyperglycemia and age-standardized disability have risen. Coupled with population aging, these changes portend that hyperglycemia will confer increasingly important risk, with its burden gradually shifting from mortality to disability. Health systems will need to adapt to the added workload.

**Keywords:** hyperglycaemia, disability-adjusted life years, mortality

**Introduction**

Diabetes is one of the leading causes of mortality and disability globally. In 2021, there were 529 million people living with diabetes worldwide, with a predicted rise to 1.31 billion by 2050 (1) (Global regional national, 2023). The concept of hyperglycemia, characterized in the Global Burden of Disease (GBD) Study as High Fasting Plasma Glucose (HFPG), permits expression of the risk of diabetes and to a lesser degree states of intermediate hyperglycemia for numerous adverse outcomes (2) (Liang, 2022). While the high prevalence and burden of diabetes have been reported in the Americas (3) (Cousin, 2022), a comprehensive analysis of the more inclusive HFPG burden in South America is lacking to date.

Given the heterogeneity of diabetes morbidity and mortality burden across countries in America, it is essential to have more detailed data for more accurate planning of public health policies. This article describes the burden of hyperglycemia in South American countries from 1990 to 2019. Furthermore, we aim to evaluate the relationship of HFPG to the level of socioeconomic development of these countries.

**Methods**

We analyzed the burden of HFPG in twelve South American countries (Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Guyana, Paraguay, Peru, Suriname, Uruguay, and Venezuela) from 1990 to 2019 using estimates from GBD 2019. The territory of French Guyana was not included since it is part of France.

The GBD 2019 organizes risk factors into four hierarchical categories. At the highest level (level 1), risk factors are split into behavioral, environmental, occupational, and metabolic groups. Within this context, HFPG is a level 2 metabolic risk factor (4) (Supplement app1 87 risk).

The GBD, based on available data, estimates the distribution of fasting plasma glucose in populations as a continuous exposure in units of mmol/L. HFPG is defined as any level above the theoretical minimum risk exposure level (TMREL), which varies from 4.8-5.4 mmol/L (86.4-97.2 mg/dL) [ref )], depending on the outcome being considered. To maximize use of available data, other measures of hyperglycemia are transformed into HFPG equivalents, permitting their incorporation in analyses.

The burden of HFPG is calculated by joining the estimated excess risk of undesirable outcomes at different levels of hyperglycemia with estimates of the frequency of these levels across the distribution of hyperglycemia. Estimated excess risk for its related outcomes across the spectrum of hyperglycemia is obtained through literature review.

We described the total burden of HFPG, as well as rank the specific burden for the fifteen GBD level 3 causes with burden attributable to HFPG in the 2019 GDB Study: diabetes, ischemic heart disease, stroke, chronic kidney disease, alzheimer’s disease, tracheal, bronchus and lung cancer, colorectal cancer, breast cancer, pancreatic cancer, tuberculosis, blindness and vision loss, peripheral artery disease bladder cancer, ovarian cancer, and liver cancer [ref ).

The HFPG burden was assessed for both nonfatal and fatal events. Fatal events were estimated as years of life lost (YLLs) due to premature death. Non-fatal events were estimated as years lived with disability (YLDs). Disability-adjusted life years (DALYs) lost, the sum of YLLs and YLDs, expresses the overall burden. YLLs were calculated subtracting the age at death from the highest life expectancy for the age in question found among countries with a population of at least five million. YLDs were calculated as the product of the prevalence of the disabilities (outcomes and their sequela) attributable to HFPG multiplied by the disability weights for those conditions. These weights express the relative valuation of the health states caused by the diverse disabilities on an interval scale, ranging between 0 (equivalent to full health) and 1 (equivalent to death) (7) (supplement 369 diseases).

To estimate the extent of population exposure to risk factors, GBD employs the Summary Exposure Value (SEV), an excess risk-weighted prevalence which is expressed as a continuous variable (9) (Murray 87 risk factors, 2020). The SEV for HFPG is calculated as the weighted prevalence of hyperglycemia, in which each level of glucose above the TMREL is weighted by the excess risk of outcomes produced at that level (8) (Supplement Cousin E, 2022). It varies from zero to 100, zero indicating a population with minimum possible risk and 100 one with maximum possible risk. Though of little use in comparisons across risk factors, it permits comparison of exposure to a given risk factor across different populations and at different times.

The Sociodemographic Index

The Socio-demographic Index (SDI) is a composite indicator of social development (4) (Supplement app1 87 risk, 2020). It is derived from the average of lag-distributed income per capita, total fertility rate in women under 25 years and average education in people over 15 years in populations (3,4) (Cousin E 2022) (Supplement app1 87 risk, 2020). The closer its value is to zero, the worse the estimated social development, with a value of zero representing a theoretical minimum level of socio-demographic development relevant to health issues and a value of one representing a theoretical maximum level of development (4) (Supplement app1 87RF, 2020).

All estimates were performed for both sexes and age-standardized, unless otherwise stated, and generated from data available from the Global Health Data Exchange GBD Results Tool (http://ghdx.healthdata.org/gbd-results-tool). The figures were done using the R package version 4.02.

We calculated annual rate of change….

95% uncertainty intervals for South American nations, when combined, were calculated….

**Results**

Considering all South American countries, in 2019, age-standardized mortality and disability attributable to HFPG were high, with xx% of all total DALYs attributable to this single risk factor. Figure 1 depicts age-standardized (left panel) and all-age (right panel) metrics forf the South American population over the period of 1990 to 2019. In 2019, considering all nations together, 2010 DALYs were attributable to HFPG. Of these, 70.4% were from YLLs and 29.6% from YLDs. Over the 30 year period, despite a 31.3% increase in the HFPG SEV, age-standardized rates for deaths (down 30%), YLLs (down 33%) and DALYs (down 17%) decreased, with this favorable trend being more prominent in the 1990s than recently. In contrast, YLDs showed a steady increase in rate, rising 24.6% over the entire period. All favorable trends were lost when one considers all-age metrics. SEV increased xxx%, with accompanying mortality increasing 48.4%, YLLs 30.1%, YLDs 110.9%, and DALYs 47.1%.

As seen in Table 1, a great deal of variabililty existed in these metrics across nations. In general, rates were greater in Venezuela, Suriname, and especially Guyana, and lower in Chile, Uruguay and especially Peru. Guyana´s 2019 DALY rate was 5.8 times that of Peru. That exposure to HFPG was three times greater in Guyana than Peru may explain a large part of this difference in burden.

Regarding the annualized rate of change of age-standardized metrics overtime, Brazil, Colombia, and Guyana had negative rates in deaths, YLLs, and DALYs, producing a shrinking burden, while Paraguay and Ecuador presented positive annualized changes. In contrast to this variability, all the countries have had a positive annualized rate of change (a growing burden) for YLDs and an increasing SEV (Figure 2), with a notable rise in the latter in Uruguay. We found no clear correlation between rate of change (1990 to 2019) of the metrics and SDI (2019) across countries (Figure 3).

Figure 4 depects the change over time of exposure (SEV) for HFPG (broader red line) along side of other risk factors for diabetes. Though the variability across nations in change in HFPG exposure seen in the previous figure is also present here, the HFPG SEV is always in ascension. What is notable in this figure are the parallel ascending tendencies of most of the subjacent risk factors. This is particularly true for a diet high in sugar-sweetened beverages and high body mass index. Though much variation exists, HFPG generally tracks in the midst of its subjacent risk factors.

Supplementary Figure 1 shows the leading 15 Level 3 causes of global DALYs due to HFPG in 1990 and 2019. Much consistency across nations is seen here, with diabetes (which englobes premature mortality due to diabetes, vision loss and blindness due to diabetic retinopathy, diabetic foot and amputation, and the burden of living with uncomplicated diabetes), ischemic heart disease, stroke, and chronic kidney disease always being the top four causes affected.

**Discussion**

This study described the age-standardised rates of deaths, DALYs, YLLs, YLDs, and SEV attributable to HFPG in South American countries from 1990 to 2019. South America´s HFPG burden is significant and heterogeneous across countries. While the age-standardized mortality burden has decreased, the underlying cause of the burden – hyperglycemia – has risen, and the combination of a rising prevalence of this risk factor and falling YLLs is producing a shift in burden from premature mortality to living with incapacity.

Our findings showed increased YLDs and SEVs between 1990 and 2019 in this region. The increase of years lived with a disability is related to the rise in prevalence and reflects the impact of HFPG on quality of life prior to leading to death. In other words, people are having more HFPG and living longer with it. SEVs evaluate the population exposure to the HFPG and consider the extent of the exposure by risk level and the severity of HFPG. Our results suggest that the prevalence of HFPG and the average population of the HFPG are increasing. The increase in these estimates is related to increased survival and worsening health behaviours. Low physical activity and poor diet are the two most important risk factors that should be targeted for primary prevention of HFPG and diabetes (3,10–13) **(Cousin E, 2022) (Danaei G, 2011) (PAHO, 2015) (Capewell S, 2018) (Duncan BB, 2017)**. The cost-effectiveness of health-style interventions has been proven favourable to health systems (14) **(Roberts S, 2018)**. Dietary factors are important causes of DALYs worldwide (15) **(Afshin A, 2019)**. The behavioral and metabolic risk factors leading up to HFPG and diabetes increased markedly over the 1990-2019 period in Brazil, with special regard to high body mass index (16) **(Stein C, 2022)**.

The Pan American Health Organization (PAHO) - the regional office for the World Health Organization (WHO) - has been applying the Country Capacity Survey, to assess the preparedness of the countries in various aspects. Pertaining to non communicable diseases, there is access to risk factors data, such as those leading to diabetes. Of the analysed countries in this article, only three (Brazil, Argentina and Chile) had specific diabetes policy, strategy, or national action plan. That comes to show that there might be little structured preventive strategies to combat this disease. On the other hand, most of the countries had essential diabetes medicines readily available, as well as guidelines, protocols or standards of care for diabetes treatment. That is, there is little incentive to decrease the disease deflagration, but many resources to deal with it, increasing its prevalence and the time spent with the disease and its associated disabilities (17) **(PAHO Snap)**.

Guyana, Suriname, and Venezuela had the highest DALY values. In contrast, the lowest were found in Peru, Uruguay and Chile. However, the annual rate of change of DALYs, YLLs, YLDs, deaths, and SEV over time showed a shrinking burden in Brazil, Colombia, and Guyana for DALYs, YLLs, and deaths in Argentina, Brazil, Chile, Colombia, Guyana, and Peru. All the countries have a growing burden for YLDs and SEV. These results show the importance of a public policy aimed at preventing HFPG and specific to the different countries of South America. These results could be associated with economic development and the health structures offered in these countries. However, most do not provide a national public health system with excellent coverage.

Furthermore, there was no clear association between the age-standardised deaths, DALYs, YLLs, YLDs, and SEV rate and the annual rate of change in SDI from 1990-2019. Previous studies have demonstrated an inverse correlation between DALYs from HFPG and SDI levels (2) **(Liang R, 2022)**. A possible justification for these differences could be that our data included only South American countries. It seems to be a trans populational phenomenon in South American countries that everybody is susceptible to regardless of the level of development one's in. In previous studies, the DALYs of stroke attributable to HFPG were higher in lower SDI countries (18) **(Liu Y, 2022)**. In contrast, NASH-related liver cancer has increased in the last decades also in regions with high SDI (19) **(Li Z, 2023)**.

The potential sequelae and adverse outcomes that stem from HFPG have personal and public costs. The longstanding association between HFPG and cancer is an example. People with HFPG and diabetes consistently have a higher risk of total mortality (20) **(Wu M, 2021)**. The burden spreads also to non-neoplastic diseases, such as stroke. The global age-standardised rate of DALY attributable to HFPG stroke did not decline significantly from 1990-2019, mainly affecting people over 50 (18) **(Liu Y, 2022)**.

This study is not free of limitations. The main limitation of the GBD assessment of the burden of diseases and injuries is lack of data. Where data are minimal, the results hang on the predictive validity of the modelling attempts. Considering the differences found between the countries of South America, there may be differences between different regions and states of each country. More specific data could further direct the public health policies of each country.

**Conclusion**

South America's high fasting plasma glucose burden is significant and heterogeneous across countries. The burden of HFPG is increasing in South America, reflected mainly in years lived with disability and summary exposure value, meaning there has been an increase in years living with disability in these countries.

The rise in HFPG prevalence has brought consequences to both the individual and the public health systems. There was meaningful progress in diagnosis and treatments over the years, but now people live longer with the disease burden. Public health measures urgently need to work on preventing HFPG to avoid its consequences. It is necessary to implement public health policies tailored to each country, to prevent the burden from increasing.

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**Authors contributions**

**Additional information**

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**Figuras e Tabelas**

**Table 1.** Age-standardised summary exposure values (SEVs), and rates of deaths, years of life lost due to premature mortality (YLLs), years of life lived with disability (YLDs), and (DALYs lostwith correspondent 95% uncertainty intervals (UI) for South American countries in 2019.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | SEV (95%IU) | Deaths (95%IU) | YLLs (95%IU) | YLDs (95%IU) | DALYs (95%IU) |
|  | % of maximum | per 100.000 | per 100.000 | per 100.000 | per 100.000 |
| exposure |
| Argentina | 11.0 (9.5 to 12.6) | 71.3 (55.1 to 92.9) | 1284.0 (1032.0 to 1599.2) | 479.8 (327.5 to 660) | 1763.8 (1456.5 to 2158.7) |
| Bolivia | 10.7 (9.2 to 12.2) | 120.5 (91.8 to 156.5) | 2191.5 (1680.0 to 2817.1) | 525.5 (354.1 to 713.6) | 2717.0 (2156.5 to 3343.5) |
| Brazil | 11.4 (10.1 to 12.8) | 77.0 (63.0 to 96.7) | 1427.2 (1204 to 1724) | 596.5 (415.9 to 808.9) | 2023.7 (1700.2 to 2419.6) |
| Chile | 13.6 (12 to 15.3) | 62.3 (48.6 to 79.8) | 1009.5 (811.5 to 1244.3) | 563.5 (376.9 to 776.1) | 1573.0 (1264.6 to 1926.3) |
| Colombia | 15.0 (13.3 to 16.7) | 62.4 (42.3 to 88.9) | 1078.2 (758.7 to 1493.7) | 738.1 (504 to 1016.3) | 1816.3 (1385.3 to 2303.9) |
| Ecuador | 12.3 (10.9 to 13.8) | 98.0 (73.9 to 131.8) | 1691.0 (1302.8 to 2242.1) | 606.9 (424.4 to 821.3) | 2298.0 (1830.7 to 2905.4) |
| Guyana | 23.2 (21.1 to 25.2) | 254.5 (193.9 to 324.1) | 5419.6 (4115.1 to 6924.2) | 1212.5 (838 to 1649.2) | 6632.1 (5237.1 to 8243.3) |
| Paraguay | 11.7 (10.2 to 13.4) | 110.1 (81.6 to 146.9) | 2072.5 (1569.6 to 2739.3) | 606.2 (414.7 to 826.4) | 2678.7 (2074.0 to 3392.3) |
| Peru | 7.7 (6.6 to 8.9) | 41.2 (29.6 to 57.0) | 746.5 (538.6 to 1035.4) | 396.6 (268.5 to 544.8) | 1143.1 (889.2 to 1445.9) |
| Suriname | 21.9 (19.9 to 23.9) | 147.5 (116.9 to 185.5) | 3052.8 (2426.9 to 3789.4) | 1166.5 (798.7 to 1599.5) | 4219.3 (3451.4 to 5046.1) |
| Uruguay | 8.3 (7.2 to 9.5) | 54.4 (42.5 to 70.7) | 958.2 (756.6 to 1211.3) | 357.9 (242.4 to 485.6) | 1316.1 (1065.7 to 1621.1) |
| Venezuela | 16.1 (14.3 to 17.9) | 126.4 (90.8 to 172.6) | 2428.8 (1748.9 to 3251.7) | 802.9 (547 to 1096.5) | 3231.8 (2478.8 to 4103.7) |

**Figure 1.** Summary exposure value (SEV), and rates of deaths, years of life lost due to premature mortality (YLLs), years of life lived with disability (YLDs), and disability-adjusted life years (DALYs) lost, from 1990-2019 for the combined South American countries from 1990 to 2019. Left panel: Age-standardized, Right Panel: All-ages.

Gráfico

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**Figure 2.** Age-standardised annual rates of change (%) for summary exposure values (SEVs) and rates of deaths, years of life lost due to premature mortality (YLLs), years of life lived with disability (YLDs), and disability-adjusted life years (DALYs) lost, from 1990-2019 in South America countries. Gráfico, Gráfico de barras

Descrição gerada automaticamente

**Figure 3.** Annual rate of change of age-standardised summary exposure values (SEVs), and rates of deaths, years of life lost due to premature mortality (YLLs), years of life lived with disability (YLDs), and disability-adjusted life years (DALYs) lost by level of socio-demographic index (SDI).

Gráfico, Gráfico de dispersão

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Figure 4. Percent change over time from 1990 to 2019 of the summary exposure value (SEV) for high fasting plasma glucose and subjacent risk factors for diabetes in South American countires.

Gráfico

Descrição gerada automaticamente

Supplementary figures.

Interface gráfica do usuário, Tabela

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Tabela

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Interface gráfica do usuário, Tabela

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