**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**

**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 metrics 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, 529 million people were living with diabetes worldwide, with a predicted rise to 1.31 billion by 2050 (1). The concept of hyperglycemia, characterized as High Fasting Plasma Glucose (HFPG) in the Global Burden of Disease (GBD) Study, permits the expression of the risk of diabetes and states of intermediate hyperglycemia for numerous adverse outcomes (2). While the high prevalence and burden of diabetes have been reported in the Americas (3), 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).

The GBD aggregates available data on measured glucose, producing summarized estimates of the distribution of fasting plasma glucose as the mean HFPG in a population as a continuous exposure in units of mmol/L. Since HFPG is along a continuum, it is defined high FPG as any level above the theoretical minimum risk exposure level (TMREL), which is 4.8-5.4 mmol/L, depending on the outcome being considered (4).

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. The estimated excess risk for its related outcomes across the spectrum of hyperglycemia is modeled based on data from 58 American literature sources (3).

We described the total burden of HFPG, as well as ranked 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, Alzheimers 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 (2)

The HFPG burden was assessed for both fatal and nonfatal 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 by 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 sequelae) attributable to HFPG multiplied by the disability weights for health states resulting from these conditions. These weights express the relative valuation of the health states on an interval scale, ranging between 0 (equivalent to full health) and 1 (equivalent to death) (2).

To estimate the extent of population exposure to risk factors, GBD employs the Summary Exposure Value (SEV) (4). 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 (3). It varies from zero to 100, zero indicating a population with minimum possible risk and 100 one with maximum possible risk. Though of limited use in comparisons across risk factors, it permits comparison of the magnitude 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). It is derived from the average lag-distributed income per capita, total fertility rate in women under 25 years, and average education in people over 15 years in populations (3). The closer its value is to zero, the worse the estimated social development is, with zero representing a theoretical minimum level of socio-demographic development relevant to health issues and one representing a theoretical maximum level of development (4).

All estimates were performed for both sexes and age-standardized unless otherwise stated. They were 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 XX 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 for the South American population for 1990 to 2019. In 2019, HFPG was responsible.

for 2010 (95IUXXX) age-standardized DALYs per 100,000 adults in the South American countries, considering. Of these, 70.4% were from YLLs and 29.6% from YLDs. Over the 30 years, 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 rate increase, rising 24.6% over the entire period. All favorable trends were lost when one considers all-age metrics. SEV increased 47%, with accompanying mortality increasing 48.4%, YLLs 30.1%, YLDs 110.9%, and DALYs 47.1%.

Table 1 shows a great deal of variability existed in these metrics across nations. In general, rates were higher in Venezuela, Suriname, and especially Guyana, and lower in Uruguay and especially in 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.

Figure 2 shows the annualized rate of change of age-standardized metrics overtime, Brazil, and Colombia, had the most negative rates in DALYs, YLLs, and deaths, producing a shrinking burden, while Paraguay and Ecuador presented the most 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 the rate of change (1990 to 2019) of the metrics and SDI (2019) across countries (Figure 3).

Figure 4 depicts the change over time of exposure (SEV) for HFPG (broader red line) alongside of similar changes of the major risk factors for diabetes. Though the variability across nations in change in HFPG exposure seen in the previous figure is also present here, HFPG's 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 during 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**

In 2019, South America's HFPG burden was large overall and markedly heterogeneous across countries. While its age-standardized mortality burden decreased from 1990 to 2019, the frequency and severity of the cause of the burden—excessive exposure to hyperglycemia—have risen. The combination of this rise in YLDs and YLLs falling has produced a slow but steady shift in burden from premature mortality to living with incapacity.

Our analysis points to important similarities and differences in country metrics. All countries have experienced a major increase in age-standardized exposure and all-age DALYs, most notably for all-age YLDs. However, Suriname, and Guyana presented SEVs, YLDs, YLLs, and DALYs above the South American mean.

Two major situations have thus produced the diabetes burden in South America: 1) a major increase in populational mean hyperglycemia level and 2) the continuous population aging. Considering the aging of the population and the worsening lifestyle, these data highlight the need for effective public policies to improve diabetes and other chronic diseases.

This transition from more locally-obtained, plant-based, calorically balanced diets composed more of *in natura* foodstuffs to the current supermarket- and restaurant-based sourcing of foodstuffs and the accompanying ubiquitous availability of snacks has permitted broad access to caloric excess and an ever-increasing input of products produced by the food industry and designed principally for their low cost and palatability rather than their nutritional quality. Within this context, the recognition of the role of ultra-processed foods (UPFs) as a risk for diabetes and other chronic diseases stands out, given the enormous population exposure to these products and the now documented risk they present not only for obesity but also for multiple chronic diseases.[refs] In parallel, the harmful role of multinational food industry actors has been increasingly recognized as a force stimulating poor nutrition to be reckoned with, much like that of the tobacco companies that created the tobacco use epidemic.

On another front, understanding the role of physical inactivity in the development of diabetes has been refined. Risk is now recognized not only from scant activity but also from sedentary behavior.[ref] Multiple types and moments of activity are now seen as beneficial within a revised conceptual framework stating that the benefit of exercise is largely independent of its intensity and the duration of its episodes.[ref] Newer risk factors such as inadequate sleep behaviors and air pollution have been added to the list. Others will likely follow.

Yet this increase in understanding of the origins of hyperglycemia has not yet seen much translation into preventive interventions with broad population reach. A wide variety of population-based interventions have been suggested, including taxes on unhealthy foods and subsidies for healthy ones, social marketing campaigns, interventions stimulating healthier foods in school and government office canteens, prohibition of the marketing of unhealthy foods to children, design and redesign of urban areas to stimulate healthy transport, and greater control of polluters. Almost all of these, for most countries, remain as ideas on paper. Their absence in practice has led to a policy vacuum permitting the large increase in hyperglycemia and many of its multiple underlying risk factors observed.

Many reasons exist for this slow translation from knowledge to action. A major one is the existence of political systems where economic interests have undue power in decision-making. A second is the lack of vibrant in-country public health communities with a strong NCD component working to stimulate the move from knowledge to action. A third is the extension of the paradigm of evidence-based medicine created in the context of clinical medicine to the realm of public health, where it is inappropriate for decision-making [ref].

The Pan American Health Organization (PAHO), the regional office of the World Health Organization (WHO) for the Americas, has been applying the Country Capacity Survey to assess preparedness to confront the challenge of the NCDs.[ref] Its results document the limited ability of most South American nations to incorporate chronic disease prevention into their practice of public health. Of the countries analyzed in our study, only three (Brazil, Argentina, and Chile) had specific diabetes policies, strategies, or national action plans.

However, most studied countries had essential diabetes medicines available, as well as guidelines, protocols, or standards of care for diabetes treatment. (17) **(PAHO Snap**). These actions likely help explain why age-standardized YLLs and DALYs have decreased over time. It is possible that the favorable ranking of Brazil in DALYs due to HFPG is largely the result of >20 years of actions to pass the central focus of diabetes care from hospitals to primary care clinics and to improve the quality of this care [refs].

A few bright notes have appeared over the past decade in efforts toward population prevention. The Brazilian government, in 2014, adopted as the focus of its nutritional guidelines avoidance of UPFs whenever possible. This initiative has expanded as Brazil has extended its guidelines to cover the pediatric population, and other countries have followed its lead. [refs] In another action, they have toughened their approach to product labeling, making it easier for individuals to identify harmful food products. Taxation of sugar-sweetened beverages has been adopted, but only in a few countries, while Brazil continues to subsidize the manufacture of these beverages.[ref] Additionally, many efforts have been taken to improve urban spaces to facilitate active transport. Yet it is too early to expect that these efforts would change GBD estimates, which are rarely based on in-country surveys undertaken in the immediate past.

Given that prevention through lifestyle involves personal decisions, poverty, leading to decreased educational attainment, constrained life choices, and more risk exposure, it likely has also played a major role. [Marmot Social determinants of health] [what is the beta and significance of the SDI, SEV reationship? From the graph they appear to be related.]The data lacks details on the paths of causality in these countries and most South American societies, which should be a stimulus for greater funding for in-country research on NCDs.

Our study is not free of limitations. The main limitation is the limited number of studies available for GBD use in creating these estimates and the metrics' ensuing wide UIs.Where data are minimal, the results hang on the predictive validity of the modeling attempts. These apply a few covariables in settings where multiple factors are known to act. Additionally, considering the differences found between the countries of South America, there may likely be differences between different regions and states of each country. More specific data could further direct the public health policies of each country. Another limitation is the lack of incorporation of more recently recognized risk factors such as UPF foods and within-country inequalities producing poverty into the GBD list of risk factors.

**Conclusion**

The burden of hyperglycemia in South America is epidemiologically significant and heterogeneous across countries, increasing and shifting slowly from mortality to disability. As rising exposure to hyperglycemia, along with the aging of the population, is the primary driver of this burden, population-based public health measures are needed to guide societies' control of the behavioral and environmental risks subjacent to hyperglycemia. While improvement of quality and access to clinical care and clinical prevention strategies have important roles to play, greater emphasis should be placed on overcoming barriers to the implementation and evaluation of these population-based measures, as they are the only ones that can be reasonably expected to stem the tide of the increasingly prevalent hyperglycemia.

**Authors contributions**

**Additional information**

ORCID

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**Figures and tables**

**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 disability-adjusted life years (DALYs) lost, with 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 to 2019 for the combined South American countries. Left panel: Age-standardized, Right Panel: All-ages.

Gráfico

Descrição gerada automaticamente

**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

Descrição gerada automaticamente

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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