

## Diabetes and Obesity Bias: Are We Intensifying the Pharmacological Treatment in Patients With and Without Obesity With Equity?

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randomly selected and then stratified into two groups according to BMI: obesity (BMI  $\geq$ 30.0 kg/m<sup>2</sup>) and without obesity (<30.0 kg/m<sup>2</sup>).

The primary outcome was the adequacy of pharmacological treatment intensification between groups, based on individualized glycemic targets. For participants under 65 years old and without major comorbidities, the HbA<sub>1c</sub> target of <7.0-7.5% (<53-58 mmol/ mol) was used. For those aged 65 or over and with major comorbidities, the Deyo-Charlson comorbidity index score was used to categorize patients into three subgroups based on the score for each comorbidity and age (3). To assess whether the provision of medical care was similar between the groups, multiple diabetes care quality indicators were evaluated. A multivariable logistic regression model was used to control for possible confounders in the interaction between the primary outcome and interest groups.

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The study was approved by the Research Ethics Committee of HSL PUCRS (no. 3.803.681), and the Research Ethics Committee of HCPA (no. 2016-0286), as well as in the Basic Health Unit and Family Health Strategy of IAPI (approved by the National Health Council in accordance with resolution 466/12, and by the Porto Alegre Municipal Health Office).

The data collected for the study, including de-identified participant data, will be available after publication of the article upon justified request and with a signed data access agreement.

According to the sample size calculation, 402 participants were included in this study. Most baseline characteristics were similar among patients without obesity (n=198) and those with obesity (n=204) (Table 1). Patients without obesity were older (68.7  $\pm$  9.0 vs. 65.2  $\pm$  8.9 years old, P<0.001), and fewer used insulin (66.7% vs. 49.5%, P<0.001) than patients with obesity. Both groups were similar regarding all

The impact of obesity on health is reflected in different spheres and includes not only metabolic consequences, such as type 2 diabetes, but also psychological consequences related to obesity stigma. Studies show that almost 40% of adults with obesity are discriminated against because of their weight (1). Weight-based stereotypes may interfere with health care decision-making in these patients (2). However, for effective management of diabetes, obesity, and associated comorbidities, health professionals must be free from cognitive bias. To better understand the scope of this problem in clinical practice, we evaluated the prevalence of pharmacological diabetes treatment intensification based on weight status.

This is a cross-sectional study of patients with type 2 diabetes who received outpatient care in Southern Brazil from October 2011 to December 2019. The study was approved by the institutional review boards. Participants who had a regular follow-up for  $\geq 1$  year, were aged  $\geq 18$  years, and had  $\geq 2$  measurements of HbA<sub>1c</sub> in the period were considered eligible. Participants were

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care.diabetesjournals.org Alessi and Associates e207

	Total ( <i>N</i> = 402)	Without obesity group $(n = 198)$	Obesity group $(n = 204)$	P value
Age (years)	66.9 ± 9.1	68.7 ± 9.0	65.2 ± 8.9	< 0.001
Sex (female)	225 (56.0)	102 (51.5)	123 (60.3)	0.08
Race/ethnicity (White)	349 (86.8)	178 (89.9)	171 (83.8)	0.07
Diabetes complications				
Retinopathy	92 (22.9)	42 (21.2)	50 (24.5)	0.43
Neuropathy	45 (11.2)	23 (11.6)	22 (10.8)	0.79
Nephropathy	109 (27.1)	53 (26.8)	56 (27.5)	0.91
Insulin use	234 (58.2)	98 (49.5)	136 (66.7)	< 0.002
Metformin use	375 (93.5)	184 (93.4)	191 (93.6)	0.92
Sulfonylurea use	211 (52.5)	111 (56.1)	100 (49.0)	0.16
Hypoglycemia§	41 (10.2)	17 (8.6)	24 (11.8)	0.29
Hypertension	357 (88.8)	169 (85.4)	188 (92.2)	0.03
Deyo-Charlson comorbidity index (%)				0.20
1 point	146 (36.3)	67 (33.8)	79 (38.7)	
2 points	134 (33.3)	67 (33.8)	67 (32.8)	
3 points	46 (11.4)	24 (12.1)	22 (10.8)	
≥4 points	76 (18.7)	40 (20.3)	36 (17.7)	
Quality indicators for diabetes care				
Number of medical appointments*		4.0 (3.0, 5.0)	3.0 (3.0, 5.0)	0.21
HbA <sub>1c</sub> † (%)		8.2 ± 1.9	8.1 ± 1.7	0.67
HbA <sub>1c</sub> (mmol/mol)		66.0 ± 20.8	65.0 ± 18.6	
Assessment of albuminuria and/or creatinine*		151 (76.3)	145 (71.1)	0.24
Assessment of lipid profile*		149 (76.3)	138 (67.6)	0.51
Assessment of sensory neuropathy*		63 (31.8)	67 (32.8)	0.83
Assessment of retinopathy*		62 (31.3)	79 (38.7)	0.12
Nutritional assessment*		46 (23.2)	48 (23.5)	0.94
Inquiry about smoking§		20 (10.1)	17 (8.3)	0.54
Primary Outcome Patients with HbA <sub>1c</sub> above the target‡ Patients who received appropriate treatment	181 (45.0)	86 (43.4)	95 (46.6)	0.53
intensification¶	109 (60.2)	58 (67.4)	51 (53.7)	0.05

Data are mean  $\pm$  SD, median (interquartile range), or n (%). HbA $_{1c}$ , hemoglobin A $_{1c}$ . §According to data registered in medical records. \*In relation to a 1-year period of follow-up. †Last test available on medical records. ‡HbA $_{1c}$  target: for participants under 65 years old and without major comorbidities, the HbA $_{1c}$  target of <7.0–7.5% (<53–58 mmol/mol) was used. For those aged 65 or over and with major comorbidities, the Deyo-Charlson comorbidity index score (CCIS) was used to categorize patients into three subgroups based on the score for each comorbidity and age (3): younger and healthier participants (age range between 65 and 79 years and CCIS 1), younger participants who are slightly ill (age range between 65 and 79 years and CCIS 2 or 3), and older and sicker participants (age range under 80 years and CCIS 4 or greater, or age above 80 years and CCIS 1 or greater). ¶The proportion of patients who had HbA $_{1c}$  above the target and who received appropriate treatment intensification. P values indicate a comparison between patients without obesity and with obesity. An  $\alpha \leq 0.05$  indicates a significant difference between groups.

quality indicators for diabetes care. According to individualized glycemic targets, 43.4% of the participants without obesity and 46.6% with obesity presented with an  $HbA_{1c}$  level above the target (P=0.53). When assessing the number of patients who received pharmacological treatment intensification when  $HbA_{1c}$  level was above the target, it was found that participants from the group without obesity more frequently received treatment intensification than those from the obesity group (67.4% vs. 53.7%, respec-

tively, P=0.05). Moreover, in a sensitivity analysis considering the  $HbA_{1c}$  target of  $\leq$ 7.0% ( $\leq$ 53 mmol/mol) for individuals younger than 65 years and without major comorbidities, 15.2% in the group without obesity and 25.0% in the group with obesity failed to receive intensification of treatment when indicated (P=0.01). Adjusted analyses, correcting for complexity of care level, age,  $HbA_{1c}$ , hypoglycemia, insulin use and hypertension, also showed that the obesity group more frequently failed in receiving

pharmacological treatment intensification when required (odds ratio 1.87, 95% Cl 1.02–3.45).

Our results suggest that patients with obesity may be more vulnerable to therapeutic inertia in the treatment of diabetes. Despite presenting an increased risk of diabetes complications and unfavorable outcomes, we found that patients with obesity more frequently fail to receive pharmacological treatment intensification when necessary. Some factors may explain the delay in intensifying

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treatment in these patients. First, many effective agents that reduce glycemia may result in weight gain (4), and this may lead to a delay in the introduction of other drugs to the pharmacological treatment. Indeed, this may have been one of the limitations of the antihyperglycemic agents used in this study population. Second, the importance of lifestyle changes and weight loss as part of treatment for these patients (4) may delay the pharmacological intensification by physicians while insisting only on lifestyle changes. Also, newer glucose-lowering medications that promote weight loss, such as glucagon-like peptide 1 receptor agonists and sodium-glucose-cotransporter 2 inhibitors, although currently available, have a high cost and are inaccessible to most of the population in developing countries (5). Furthermore, the stigma of obesity has the potential to disrupt the health process and prevent many professionals from providing highquality care to these patients (2).

The mental processes and cognitive biases that guide medical decision-making when treating patients with obesity are still poorly studied and not fully understood. Despite this, our findings suggest that patients with obesity may have some of their disease aspects neglected and that the limits of glycemic control in patients with type 2 diabetes and obesity are more permissive, which reflect the need to carefully revisit therapeutic decisions in these patients.

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reviewing, and editing. All authors have reviewed the final version of the manuscript and agree with the publication of the results presented. J.A. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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