

# The burden of diabetes and hyperglycemia in Brazil and its states: findings from the Global Burden of Disease Study 2015

## *A carga de doença devido ao diabetes e à hiperglicemia no Brasil e seus estados: achados do Global Burden of Disease Study 2015*

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**ABSTRACT: Introduction and objective:** The global burden of disease (GBD) 2015 project, extends GBD analyses to include Brazilian federative units separately. We take advantage of GBD methodological advances to describe the current burden of diabetes and hyperglycemia in Brazil. **Methods:** Using standard GBD 2015 methods, we analyzed the burden of diabetes, chronic kidney disease due to diabetes and high fasting plasma glucose in Brazil and its states. **Results:** The age-standardized rate of disability-adjusted life years (DALYs) which was lost to high fasting plasma glucose, a category which encompasses burdens of diabetes and of lesser hyperglycemia, were 2448.85 (95% UI 2165.96-2778.69) / 100000 for males, and 1863.90 (95% UI 1648.18-2123.47) / 100000 for females in 2015. This rate was more than twice as great in states with highest burden, these being overwhelmingly in the northeast and north, compared with those with lowest rates. The rate of crude DALYs for high fasting plasma glucose, increased by 35% since 1990, while DALYs due to all non-communicable diseases increased only by 12.7%, and DALYs from all causes declined by 20.5%. **Discussion:** The worldwide pandemic of diabetes and hyperglycemia now causes a major and growing disease burden in Brazil, especially in states with greater poverty and a lesser educational level. **Conclusion:** Diabetes and chronic kidney disease due to diabetes, as well as high fasting plasma glucose in general, currently constitute a major and growing public health problem in Brazil. Actions to date for their prevention and control have been slow considering the magnitude of this burden.

**Keywords:** Diabetes mellitus. Hyperglycemia. Epidemiology. Brazil.

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**RESUMO: Introdução e objetivo:** O projeto Global Burden of Disease (GBD) 2015 estendeu suas análises para incluir unidades federativas brasileiras de maneira separada. Aproveitamos os avanços metodológicos do GBD para descrever a carga atual de diabetes e hiperglicemia no Brasil. **Métodos:** Utilizando os métodos padrão GBD 2015, analisamos a carga de diabetes, de doença renal crônica por diabetes e de glicemia de jejum elevada no Brasil e seus estados. **Resultados:** A taxa padronizada por idade de anos de vida ajustados por morte ou incapacidade (DALYs) perdidos devido à glicemia de jejum elevada foi de 2448,85 (95% IU 2165,96-2778,69) / 100000 para homens e 1863,90 (95% IU 1648,18-2123,47) / 100.000 para as mulheres em 2015. Esta taxa foi mais do que o dobro em estados com maior carga, quase sempre no Nordeste e Norte, em comparação com aqueles com as taxas mais baixas. A taxa bruta de DALYs devido à glicose de jejum elevada aumentou 35% desde 1990, enquanto que a dos DALYs devido a todas as doenças não transmissíveis aumentou apenas 12,7% e a taxa dos DALYs devido a todas as causas diminuiu 20,5%. **Discussão:** A pandemia mundial de diabetes e hiperglicemia atualmente causa uma grande e crescente carga de doenças no Brasil, especialmente em estados com maior pobreza e menor escolaridade. **Conclusão:** O diabetes e a doença renal crônica por diabetes, bem como a glicemia de jejum elevada constituem atualmente um grande e crescente problema de saúde pública no Brasil. As ações até o momento para sua prevenção e controle tem sido tímidas considerando a magnitude dessa carga.

**Palavras-chave:** Diabetes mellitus. Hiperglicemia. Epidemiologia. Brasil.

## INTRODUCTION

Over the past several decades, diabetes mellitus has become increasingly prevalent around the world<sup>1</sup>. Given its major impact in increasing the risk for a series of diseases, including cardiovascular diseases, it has also risen as a leading cause of death and disability. The GBD2015 study estimates that diabetes is now the 11th leading cause of disability adjusted life years (DALYs) in the world, and that high fasting plasma glucose is the fifth leading risk, causing DALYs in women, and seventh leading risk in men.

Brazil is no exception in this regard, and currently is the fourth leading country, in terms of the absolute number of people with diabetes<sup>2</sup>.

In recent years, the Global Burden of Disease Project has established itself as the world's leader in the descriptive epidemiology of disease burden. The GBD 2015 project, for the first time, extends GBD analyses for Brazil beyond the country level to include each Brazilian federative unit separately.

The objective of this report is to take advantage of the methodological advances afforded by GBD 2015, to describe the current burden of diabetes and hyperglycemia in Brazil, expressing not just overall burden, but highlighting the surprisingly large differences that exist across states.

## METHODS

The GBD 2015 includes multiple assessments of disease burden, from 1990 to the present. Detailed descriptions of methodology and approach of GBD 2015 have been published

elsewhere<sup>3-6</sup>. We generated the estimates presented here with the Institute for Health Metrics and Evaluation GBD 2015 visualizations<sup>7</sup>.

The GBD 2015 framework recognizes diabetes both as a disease, with its proper outcomes, as a distinct cause of chronic kidney disease, and as one of the multiple causes of a series of other diseases<sup>8</sup>. This latter expression of its pathology is accounted for within the risk factor category of high fasting plasma glucose, which also encompasses the effects of lower levels of hyperglycemia. Figure 1 shows this GBD combined burden approach. Within it, part of the burden is ascribed directly to diabetes — defined through ICD codes E10-13, except “.2” codes, related to renal disease — and includes that due to living with diabetes (“uncomplicated diabetes”), to inherent complications such as hypoglycemic and hyperglycemic coma and death, and to its traditional, “microvascular” complications (vision loss, including severe low vision and blindness; neuropathy; and amputation)<sup>9</sup>. This direct burden is shown in the part of Figure 1 highlighted by the dotted red line<sup>3</sup>. Chronic kidney disease due to diabetes is treated as a separate item. The rest of the burden, which results from the other recognized complications of both diabetes and lesser hyperglycemia<sup>10</sup> — ischemic heart disease, ischemic stroke, hemorrhagic stroke, other CKD (hypertensive CKD, glomerulonephritis CKD, and other CKD) and tuberculosis<sup>4</sup> — is accounted for through high fasting plasma glucose. In these latter calculations, the theoretical minimum risk exposure level of glucose is taken to be 4.8–5.4 mmol/L or 86.4–97.2 mg/dl<sup>11</sup>.

The GBD uses four main indicators to calculate disease burden – mortality, years of life lost due to premature mortality (YLLs), years of life lived with disability (YLDs), and the sum of the latter two — disability-adjusted life years (DALYs). In brief, YLLs are calculated multiplying the number of deaths from diabetes or due to high fasting plasma glucose in each age group by the reference life expectancy at the average age of death for those who die in that age group<sup>5</sup>. YLDs were obtained initially for each diabetes sequelae by multiplying its prevalence times, to its disability weight in each age-, sex-, and year-specific strata, with total YLDs then being aggregated across strata and sequelae<sup>10</sup>. Disability weights were derived from population-based surveys of the general public<sup>12</sup>. All results are standardized to the world population<sup>5</sup>. In addition, in order to take into account differences in socioeconomic level, when comparing disease burden across geographies, the GBD 2015 created its so-called socio demographic index, based on the average income per person, educational qualifications, and total fertility rate<sup>5</sup>. To describe the degree of confidence in the indicators presented, and given the uncertainty in the initial data and subsequent calculations, the GBD generates 95% uncertainty intervals for its metrics. These estimate and sum up uncertainty across the key steps of estimation frequently, by repeating the estimation step 1,000 times and characterizing the 95% boundaries of the data so generated. The data are presented for Brazil as a whole, and frequently also separately for Brazilian states and the Federal District.

Results are presented overall for Brazil and separately for each of its federative units (states and the Federal District, hereafter called “states”).

This study required no approval by a research ethics committee as it utilized only secondary databases which are publicly available, while obeying the ethical principles of Resolution n° 466/2012 of the Brazilian Conselho Nacional de Saúde.

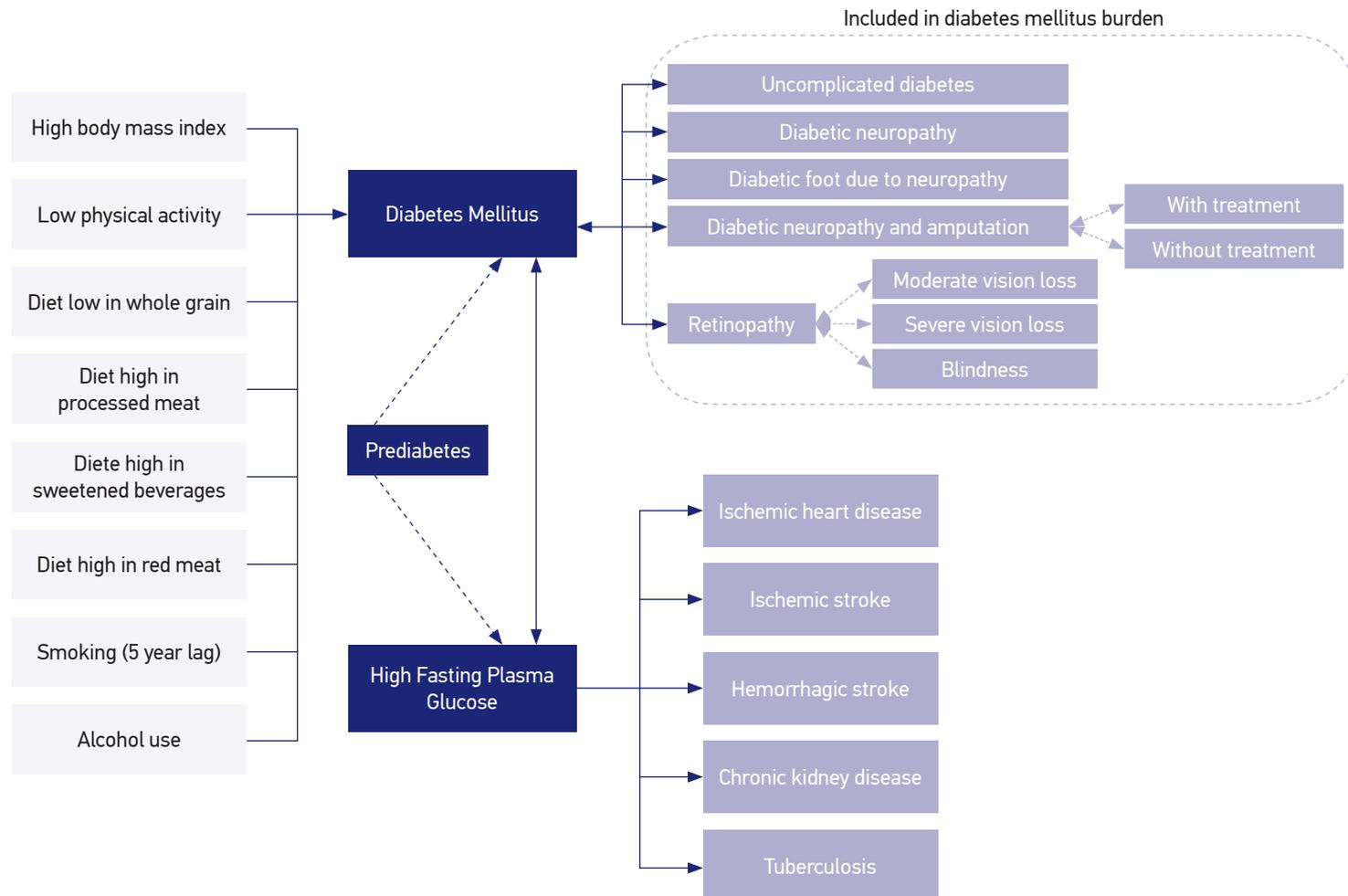


Figure 1. Dimensions of assessment of the disease burden of diabetes and high fasting plasma glucose, and burden attributable to its risk factors in the Global Burden of Disease 2015 (GBD 2015) study<sup>3</sup>.

## RESULTS

Figure 2 shows the crude rate of death in Brazil and its states due to diabetes and to chronic kidney disease due to diabetes. In Brazil, in 2015, the coefficient of mortality due to diabetes was 26.82 (95% UI 25.01–28.55)/100,000 for males, and 33.18 (95% UI 31.06–35.23)/100,000 for females, and for chronic kidney disease due to diabetes, 11.08 (95% UI 9.86–13.65)/100,000 for males, and 9.65 (95% UI 8.95–10.42)/100,000 for females.

Among the states, considering the two causes jointly, coefficients varied over a wide range, that of Paraíba, for instance, being more than 2.5 times in those of Amapá or the Federal District. In general, in the crude analyses, lesser mortality was seen in the north region and in isolated states, such as São Paulo and Goiás, among other regions. Greater mortality was

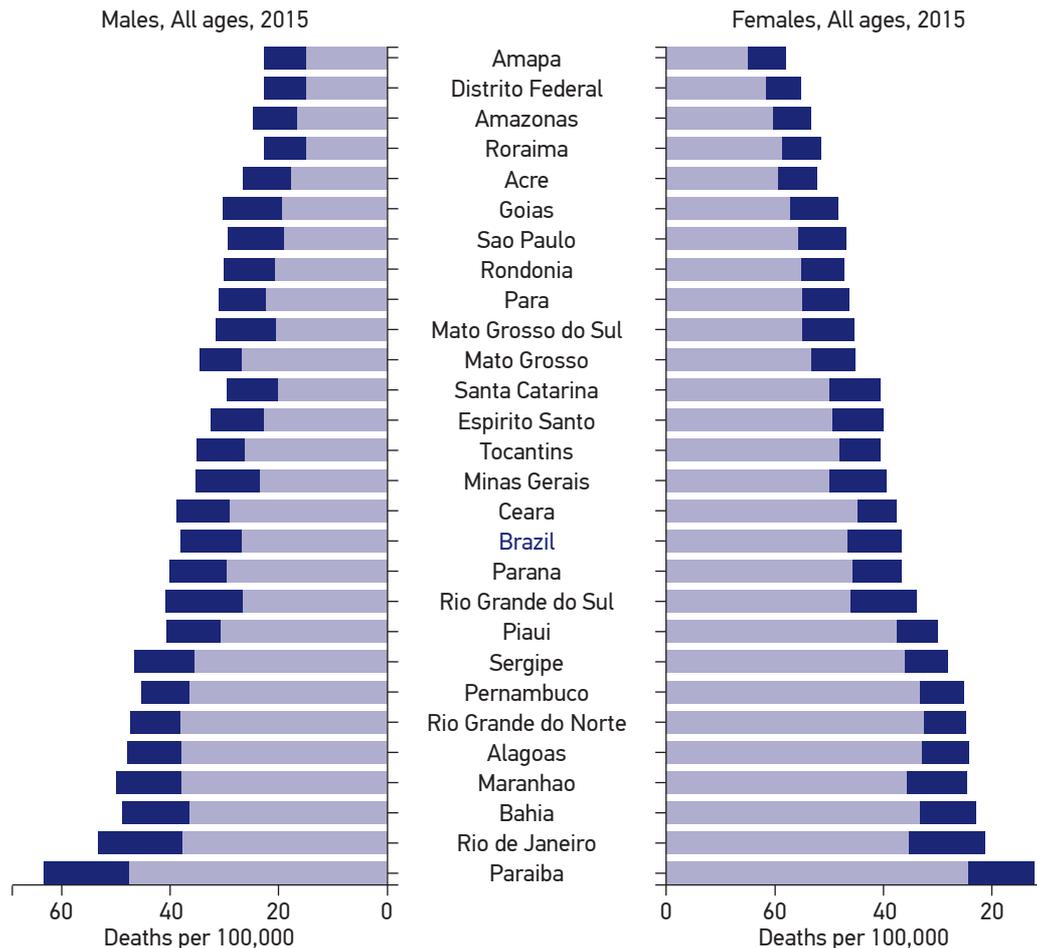


Figure 2. Crude death rates (per 100,000) for males and females resulting from diabetes (light bars) and chronic kidney disease due to diabetes (dark bars), Brazil and its states, 2015.

present generally in the Northeast region and notably in Rio de Janeiro. Considering the individual causes of death, one sees that crude diabetes mortality coefficients were higher in the northeast, and CKD due to diabetes especially high in Rio de Janeiro. When these data are age-standardized, the joint mortality of these two conditions is higher in the states of the northeast, generally followed by states in the north (data not shown).

Figure 3 shows similar data, now for the crude rate of DALYs. Overall, this rate for diabetes was 998.17 (95% UI 851.77–1171.37)/100,000 for males, and 1031.85 (95% UI 871.17–1216.03)/100,000 for females, and for chronic kidney disease due to diabetes, it is 282.83 (95% UI 252.41–354.84)/100,000 for males, and 239.29 (95% UI 220.03–258.44)/100,000 for females. The distribution by states was similar to that for crude deaths.

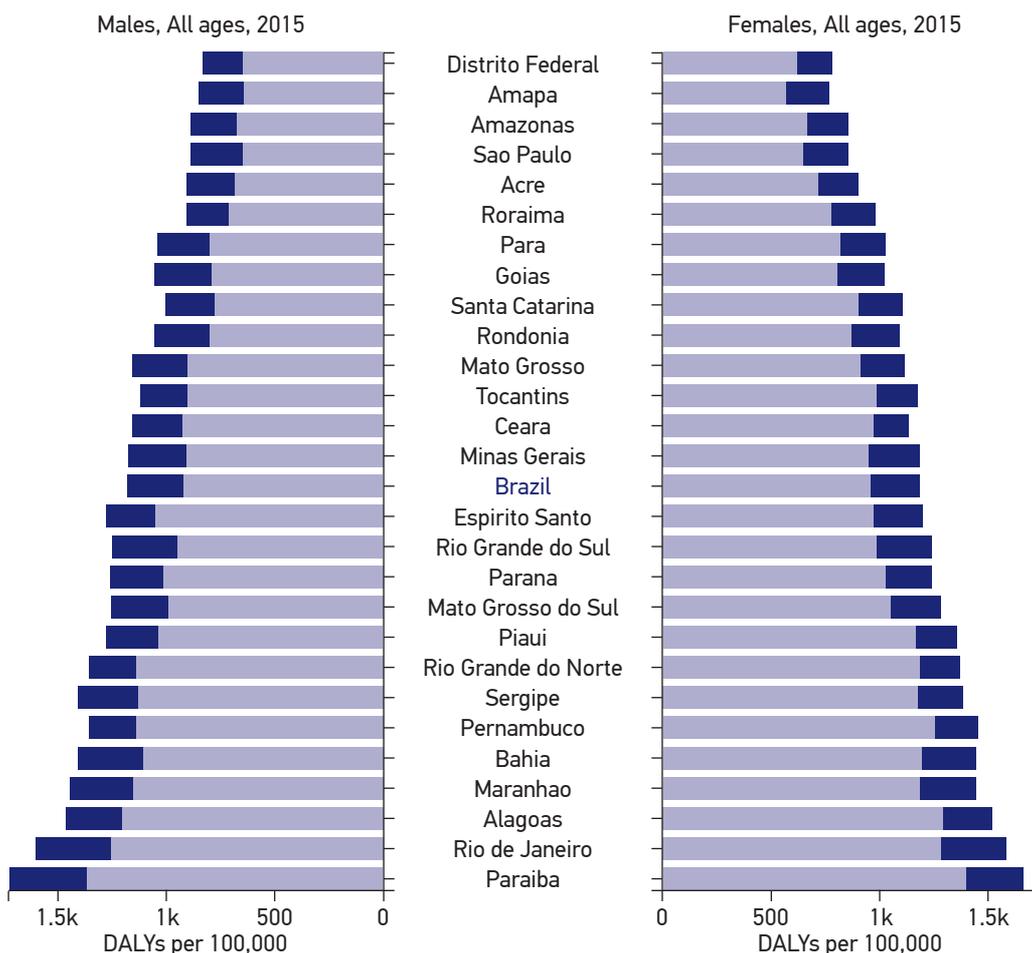


Figure 3. Crude rates of disability adjusted life years lost (per 100,000 person-years) by males and females as a result of diabetes (light bars) and of chronic kidney disease due to diabetes (dark bars), Brazil and its states, 2015.

Figure 4 also shows rates of DALYs, now age standardized. For Brazil, the age-standardized rate for diabetes was 1158.02 (95% UI 999.88–1347.11)/100,000 for males, and 1054.43 (95% UI 897.09–1238.27)/100,000 for females, and for chronic kidney disease due to diabetes 331.53 (95% UI 293.31–408.40)/100,000 for males, and 242.06 (95% UI 222.84–260.89)/100,000 for females. As can be seen when comparing this figure with the previous one, controlling for the age structure in state populations produces important differences in the relative ranking of states. DALY rates, similar to those seen for age-standardized mortality, are generally higher in the northeast, and lower in the wealthier and more socioeconomically developed states, such as São Paulo, the Federal District, and those of the southern region and Minas Gerais.

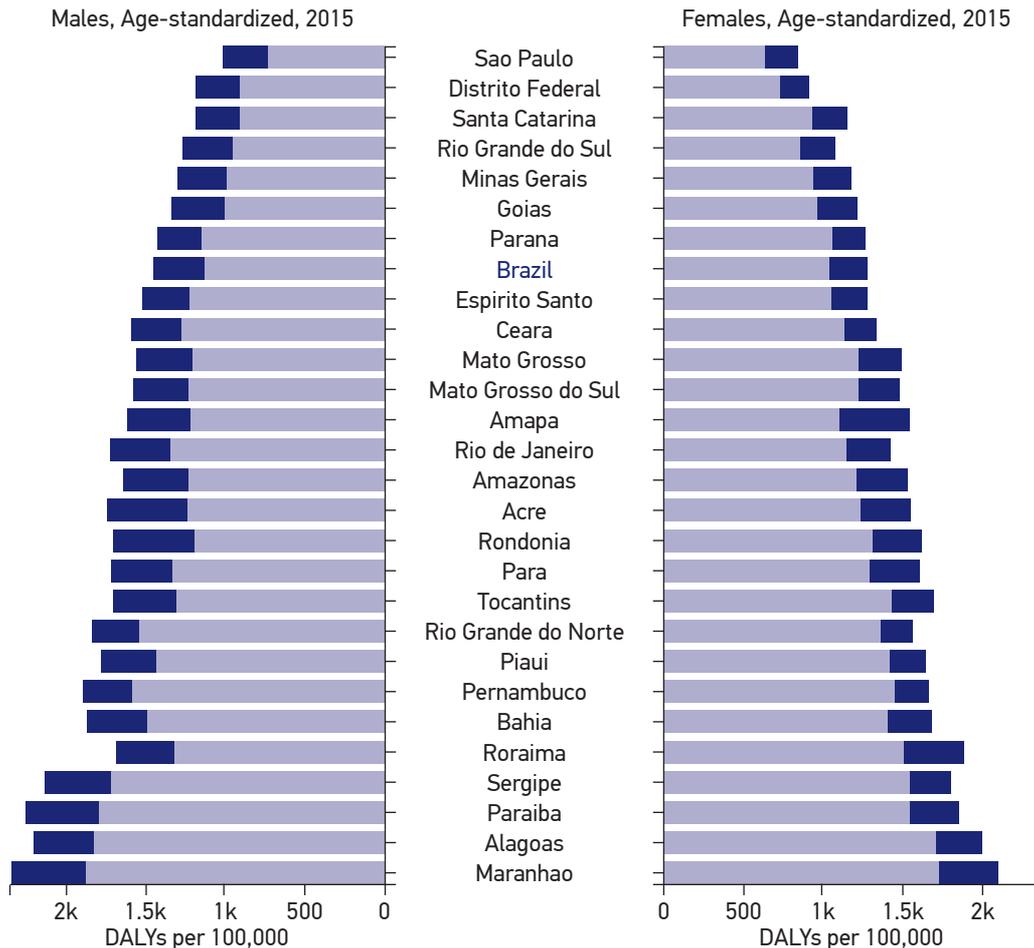


Figure 4. Age-standardized rates of disability-adjusted life years lost (per 100,000 person-years) by males and females as a result of diabetes (light bars) and of chronic kidney disease due to diabetes (dark bars), Brazil and its states, 2015.

Figure 5 shows age-standardized DALYs for high fasting plasma glucose. As shown in Figure 1, this approach captures the burden shown in the previous figure, and additionally the large burden of diabetes expressed via cardiovascular disease, the moderate-sized burden of diabetes expressed via other causes of CKD and the much smaller burden expressed via tuberculosis. Overall, the age-standardized rate for high fasting plasma glucose was 2448.85 (95% UI 2165.96–2778.69)/100,000 for males, and 1863.90 (95% UI 1648.18–2123.47)/100,000 for females, the overall burden being 64.4% and 43.8% respectively, which is greater when one considers only deaths and sequelae directly due to diabetes, and to CKD due to diabetes. In terms of rank, all of the top 10 and none of the lowest 9 Brazilian states are located in the northeast or the north. In 1990 (data not shown), the risk was more equally distributed across Brazil's regions, with 7 of the top 10 ranked states and 7 of the 9 lowest ranked states being located in the northeast and the north.

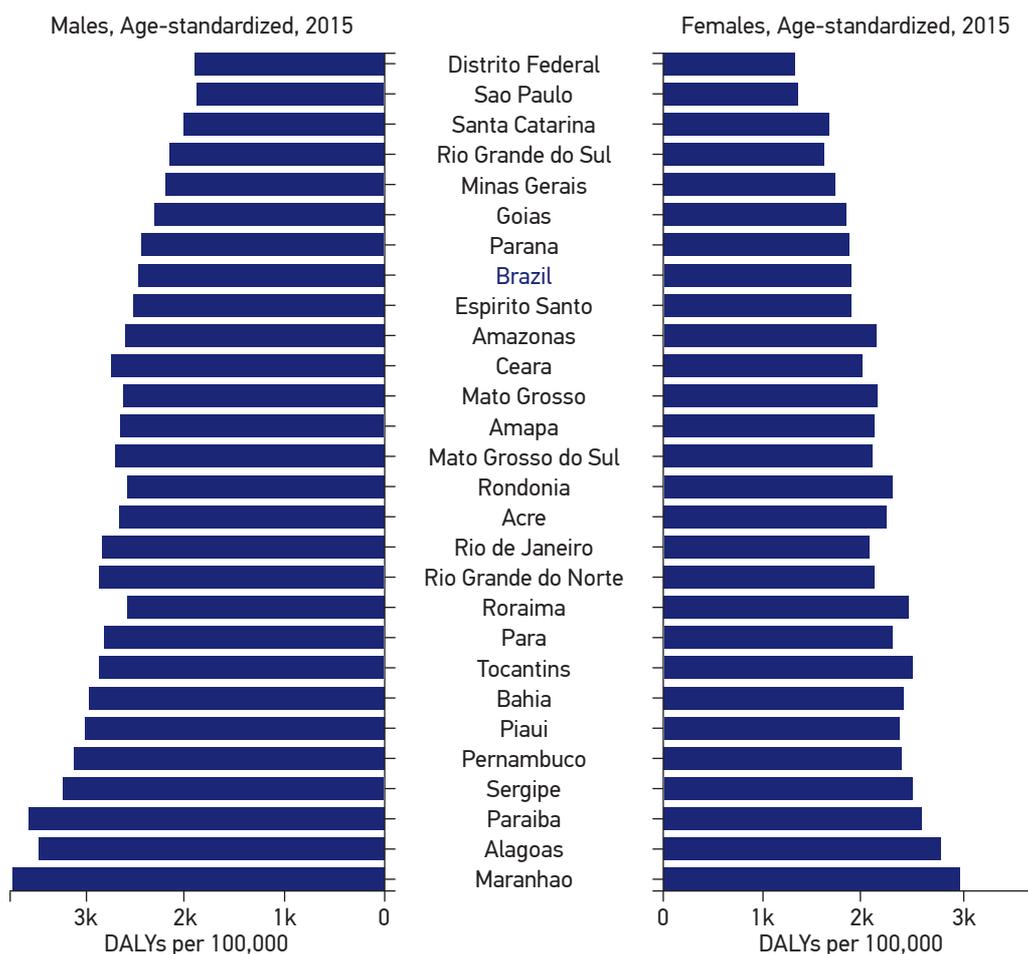


Figure 5. Age-standardized rates of disability adjusted life years lost (per 100,000 person-years) by males and females as a result of high fasting plasma glucose, Brazil and its states, 2015.

These age-standardized DALYs, for Brazil, were virtually unchanged from 1990 (2,089/100,000) to 2015 (2,091/100,000). However, with the aging of the population over this period, the overall crude rate of DALYs due to high fasting plasma glucose in Brazil increased to 35.2%, from 1,441/100,000 in 1990, to 1,948/100,000 in 2015. This compares to a smaller increase, 12.7%, in DALYs due to all NCDs, and contrasts markedly with the 20.5% decrease in crude DALYs from all causes over this same period.

To place the Brazilian burden of high fasting plasma glucose in an international context, it is 11% and 8% lower for males and females, respectively, than the average among socio-demographically similar countries (having a middle level socio-demographic index), 22% and 35% higher, respectively, than in the GBD-defined southern Latin American countries – Chile, Argentina and Uruguay; and 42% and 52% lower, respectively, than in the GBD-defined Central American countries, which span from Mexico to Columbia and Venezuela.

## DISCUSSION

The data presented here show a large and unevenly distributed burden of diabetes and high fasting plasma glucose in Brazil. For every 100 person-years lived, almost a potentially additional 2 years of high-quality life is lost to death and complications of diabetes and lesser states of hyperglycemia. With the population which is aging, the crude burden is growing at a rate greater than that of NCDs overall and in marked contrast to that of the crude overall burden from all diseases, which is falling. The disease burden of diabetes and hyperglycemia, vary markedly across Brazilian states.

These findings in Brazil are a consequence of the worldwide pandemics of diabetes and of its main biologic risk factor – obesity. Considering all nations, from 1990 to 2015, high body mass index has risen from the world's 13th to its 4th leading risk factor, in terms of DALYs, and high fasting plasma glucose from the world's 10th to the 3rd leading risk factor<sup>4</sup>.

Diabetes, which, from an international public health standpoint, was a curiosity 40 years ago, presenting high prevalence only in select native American and Pacific islander populations, has grown to be a major and ever escalating concern. Although the increased prevalence of diabetes in the United States has frequently been cited, a considerably higher prevalence of diabetes is now seen throughout most of the Middle East and Central Asia, Mexico and some countries in the Caribbean, and in several other countries in Asia<sup>1</sup>. It is now estimated that between 30% and 70% of adults living in the United States, Canada, Australia, Mexico and Denmark will develop diabetes during their lifetime<sup>13-17</sup>. Preliminary data from the ELSA-Brasil cohort, which show a high prevalence above 60 years of age, and suggest that at least a third of Brazilian adults will develop diabetes during their lifetime<sup>18</sup>.

The geographic differences in burden found across Brazilian states, with some showing rates of DALYs more than twice those of others, are perhaps larger than expected. Diabetes has now shifted to the poor, as evidenced by the highest burden being found in states of the northeast region, which is Brazil's poorest. Data from ELSA-Brasil demonstrate a large

gradient across educational levels, with those having less than a complete elementary school education and having a 59% greater prevalence of diabetes, after adjustment of age, sex, body mass index, and ethnicity<sup>18</sup>. One might speculate that this rise in burden in the northeast is in part due to the greater risk of diabetes in those suffering under nutrition in fetal and early life and who are now exposed to the nutritional inadequacies and caloric excess of an unhealthy food environment<sup>19</sup>. Might this shift have been blunted if greater attention to the risks of obesity and diabetes and greater public health measures to prevent them had been coupled with anti-poverty efforts implemented principally in these regions over recent decades?

Perhaps due to the slow rise over decades in the prevalence of obesity and of diabetes, these diseases have received less attention than they merit, considering the burden they currently exert. In this regard, our data are an additional demonstration of the urgent need for the Brazilian Ministry of Health, the health sector, and the Brazilian society in general to effectively confront the problem. Although stimulating lifestyle change in high risk individuals has been shown to be effective in preventing diabetes<sup>20,21</sup>, this clinical strategy, in and of itself, will be inadequate, given that much of the “prevented” disease is in fact merely delayed, many will be unwilling to undertake the changes necessary within the current social context, and an important fraction of diabetes develops in individuals who would not have been identified as at high risk only a few years earlier<sup>22</sup>. In addition, as most importantly, the limitations of the so-called high risk strategy become even clearer within the vision of diabetes as a life course disease, that is to say, a disease that develops slowly over the full lifespan of an individual<sup>23,24</sup>. In consonance with this reality, preventive measures should span the life course, beginning with actions related to an individual’s fetal experience, e.g. guaranteeing a healthy birth weight. Others must occur during infancy, e.g. stimulation of exclusive breastfeeding and avoidance of sweet foods, and in childhood and adolescence, when lifelong dietary and physical activity habits are developed. Avoiding weight gain and obesity in childhood and early adulthood are further steps in this process. Finally, early identification of high-risk individuals, mainly in mid- and late adulthood, and adequate orientation and support for lifestyle change are necessary. Aside from all of this, adequate health care provision for the prevention of complications once diabetes developed will be required.

However, as most of the above-mentioned actions deal with healthy individuals, they fall mainly within the realm of population-based rather than clinical interventions, involving making healthy choices easier, and more prevalent in terms of nutrition and physical activity, among others. In addition, if present concerns of a role for environmental pollutants in the etiology of diabetes are confirmed<sup>25,26</sup>, public health actions of another nature will also be necessary.

Our report is not without its limitations. Analyses are based on the assumption that problems in incompleteness and inaccuracy in Brazilian mortality data are adequately corrected by the GBD 2015 approaches. In this regard, the standardized and sophisticated approaches taken by a critical mass of demographers, statisticians, and epidemiologists aggregated to produce GBD 2015 make these estimates the best available. In addition, they assume that estimates of diabetes prevalence across states are correct, given that most available data involve

only a self-reported diagnosis, and differential access to medical care alter the probability that diabetes will be detected when present. As the quality of reporting and access to medical care are worse in the north region, estimates for states of this region are subject to greater error. Of final note, these estimates of the disease burden of diabetes and hyperglycemia are likely to be seriously underestimated, as about 40% of deaths due to diabetes are currently believed to result from non-vascular complications, most of which are not taken into consideration in GBD 2015 calculations. These complications include many types of cancer, chronic obstructive pulmonary disease, pneumonia, and other infections. Although they also include CKD, this category represents a relatively small fraction of total non-vascular deaths<sup>27</sup>.

## CONCLUSION

Diabetes, chronic kidney disease due to diabetes, as well as high fasting plasma glucose in general, cause a large and growing burden of disease in Brazil. Public health and clinical actions to date for the prevention and control of diabetes and obesity, its main risk factor, have been slow considering the current and growing disease burden presented in this report.

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