

## Glycemic control and associated factors in patients with type 1 diabetes mellitus in primary care in Southeastern Brazil

Heverton Alves Peres<sup>1</sup>, Edson Zangiacomi Martinez<sup>2</sup>,  
Carlos Manuel Viana<sup>3</sup>, Leonardo Régis Leira Pereira<sup>1</sup>

<sup>1</sup>Department of Pharmaceutical Sciences, School of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo, Ribeirão Preto, São Paulo, Brazil,

<sup>2</sup>Department of Social Medicine, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, São Paulo, Brazil, <sup>3</sup>Viana Health Center, Aruba

Diabetes is a self-managed condition with knowledge, attitudes and practices that can influence the overall treatment and outcomes delay the complications of diabetes. However, the few reported studies published point out that: low education level, poor adherence to pharmacotherapy and diet recommendations, infrequent monitoring of blood glucose, and insulin dosage regimen are associated with higher hemoglobin levels. This study aimed to assess the knowledge, adherence medication, and complexity of pharmacotherapy in T1DM patients in Brazil. A cross-sectional study was conducted involving 156 T1DM patients who were attending in primary care. Logistic regression analyses were conducted to assess the variables associated with glycemic control. The overall assessments of T1DM patients for the glycemic control were bad (121, 77.6%). However, T1DM patients with high MedTake Test (OR=2.4, CI=1.1-5.7) and Morisky-Green Test (OR= 2.5, CI=1.1-6.1), and in the use of dosage insulin (>40 units, OR=0.3, CI=0.1-0.7) and postprandial glucose (100-125mg/dl, OR=3.8, CI=1.1-14.6) had better glycemic control compared to uncontrolled patients. Glycemic control in Brazilians adults with T1DM is low. We suggested the screening patients with low MedTake and Morisky-Green Tests, increasing patient knowledge as part of a complex intervention that may lead to substantially improved treatment outcomes in primary care.

**Keywords:** Medication adherence. Glycemic control. Diabetes. Knowledge. Brazil.

### INTRODUCTION

Diabetes mellitus (DM) it's one of four priorities highlighted for intervention by the Strategic Action Plan Tackling NCDs, 2011-2022 and by the World Health Organization (WHO, 2014). The resultant chronic associated complications and hospitalizations produce high costs for the health systems, consuming 5-15% of annual health care budgets (Malta *et al.*, 2019). Type 1 diabetes mellitus (T1DM) hallmark is insulin deficiency, destruction of the insulin producing pancreatic  $\beta$  cells, producing a hyperglycemic state. Treatment for T1DM requires continued

use of exogenous insulin to prevent acute and chronic, life-threatening complications. Even under ongoing medical care, T1DM patients can develop peripheral neuropathy nerve damage, retinopathy and an increased risk for cardiovascular disease, resulting in a reduced life expectancy. In patients not properly treated, comorbid outcomes are more severe. In Brazil, the reported incidence is 10.4 cases of T1DM per 100,000 inhabitants (Souza *et al.*, 2020; International Diabetes Federation, 2019). The annual incidence of T1DM varies greatly between countries, ranging from 1.1 to 39.9 per 100,000 people age 15-19 years. However, globally T1DM rates are increasing at a rate of 3% per year, predicting long-term T1DM comorbidities resulting in increasing health care costs while negatively impacting quality of life (Tuomilehto, 2013; Diaz-Valencia, Bougnères, Valleron, 2015).

\*Correspondence: H. A. Peres. Departamento de Ciências Farmacêuticas. Faculdade de Ciências Farmacêuticas de Ribeirão Preto. Universidade de São Paulo. Av do Café, s/n 14040-903 – Ribeirão Preto – SP, Brasil. Phone: 55 16 99215-4036. E-mail: pereshevertonalves@gmail.com. ORCID: <https://orcid.org/0000-0002-2089-6559>

The targets in T1DM management can be achieved through intensive insulin therapy and healthy habits. It is evident that adherence to recommended pharmacotherapy and medical recommendations contribute to maintaining adequate glycated hemoglobin (HbA1c) levels. Achieving and maintaining ideal HbA1c of less than seven <7.0% delays diabetes-related chronic complications (Gomes *et al.*, 2017; Nathan, 2014). Unfortunately, most T1DM patients in primary care have HbA1c values above this target (Peres *et al.*, 2020, Peres *et al.*, 2019). Various studies are reporting a disturbing scenario where up to 90% T1DM patients have inadequate glycemic control (HbA1c levels >7.0%) (McCarthy, Funk, Grey, 2016; Braga de Souza *et al.*, 2015; Mendes *et al.*, 2010).

Appreciating and being familiar with the factors influencing glycemic control in primary care T1DM patients should be relevant within health systems, and yet, presents an ongoing challenge for health professionals. A literature review reveals that most investigating studies of glycemic control determinants had enrolled patients with T1DM and T2DM combined or studied patient with T2DM. Thus, there is a research paucity exploring determining factor to achieve glycemic control in patients with T1DM in primary care. The few reported studies published point out that: low education level, poor adherence to pharmacotherapy and diet recommendations, infrequent monitoring of blood glucose, and insulin dosage regimen are associated with higher HbA1c levels (Peres *et al.*, 2015). Useful would be to study T1DM patients with inadequate glycemic control in vis-a-vis with the variables: patient's understanding of their recommended therapy, the complexity of their medical regimes, drug load, and length in medical attendance.

Almost 80% of the Brazilian population requests DM treatment within the public health sector (Peres *et al.*, 2020). With sample data from a basic health unit, we researched the consequences of the variables that may influence glycemic control in primary care T1DM patients. Our hypothesis: patients with better MedTake (MT) scores, lower Pharmacotherapy Complexity Index (PCI) scores and lower complications of diabetes (DCSI) would have better glycemic control. This study aimed to evaluate what variables in T1DM patients in the primary care influencing their glycemic control Southeast Region of Brazil.

## MATERIAL AND METHODS

### Study design and participants

This was a cross-sectional study conducted in Franca in the Brazilian state of Sao Paulo, from August 2017 to February 2018. Participants for the study were recruited from the basic health unit known as House Diabetes. Since much of our medical research data was going to be observational, in this study we followed the guidelines in Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement. In Brazil, unidade básica de saúde (UBS), also called Basic Health Unit, is the preferred medical treatment entry point into the Unified Health Service (*Sistema Único de Saúde (SUS)*), that manages the organization and integration of Brazilian healthcare networks. Participants with confirmed T1DM, aged 18 to 90 years, using isophane insulin (NPH) or regular insulin, and having earned a basic or more advanced education level were included in the study. Patients with T2DM, or those who had cognitive impairment, chronic diseases of greater complexity (i.e. cancer, kidney disease) pregnancy and all patients missing HbA1c results in their medical records were excluded. Subsequently, clinical parameters and variables for factual data were collected from medical records, including fasting and postprandial blood glucose levels, and HbA1c scores during the previous six months.

### Sample description

The sample size of our study was calculated using epidemiological information of Basic Health Unit. Non-probabilistic sampling was applied: the sample was obtained by convenience and comprised patients with T1DM who attended medical visits in the Basic Health Unit. The sample calculation in the present study was based on the following parameters: confidence level of 95%, error of 5%, and prevalence of 50%. These parameters considered the heterogeneity of the events to be measured. At the end a minimum sample size of 147 patients was required. After the pilot interview a loss of 30% was assumed and a sample of 210 patients with T1DM was targeted for interviews.

## Data collection

All data were collected by one researcher. All qualifying patients were given an open questions research questionnaire. Previously, to correct differences of language interpretation, the questionnaire was studied and standardized by twenty patients. These editing volunteers were excluded from the study.

Selected patients were first interviewed an average of 20 minutes in a room separate from the doctor's office. The variables collected through the questionnaire included: gender, age, marital status, per capita income, co- morbidities, education level, duration of diabetes diagnosis, number of drugs prescribed, time in treatment, body mass index (BMI), waist circumference, levels of fasting blood glucose, postprandial glucose, and Hb1Ac. After the interview, participants had a medical consultation.

## Questionnaires

To evaluate patient's compliance to pharmacotherapy recommendations, number of insulin injections missed, the patient's knowledge of the prescribed drugs, and pharmacotherapy complexity, the following tests were applied: Diabetes Complications Index (DCSI) Morisky Green Test modified (MGT), Pharmacotherapy Complexity Index (PCI), MedTake (MT), and the Auto-Compliance Test (ACT).

Associated diabetes complications were evaluated using the Diabetes Complications Index (DCSI) diagnostic tool. The DCSI tool is composed of seventeen (17) questions: five (5) questions evaluate coronary heart disease, three (3) questions are stroke specific, two (2) questions explore peripheral vascular disease, two (2) question neuropathy, three (3) questions deal with problems with the lower extremities, and two (2) questions deal with diabetic retinopathy (Fincke *et al.*, 2005). Each complication is determined by two or more questions, e.g., coronary heart disease is present if the patient reported having a myocardial infarction, symptoms of angina pectoris, or having been diagnosed by a doctor as having coronary heart disease. The DCSI tool calculates the sum of any complications that are present, resulting

in ascending scores from 0 to 6, where '0' indicates no complications and '6' reflects many complications.

To evaluate therapy compliance the Morisky Medication Adherence Scale modified (MMAS-6) was applied (Morisky, Green, Levine, 1986). Four questions with Yes/No answers comprise this test: (1) Have you ever forgotten to take your medicine for diabetes? (2) At times, are you not careful about taking your medicine for diabetes? (3) When you feel better, do you sometimes stop taking your medicine? (4) At times, if you feel worse when you take your medicine, do you stop taking it? (5) Do you know the long-term benefits of taking your medicine? (6). At times do you forget to refill your medicines in a timely manner? The patient only answers questions five and six only if they answer 'yes' to all of questions one to four. The patients with scores of more than eighty percent ( $\geq 80\%$ ) in the MGT, that evaluates their adherence to recommended medication were considered 'compliant'.

Quantifying drug regimen complexity was based on the quantity of medications, dosage frequency, dosage form and additional instructional (e.g., to take medication at a specified time, timing with food/liquid and whether to break/crush the tablet), we used the PCI. This tool is divided into three sections and was translated and validated from the MRCI (Medication Regimen Complexity Index) for Portuguese. The PCI is obtained by the sum of all three sections (A+B+C) scores. High section scores are defined as greater complexity and possible increased medication side effects (Melchior, Correr, Fernández-Llamos, 2007).

The Medtake (MT) tool was used to determine patient's knowledge of their prescribed medications. The MT evaluates indication, regime, dosage (units), and knowledge about the drug-interaction or food-drug interaction of medications prescribed (Raehl *et al.*, 2002). Scores range from 0 to 100 % and the mean of all test scores for each patient is calculated, that assesses patients' ability to safely use their prescribed drugs. Patients who correctly answered the four questions have a score of one hundred percent (100%) and participants who answered only three questions receive a score of seventy- five percent (75%).

The Anatomical Therapeutic Chemical Classification (ATC) system was compared with the Defined Daily Dose (DDD) system, and the ATC: DDD

ratio serves as a tool for drug utilization research, that when employed can improving drug utilization quality. The foundation of this system is the comparison and presentation of drug consumption statistics with international and other levels. The drug dosage taken by the patient was divided by defining the daily dose according to international drug utilization research. When the subject takes more of one drug, the ATC: DDD ratio values increase. Subjects with high drug load values are over-medicated and risk a probability of high adverse effect (Available: <http://www.whooc.no/>).

To evaluate the number of insulin injections missed in the previous months, we used the Auto compliance test (ACT) instrument. ACT instrument assesses the patient's self-reporting of the difficulty of applying insulin by asking two open questions: (1) "Did you have any difficulties with your insulin injection?" and (2) "How many times did you skip insulin injection in the last month?" The ACT was calculated using the following formula: Total number of insulin injections prescribed/actual number of prescribed insulin injections x 100. Subjects who affirmed taking more than eighty percent (>80%) of the total of number of prescribed insulin injections were labeled 'compliant' with their recommended protocol (Farsaei *et al.*, 2014).

### Ethics approval

This study was approved by the Research Ethics Committee of the the School of Medicine of Ribeirão Preto, University of São Paulo (technical opinion number 049698/2015), and all patients provided informed consent prior to participating.

### Data analyses

Patients selected for this study were initially divided into two groups: one group controlled with good glycated hemoglobin levels of or less than seven percent ( $\leq 7.0\%$ ) and other group with patients with glycated hemoglobin Greater than seven percent ( $> 7.0\%$ ). The continuous variables were reported as the mean and the standard deviation and variables were categorized as frequency and percentage around the mean.

To evaluate the effect of variables exerted in the controlled and uncontrolled group, a logistic regression model was executed. We used Hb1Ac as the dependent variable while the independent variables included relevant clinical, demographics, and medication data.

Associating glycemic control with the independent variables, a logistic regression model was used. This model produces odds ratios (OR) as a relationship measure, with a respective ninety percent confidence intervals (95% CI). A confidence interval not including 1 were considered statistically significant (analogous to p-value when less than  $<0.05$ , the null hypothesis is rejected since there is no difference between the means). For all statistic procedures, SAS (previously "Statistical Analysis System") software version 9.0 was used.

## RESULTS AND DISCUSSION

Out of 210 diabetic patients approached, 156 were within our inclusion criteria and agreed to participate in this study. Of the 156 (100%) patients with T1DM enrolled in the study, 22.4% (35/156) have achieved the target Hb1Ac level equal or less than seven percent ( $\leq 7.0\%$ ) and 77.6% (121/156) have poorly controlled diabetes with high levels of Hb1ac greater than seven percent ( $> 7.0\%$ ). In the controlled group, those with target levels of Hb1Ac ( $\leq 7.0\%$ ), males were a slight majority (60%), lighter skin color (57%), and average age of 59 (SD= 15.5) years, basic education earned 0-8 years (62.8%), per capita income in Brazilian Reais (BRL) 581.2 (SD = 251) and marital status single/divorced (57.2%). The number of comorbidities was 3.5 (SD=1.7) and the time since being diagnosed was 216 (SD=122) months.

The main comorbidities related to DM were hypertension (25.5%), dyslipidemia (18.3%), depression (10.6%) and congestive heart failure (10%). There was significant difference in myocardial infarction rates between controlled group where eight participants had a heart attack compared to uncontrolled group where fifteen had a cardiac incident (8 vs. 15,  $p<0.04$ ) within chronic complications, retinopathy (19%) was emphasized by participants. Patients of both groups are overweight, but obesity predominated in the uncontrolled group 29.4kg / m<sup>2</sup> (SD =5.8). Lower levels of fasting blood glucose

( $134.5 \pm 60$  vs.  $169.6 \pm 80$ ,  $p < 0.02$ ) and postprandial glycaemia ( $165.5 \pm 55.6$  vs.  $237.4 \pm 101$ ,  $p < 0.01$ ) were

found in controlled group compared to the uncontrolled group, highlighting a significant difference (Table I).

**TABLE I -** Baseline demographic and clinical characteristics of T1DM patients (n=156)

|                                  | Controlled n=35 | Uncontrolled n=121 | OR(CI)       | P value <sup>(a)</sup> |
|----------------------------------|-----------------|--------------------|--------------|------------------------|
| Gender <sup>a</sup>              |                 |                    |              |                        |
| Male                             | 21(60.0)        | 63(52.1)           | 1.4(0.5-2.1) | 0.40                   |
| Female                           | 14(40.0)        | 58(47.9)           |              |                        |
| Race <sup>a</sup>                |                 |                    |              |                        |
| White                            | 20(57.0)        | 51(42.1)           | 1.7(0.5-5.8) | 0.33                   |
| Black                            | 4(11.5)         | 18(14.8)           |              |                        |
| Brown                            | 11(31.5)        | 52(42.9)           | 1.0(0.3-3.7) | 0.93                   |
| Marital Status <sup>a</sup>      |                 |                    |              |                        |
| Married                          | 20(57.2)        | 62(51.2)           | 1.2(0.6-2.7) | 0.51                   |
| Single/Divorced                  | 15(42.8)        | 59(48.8)           |              |                        |
| Schooling (years) <sup>a</sup>   |                 |                    |              |                        |
| 0-8                              | 22(62.8)        | 73(60.3)           | 1.1(0.5-2.4) | 0.78                   |
| 9-12                             | 13(37.2)        | 48(39.7)           |              |                        |
| Clinical Parameters <sup>b</sup> |                 |                    |              |                        |
| Time diagnosis(months)           | 216±122         | 202±107            |              | 0.69                   |
| Number of comorbidities          | 3.4±2.1         | 4.1±2.1            |              | 0.05                   |
| Per capita income                | 581.2±251       | 577.5±259          |              | 0.81                   |
| Age                              | 59±15.5         | 56.7±17.4          |              | 0.45                   |
| Body mass Index                  | 28.2±5.7        | 29.4±5.8           |              | 0.20                   |
| Fasting blood glucose (mg)       | 134.5±60        | 169.6±78           |              | 0.02*                  |
| Drug load                        | 1.5±1.1         | 1.7±0.7            |              | 0.08                   |
| Number of medicines              | 4.4±2.4         | 5.4±2.7            |              | 0.02*                  |
| Postprandial glucose (mg)        | 165.5±56.2      | 237.4±101          |              | 0.01*                  |
| Time medical services (minutes)  | 11.2±3.9        | 11.1±4.6           |              | 0.83                   |
| MedTake test                     | 65.9±17.4       | 55.4±22.8          |              | 0.03*                  |
| Morisky-Green modified           | 85.5±16.3       | 76.8±17.8          |              | 0.02*                  |
| Pharmacotherapy Complexity Index | 14.9±4.5        | 18±6               |              | 0.01*                  |
| Diabetes Complications Index     | 1.9±1.4         | 2.2±1.5            |              | 0.29                   |
| Auto Compliance Test             | 99.7±0.6        | 97.7±5.5           |              | 0.06                   |
| Comorbidities <sup>a</sup>       | 3.5±1.7         | 4.1±1.8            |              | 0.10                   |
| Hypertension                     | 21(24.1)        | 82(25.5)           |              | 0.20                   |
| Dyslipidemia                     | 12(13.8)        | 59(18.3)           |              | 0.06                   |

**TABLE I - Baseline demographic and clinical characteristics of T1DM patients (n=156)**

|                               | <b>Controlled n=35</b> | <b>Uncontrolled n=121</b> | <b>OR(CI)</b> | <b>P value <sup>(a)</sup></b> |
|-------------------------------|------------------------|---------------------------|---------------|-------------------------------|
| Congestive heart failure      | 15(17.0)               | 29(10.0)                  |               | 0.83                          |
| Heart attack                  | 8(10.0)                | 15(4.7)                   |               | 0.04*                         |
| Stroke                        | 3(3.0)                 | 11(3.4)                   |               | 0.89                          |
| Depression                    | 6(6.0)                 | 34(10.6)                  |               | 0.11                          |
| Retinopathy                   | 14(16.1)               | 61(19.0)                  |               | 0.24                          |
| Thyroid                       | 8(10.0)                | 30(9.4)                   |               | 0.72                          |
| Pharmacotherapy <sup>ab</sup> |                        |                           |               |                               |
| NPH Insulin dosage (mg)       | 47.3±25.3              | 55.3±22.5                 |               | 0.06                          |
| Regular Insulin dosage (mg)   | 12.5±6.1               | 15.5±8.6                  |               | 0.18                          |
| Captopril                     | 2(3.7)                 | 4(1.9)                    |               |                               |
| Hydrochlorothiazide           | 5(9.3)                 | 15(7.2)                   |               |                               |
| Losartan                      | 9(16.6)                | 34(16.4)                  |               |                               |
| Sinvastatin                   | 5(9.3)                 | 34(16.4)                  |               |                               |
| Levothyroxine                 | 6(11.2)                | 29(14.0)                  |               |                               |
| Acetylsalicylic acid          | 9(16.6)                | 49(23.7)                  |               |                               |
| Carvedilol                    | 5(9.3)                 | 16(7.7)                   |               |                               |
| Amlodipine                    | 2(3.7)                 | 11(5.3)                   |               |                               |
| Omeprazole                    | 4(7.4)                 | 15(7.2)                   |               |                               |
| Enalapril Maleate             | 7(12.9)                | 21                        |               |                               |

Legends: Bold values indicate significant difference.

a=frequency and percentage;

b=mean and standard deviation.

There was significant difference between groups in the following drug-related variables: number of medications ( $4.4 \pm 2.4$  vs.  $5.4 \pm 2.7$ ,  $p < 0.02$ ). Determining patient's knowledge of their prescribed medications, MT ( $65.9 \pm 17.4$  vs.  $55.4 \pm 22.8$ ,  $p < 0.03$ ). Evaluating compliance to therapy protocol, MGT ( $85.5 \pm 16.3$  vs.  $76.8 \pm 17.8$ ,  $p < 0.02$ ). Quantifying drug regimen complexity, the PCI was ( $14.9 \pm 4.5$  vs.  $18 \pm 6$ ,  $p < 0.01$ ).

To treat comorbidities, most used medications in both groups were: Levothyroxine (L-thyroxine), Omeprazole, Acetylsalicylic Acid, Enalapril (enalapril maleate), Hydrochlorothiazide, Simvastatin, Carvedilol and Losartan (losartan potassium) (Table I).

Variables in the regression model included fasting blood glucose (odds ratio (OR)=3.8, confidence interval (CI) =1.1-14.6), MT(OR=2.4, CI=1.1-5.7) and MGT(OR=2.5, CI=1.1-6.1). These variables were significantly associated with increased odds of achieving better glycemic control in patients with T1DM (Table II). Postprandial glucose variables (OR=0.3, CI=0.1-0.7) and insulin dosage (insulin NPH) greater than forty (>40) units (OR=0.3, CI=0.1-0.7) showing a protective, prophylactic effect for the controlled group.

**TABLE II** - Logistic regression of the Hb1Ac variable with the comorbidities

|                          | Controlled<br>n=35 | Uncontrolled<br>n=121 | Crude OR<br>(95%CI) | Adjusted OR <sup>(a)</sup><br>(95%CI) |
|--------------------------|--------------------|-----------------------|---------------------|---------------------------------------|
| Age (years)              |                    |                       |                     |                                       |
| ≤ 40                     | 5 (14.3)           | 20 (16.5)             | Ref.                | Ref.                                  |
| 41 – 60                  | 12 (34.3)          | 48 (39.7)             | 1.0 (0.3 – 3.2)     | 1.4 (0.3 – 4.9)                       |
| > 60                     | 18 (51.4)          | 53 (43.8)             | 1.4 (0.4 – 4.1)     | 1.8 (0.5 – 6.0)                       |
| Gender                   |                    |                       |                     |                                       |
| Male                     | 14 (40.0)          | 63 (52.1)             | Ref.                | Ref.                                  |
| Female                   | 21 (60.0)          | 58 (47.9)             | 1.6 (0.7 – 3.5)     | 1.6 (0.7 – 3.5)                       |
| Race                     |                    |                       |                     |                                       |
| White                    | 20 (57.1)          | 51 (42.1)             | Ref.                | Ref.                                  |
| Black                    | 4 (11.4)           | 18 (14.9)             | 0.6 (0.1 – 1.9)     | 0.6 (0.1 – 2.1)                       |
| Brown                    | 11 (31.4)          | 52 (43.0)             | 0.5 (0.2 – 1.2)     | 0.6 (0.2 – 1.3)                       |
| Marital Status           |                    |                       |                     |                                       |
| Married                  | 20 (57.1)          | 62 (51.2)             | Ref.                | Ref.                                  |
| Single/Divorced          | 15 (42.9)          | 59 (48.8)             | 0.8 (0.3 – 1.7)     | 0.9 (0.3 – 2.5)                       |
| Schooling (years)        |                    |                       |                     |                                       |
| 0-8                      | 22 (62.9)          | 73 (60.3)             | Ref.                | Ref.                                  |
| 9-12                     | 13 (37.1)          | 48 (39.7)             | 0.9 (0.4 – 2.0)     | 0.7 (0.3 – 1.7)                       |
| Diagnosis (months)       |                    |                       |                     |                                       |
| <120                     | 10 (28.6)          | 25 (20.7)             | Ref.                | Ref.                                  |
| 120–240                  | 12 (34.3)          | 63 (52.1)             | 0.5 (0.1 – 1.2)     | 0.4 (0.1 – 1.2)                       |
| >400                     | 13 (37.1)          | 33 (27.3)             | 1.0 (0.3 – 2.6)     | 0.8 (0.3 – 2.5)                       |
| Income                   |                    |                       |                     |                                       |
| <400                     | 15 (42.9)          | 46 (38.0)             | Ref.                | Ref.                                  |
| 400-600                  | 5 (14.3)           | 28 (23.1)             | 0.5 (0.1 – 1.7)     | 0.5 (0.1 – 1.6)                       |
| >600                     | 15 (42.9)          | 47 (38.8)             | 1.0 (0.4 – 2.2)     | 0.8 (0.3 – 1.9)                       |
| BMI (kg/m <sup>2</sup> ) |                    |                       |                     |                                       |
| ≤ 25                     | 8 (22.9)           | 28 (23.1)             | Ref.                | Ref.                                  |
| (25 – 30]                | 19 (54.3)          | 34 (28.1)             | 1.9 (0.7 – 5.2)     | 1.9 (0.5 – 6.3)                       |
| >30                      | 8 (22.9)           | 59 (48.8)             | 0.5 (0.1 – 1.4)     | 0.4 (0.1 – 1.4)                       |
| Hypertension             |                    |                       |                     |                                       |
| No                       | 14 (40.0)          | 39 (32.2)             | Ref.                | Ref.                                  |
| Yes                      | 21 (60.0)          | 82 (67.8)             | 0.7 (0.3 – 1.5)     | 0.6 (0.2 – 1.4)                       |
| Dyslipidemia             |                    |                       |                     |                                       |
| No                       | 23 (65.7)          | 62 (51.2)             | Ref.                | Ref.                                  |

**TABLE II** - Logistic regression of the HB1Ac variable with the comorbidities

|                            | <b>Controlled<br/>n=35</b> | <b>Uncontrolled<br/>n=121</b> | <b>Crude OR<br/>(95%CI)</b> | <b>Adjusted OR <sup>(a)</sup><br/>(95%CI)</b> |
|----------------------------|----------------------------|-------------------------------|-----------------------------|-----------------------------------------------|
| Yes                        | 12 (34.3)                  | 59 (48.8)                     | 0.5 (0.2 – 1.2)             | 0.4 (0.1 – 1.1)                               |
| Congestive heart failure   |                            |                               |                             |                                               |
| No                         | 26 (74.3)                  | 91 (75.2)                     | Ref.                        | Ref.                                          |
| Yes                        | 9 (25.7)                   | 30 (24.8)                     | 1.1 (0.4 – 2.5)             | 1.1 (0.4 – 2.7)                               |
| Heart attack               |                            |                               |                             |                                               |
| No                         | 27 (77.1)                  | 106 (87.6)                    | Ref.                        | Ref.                                          |
| Yes                        | 8 (22.9)                   | 15 (12.4)                     | 2.1 (0.8 – 5.4)             | 2.8 (0.9 – 8.4)                               |
| Stroke                     |                            |                               |                             |                                               |
| No                         | 32 (91.4)                  | 110 (90.9)                    | Ref.                        | Ref.                                          |
| Yes                        | 3 (8.6)                    | 11 (9.1)                      | 0.9 (0.2 – 3.6)             | 1.0 (0.2 – 4.0)                               |
| Depression                 |                            |                               |                             |                                               |
| No                         | 29 (82.9)                  | 87 (71.9)                     | Ref.                        | Ref.                                          |
| Yes                        | 6 (17.1)                   | 34 (28.1)                     | 0.5 (0.2 – 1.4)             | 0.4 (0.1 – 1.2)                               |
| Retinopathy                |                            |                               |                             |                                               |
| No                         | 21 (60.0)                  | 58 (47.9)                     | Ref.                        | Ref.                                          |
| Yes                        | 14 (40.0)                  | 63 (52.1)                     | 0.6 (0.2 – 1.3)             | 0.5 (0.2 – 1.5)                               |
| Thyroid                    |                            |                               |                             |                                               |
| No                         | 27 (77.1)                  | 93 (76.9)                     | Ref.                        | Ref.                                          |
| Yes                        | 8 (22.9)                   | 28 (23.1)                     | 1.0 (0.4 – 2.4)             | 0.8 (0.3 – 2.3)                               |
| Fasting blood glucose (mg) |                            |                               |                             |                                               |
| <100                       | 7 (20.0)                   | 21 (21.6)                     | Ref.                        | Ref.                                          |
| 100-125                    | 10 (28.6)                  | 9 (9.3)                       | 3.3 (0.9 – 11.5)            | 3.8 (1.1 – 14.6)*                             |
| >125                       | 18 (51.4)                  | 67 (69.1)                     | 0.8 (0.3 – 2.2)             | 0.8 (0.2 – 2.4)                               |
| Postprandial glucose (mg)  |                            |                               |                             |                                               |
| <140                       | 12 (34.3)                  | 17 (15.2)                     | Ref.                        | Ref.                                          |
| ≥140                       | 23 (65.7)                  | 95 (84.7)                     | 0.3 (0.1 – 0.8)*            | 0.3 (0.1 – 0.7)*                              |
| Insulin NPH (units)        |                            |                               |                             |                                               |
| <40                        | 17 (48.6)                  | 31 (25.6)                     | Ref.                        | Ref.                                          |
| ≥40                        | 18 (51.4)                  | 90 (74.4)                     | 0.4 (0.1 – 0.8)*            | 0.3 (0.1 – 0.7)*                              |
| Insulin regular (units)    |                            |                               |                             |                                               |
| <10                        | 6 (25.0)                   | 26 (25.5)                     | Ref.                        | Ref.                                          |
| ≥10                        | 18 (75.0)                  | 76 (74.5)                     | 1.0 (0.3 – 2.9)             | 1.0 (0.3 – 3.0)                               |
| Medical care time (min)    |                            |                               |                             |                                               |
| <10                        | 18 (52.9)                  | 50 (43.9)                     | Ref.                        | Ref.                                          |

**TABLE II** - Logistic regression of the Hb1Ac variable with the comorbidities

|               | Controlled<br>n=35 | Uncontrolled<br>n=121 | Crude OR<br>(95%CI) | Adjusted OR <sup>(a)</sup><br>(95%CI) |
|---------------|--------------------|-----------------------|---------------------|---------------------------------------|
| ≥10           | 16 (47.1)          | 64 (56.1)             | 0.7 (0.3 – 1.5)     | 0.6 (0.2 – 1.3)                       |
| Medtake       |                    |                       |                     |                                       |
| <70           | 10 (28.6)          | 61 (51.3)             | Ref.                | Ref.                                  |
| ≥70           | 25 (71.4)          | 58 (48.7)             | 2.6 (1.2 – 5.9) *   | 2.4 (1.1 – 5.7)*                      |
| PCI           |                    |                       |                     |                                       |
| 5-10          | 3 (8.8)            | 5 (4.2)               | Ref.                | Ref.                                  |
| >10           | 31 (91.2)          | 113 (95.8)            | 0.4 (0.1 – 2.0)     | 0.3 (0.1 – 1.7)                       |
| DCI           |                    |                       |                     |                                       |
| <2            | 13 (37.1)          | 43 (35.5)             | Ref.                | Ref.                                  |
| ≥2            | 22 (62.9)          | 78 (64.5)             | 0.9 (0.4 – 2.0)     | 0.8 (0.3 – 2.0)                       |
| Morisky Green |                    |                       |                     |                                       |
| <80           | 8 (22.9)           | 52 (43.0)             | Ref.                | Ref.                                  |
| ≥80           | 27 (77.1)          | 69 (57.0)             | 2.5 (1.1 – 6.1) *   | 2.3 (0.9 – 5.6)                       |

Legends:(a) adjusted OR for gender, age and time of diagnosis, MT = Medtake, PCI = Pharmacotherapy Complexity Index, DCI = Diabetes Complication Index.

Our reporting provides clinical significance to current research literature by highlighting the practical importance of treatment plans effected by new reported factors associated with poor glycemic control, fasting blood glucose, postprandial glucose from low patient's knowledge of their prescribed medications, MT and not being compliant to therapy protocol, (MGT scores). Intriguingly, the postprandial glucose levels and insulin NPH dosage greater than forty (>40) units in the controlled group's analyzed regression model showed a prophylactic, protective result. We can see relevant therapeutic compliance and a good working knowledge of their prescribed medications (high MT scores) contributes to better glycemic control, decreased diabetes complications, and lower public health costs. We found the controlled group, those that achieved target Hb1Ac level equal or less than seven percent ( $\leq 7.0\%$ ) had lower levels of fasting blood glucose, postprandial, more compliance to therapy protocol (MGT) and a working knowledge of their prescribed medications (MT

scores), confirming our initial hypothesis. Additionally, we founded significant differences for all the following variables in the control group: lower Pharmacotherapy Complexity Index (PCI) scores, lower drug load, lower insulin dose and having to take less pharmaceuticals.

Clinically, the findings above contribute to identifying individual patient characteristics and clinical aspects related to helping T1DM patients achieve ideal Hb1Ac level equal or less than seven percent ( $\leq 7.0\%$ ). We have shown that T1DM patients in basic health units (PC) clinics that are compliance and knowledgeable about their therapeutic recommendations get along much better health wise. These findings stress that increasing patient's knowledge of their prescribed medications, MT scores, and encouraging a higher compliance to therapy protocol, MGT, are modifiable factors possibly accomplished by specific treatment actions and providing relevant pharmaceutical care, non-compliant patients could be educated, improving their health status. Indeed, our findings add valuable treatment information for a better

understanding of the barriers to T1DM patients achieving adequate glycemic levels. Understanding the impact of these variables on T1DM patients should aid health professionals take into consideration the influencing variables and improve T1DM patient health status. Besides that, the risk of developing DM complications are influenced by patient's knowledge of disease (American Diabetes Association, 2018; Simard *et al.*, 2015).

The macrovascular and microvascular complications associated with poor glycemic control in patients with DM and majority of patients with T1DM worldwide reflect the consequences of inadequate glycemic control (American Diabetes Association, 2018; Andrade *et al.*, 2017; Angamo, Melese, Ayen, 2013). This study, the average HbA1c level was a high nine-point eight percent (9.8%) for the uncontrolled group. Results of data similarly reported in a multicenter, T1DM study, conducted between 2008 and 2010 in 20 Brazilian cities (Braga de Souza *et al.*, 2015). A recent study done in Brazil reported that for the patient to achieve normoglycemia or euglycemia HbA1c levels seven or less percent ( $\leq 7.0\%$ ), an investment of US\$ 2,419.06 (value/patient/year) is necessary and as the value of HbA1c decreases, costs are reduced (Gonçalves *et al.*, 2019).

In most Brazilian basic health units, medications are dispensed and are only delivered to the patient without pharmaceutical instruction. Lacking patient education on their medication and helping DM patients understand the need for strict compliance to treatment recommendations, results in high probability of treatment failure. Low adherence to therapy and resulting adverse effects increases repeat visits to the basic health units, the need for more medication and higher public health system cost. Patient education works when a pharmaceutical care program was provided to patients with DM and hypertension a seven- tenth percent (0.7%) reduction in HbA1c levels provides a saving of US\$ 660.00 per patient per year (Obreli-Neto *et al.*, 2011).

There is a paucity of MedTake (MT) studies to evaluate in primary care diabetes patient's knowledge of their prescribed medications. In the last years, our research group has published various research articles that used MT tool to determine patient's knowledge of their prescribed medications and the MGT questionnaire

to evaluate medication adherence. The results of these studies have demonstrating T1DM and T2DM patients with high MT and MGT scores have better glycemic control (Peres, Pereira, Foss, 2017, Peres *et al.*, 2017). Pertain to MT and MGT scores, our data agrees with other research that conclude patients with higher MT and MGT have better glycemic control (Peres *et al.*, 2020, Peres *et al.*, 2019). Our study establishes an association for MT and MGT scores with better glycemic control in patients with T1DM (Table II).

The challenge for Brazil and public health providers worldwide, mainly in primary care, is to better educate diabetic patients. Other studies reinforce what we found, diabetes education programs in patients with T1DM was associated with better glycemic control (Speight *et al.*, 2016; Ba-Essa *et al.*, 2015). This baseline demonstrates pharmaceutical care may contribute to better pharmacotherapy compliance, improving knowledge about DM and improving confidence to better self-manage the consequences of deficient insulin secretion. Treatment education of how to better manage T1DM and information on how to adopt better lifestyle habits go a long way in helping patients achieved adequate glycemic goals. Thus, to achieve better glycemic control, patient knowledge about their disease is crucial to improve compliance and to better understand the recommendations provided by the multi-professional health team.

Our data are in line with studies that found no association between level of education vis-à-vis glycemic control (Andrade *et al.*, 2017; Tiv *et al.*, 2012; Zhu *et al.*, 2011). However, a cohort Brazilian study of T1DM patients did report an association between higher education and better glycemic control (Andrade *et al.*, 2017). Although, no association between education level and antihyperglycemic issues has been established thus far, the topic deserves analysis from health professionals and researchers, and could greatly contribute to the planning education activities and evaluation recommendations to local health services.

We suggest a method in primary care to simplify patient understanding about their diabetes disease is to produce and disseminate graphic stories told mostly in pictures with some plain writing. A "comic book" format provides a simplified but powerful visual message which

conveys immediate intuitive understanding. Widely distributed graphic stories providing diabetes information and lifestyle recommendations would result in better diabetic patient care and education on prescription medication (Peres *et al.*, 2017).

Reaching healthy glycemic goals, the cornerstone of T1DM patient management involves intensive insulin therapy, non-pharmacological therapy (i.e. medical nutrition advises) and regular physical activity. Achieving these goals will delay macrovascular and microvascular diabetic complications. T1DM patients require continued reevaluation of scripted exogenous insulin to better control glycemic levels, thus preventing acute and chronic complications. Significantly appropriate and adequate insulin dosage is dependent on the glycemic response of the individual's food choices, lifestyle and exercise regimes. Consequently, individual T1DM patient insulin dosage algorithm tailored to the specific needs and glycemic goals should be developed.

In our study, we found that insulin NPH dosage greater than forty ( $>40$ ) units and postprandial glucose levels greater than one hundred forty milliliters per deciliter ( $>140\text{mg/dl}$ ) analyzes in the regression model of the control group showed a prophylactic effect. Our data reflects what is being reported in current articles, patients with T1DM that have good adherence to recommended diet and insulin therapy and who have postprandial glucose levels ( $140\text{--}200\text{ mg/dl}$ ) achieve recommended glycemic goals (Gomes *et al.*, 2018; Gomes *et al.*, 2017; Andrade *et al.*, 2017). In a mirror result, substantiating our hypothesis, some studies have reported that patients with T1DM that use dosage of insulin less than forty units ( $<40$ ) have poor glycemic control (Angamo, Melese, Ayen, 2013). Here we can appreciate the results of lacking diabetes education for both healthcare providers and T1DM patients. In this spirit, the often quoted prediction of Sir Muir Gray, Director United Kingdom's National Knowledge Service predicted correctly "Knowledge is the enemy of disease, the application of what we know will have a bigger impact than any drug or technology likely to be introduced in the next decade."

Reflecting the findings in current literature, no significant difference is found between clinical and social demographic variables when compared with good

glycemic control (Andrade *et al.*, 2017; Braga *et al.*, 2015). Studies on 'time to diagnosis' indicate patients with a greater time since being diagnosed have greater diabetes knowledge, becoming more secure and self-confident vis-à-vis recommended therapeutic recommendations (Zhu *et al.*, 2011). Similarly, our data also reflects what is found in the current literature, but we did not find an association with this variable. Conversely, patients with less time of diagnosis and starting treatment are less compliant to recommended therapy. Gradually, neglect occurs with follow-up treatment recommendations due to patient's perception of negative results, lack of motivation, lack of family support, cultural issues and comorbid symptoms (Khattab *et al.*, 2010; Simard *et al.*, 2015). Thus, providing recently diagnosed T1DM patients a fully explained pharmaceutical protocols could increase therapy compliance and would decrease drug related problems.

Our study designed as an exploratory endeavor, has inherent limitations. Thus, the results might not be exempt from drawing conclusions about a causal connection, inference causality, or possible biases that might affect resulting values. Unfortunately, the study design does not allow to establish a causal relationship between the two events, a 'relation of causality'. Secondly, self-reporting generally tends to yield inflated estimates in test values and could have been somewhat lower than we observed. However, even though self-reporting has been criticized as an excessively subjective and upwardly based approach, we feel longitudinal analysis of symptoms and glycemic control in diabetes, the Aikens and Piette analysis strengthens the use of self-reporting in evaluating a diabetic patient (Aikens *et al.*, 2013). Thirdly, since our study was conducted in the same basic health unit, unidade básica de saúde (UBS) the generalization of data should be performed with caution. However, as cautious we are due to sample size, the results clearly show patient's knowledge of their prescribed medications, MT, and the evaluation to medication adherence, MGT results validate our hypothesis. Despite these limitations, the results of this study provide a basis for further planning in the development of strategic plans in clinical management and education in T1DM patients.

## CONCLUSION

This study assessed the knowledge, adherence medication, and complexity of pharmacotherapy among T1DM patients in the primary care setting southeast Brazil. Our results demonstrated that T1DM patients with higher MT and MGT scores using more than forty units (>40) insulin dosages and postprandial glucose greater than one hundred forty milligrams per deciliter (>140mg/dl) have good glycemic control. The challenge in clinical practice is to educate and inspire diabetes patients, cultivating a positive attitude in reaching and maintaining better glycemic control. Screening and intervening at risk T1DM patients with low MT and MGT scores, providing education could lower adverse effects, improve quality of life and reduce health costs. Recommendations for future clinical research should include larger data sets in different locations to add to the diabetes care knowledge base enhancing the knowledge of patients and health professionals in primary care. Finally, we suggested the development of more enlightening programs and campaigns focused in DM education, both T1DM patients and health care provider.

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## REFERENCES

Aikens JE, Piette JD. Longitudinal association between medication compliance and glycaemic control in Type 2 diabetes. *Diabet Med*. 2013;30(3):338-44.

American Diabetes Association AD. 6. Glycemic Targets: Standards of Medical Care in Diabetes-2018. *Diabetes Care*. 2018;41(Supl 1):S55-S64.

Andrade CS, Ribeiro GS, Santos CAST, Neves RCS, Moreira ED. Factors associated with high levels of glycated haemoglobin in patients with type 1 diabetes: a multicentre study in Brazil. *BMJ Open*. 2017;7(12):e018094.

Angamo MT, Melese BH, Ayen WY. Determinants of glycemic control among insulin treated diabetic patients in Southwest Ethiopia: hospital based cross sectional study. *PLoS One*. 2013;8(4):e61759.

Ba-Essa EM, Mobarak EI, Alghamdi A, Al-Daghri NM. Intensified glucose selfmonitoring with education in Saudi DM patients. *Int J Clin Exp Med*. 2015;8(10):19374-80.

Braga de Souza AC, Felício JS, Koury CC, Neto JF, Milléo KB, Santos FM, et al. Health-related quality of life in people with type 1 Diabetes Mellitus: data from the Brazilian Type 1 Diabetes Study Group. *Health Qual Life Outcomes*. 2015;13:204.

Diaz-Valencia PA, Bougnères P, Valleron AJ. Global epidemiology of type 1 diabetes in young adults and adults: a systematic review. *BMC Public Health*. 2015;15:255.

Farsaei S, Radfar M, Heydari Z, Abbasi F, Qorbani M. Insulin compliance in patients with diabetes: risk factors for injection omission. *Prim Care Diabetes*. 2014;8(4):338-45.

Fincke BG, Clark JA, Linzer M, Spiro A 3rd, Miller DR, Lee A, et al. Assessment of long-term complications due to type 2 diabetes using patient self-report: the diabetes complications index. *J Ambul Care Manag*. 2005;28(3):262-273.

Gomes MB, Rodacki M, Pavin EJ, Cobas RA, Felício JS, Zajdenverg L, et al. The impact of ethnicity, educational and economic status on the prescription of insulin therapeutic regimens and on glycemic control in patients with type 1 diabetes. A nationwide study in Brazil. *Diabetes Res Clin Pract*. 2017;134:44-52.

Gomes MB, Santos DC, Pizarro MH, Barros BSV, de Melo LGN, Negrato CA. Does knowledge on diabetes management influence glycemic control? A nationwide study in patients with type 1 diabetes in Brazil. *Patient Prefer Adherence*. 2018;12:53-62.

Gonçalves ACDO, Cazarim MDS, Sanches C, Pereira LRL, Baldoni ADO. How much to invest in glycemic control of a patient with diabetes mellitus type 2? A constant dilemma for the Brazilian Public Health System (SUS). *Braz J Pharm Sci*. 2019;55:e17197.

International Diabetes Federation. IDF Diabetes Atlas Ninth edition. 2019. <https://www.diabetesatlas.org/en/>. Accessed 28 Oct 2021.

Khattab M, Khader YS, Al-Khawaldeh A, Ajlouni K. Factors associated with poor glycemic control among patients with Type II diabetes. *J Diabetes Complicat*. 2010;24(2):84-89.

Malta DC, Duncan BB, Schmidt MI, Machado ÍE, Silva AGD, Bernal RTI, et al. Prevalence of diabetes mellitus as determined by glycated hemoglobin in the Brazilian adult population, National Health Survey. *Rev Bras Epidemiol*. 2019;22:E190006-SUPL.

McCarthy MM, Funk M, Grey M. Cardiovascular health in adults with type 1 diabetes. *Prev Med*. 2016;91:138-143.

- Melchior AC, Correr CJ, Fernández-Llamos F. Translation and validation into Portuguese language of the medication regimen complexity index. *Arq Bras Cardiol.* 2007;89(4):210-8.
- Mendes AB, Fittipaldi JA, Neves RC, Chacra AR, Moreira ED. Prevalence and correlates of inadequate glycaemic control: results from a nationwide survey in 6,671 adults with diabetes in Brazil. *Acta Diabetol.* 2010;47(2):137-45.
- Morisky DE, Green LW, Levine DM. Concurrent and Predictive Validity of a Self-Reported Measure of Medication Compliance. *Med Care.* 1986;24(1):67-74.
- Nathan DM. The Diabetes Control and Complications Trial/ Epidemiology of Diabetes Interventions and Complications Study at 30 Years: Overview. *Diabetes Care.* 2014;37(1):9-16.
- Obreli-Neto PR, Guidoni CM, Baldoni AO, Pilger D, CruciolSouza JM, Gaeti-Franco WP, et al. Effect of a 36-month pharmaceutical care program on pharmacotherapy adherence in elderly diabetic and hypertensive patients. *Int J Clin Pharm.* 2011;33(4):642-649.
- Peres HA, Freitas-Foss MC, Pereira LRL, Viana CM. New insights for the polypharmacy use in elderly with diabetes-an update about effect of education level. *J Endocrinol Diabetes.* 2017;4(5):1-6.
- Peres HA, Martinez EZ, Pereira LRL, Freitas-Foss MC. Age, the Number of Medicines Taken and Comorbidities are Associated with Changes of Fasting Blood Glucose Levels in Elderly Diabetics Taking Propranolol and Hydrochlorothiazide. *J Bioanal Biomed.* 2017;9(5):240-243.
- Peres HA, Pereira LRL, Martinez EZ, Viana CM, Foss-Freitas MC. Heart failure is associated with non-adherence to pharmacotherapy in elderly with type 2 diabetes mellitus in public health system Brazilians. *Diabetes Metab Syndr.* 2019;13(2):939-946.
- Peres HA, Pereira LRL, Martinez EZ, Viana CM, Foss-Freitas MC. Elucidating factors associated with non-adherence among Type 1 diabetes patients in primary care setting in Southeastern Brazil. *Prim Care Diabetes.* 2020;14(1):85-92. <https://pubmed.ncbi.nlm.nih.gov/31262602/>
- Raehl CL, Bond CA, Woods T, Patry RA, Sleeper RB. Individualized drug use assessment in the elderly. *Pharmacotherapy.* 2002;22(10):1239-48.
- Simard P, Presse N, Roy L, Dorais M, White-Guay B, Räkel A, et al. Persistence and compliance to oral diabetes: a population-based cohort study. *Acta Diabetol.* 2015;52(3):547-556.
- Souza LCVFD, Kraemer GDC, Koliski A, Carreiro JE, Cat MNL, Lacerda LD, et al. Diabetic ketoacidosis as the initial presentation of type 1 diabetes in children and adolescents: epidemiological study in southern Brazil. *Rev Paul Pediatr.* 2020;38:e2018204.
- Speight J, Holmes-Truscott E, Harvey DM, Hendrieckx C, Hagger VL, Harris SE, et al. Structured type 1 diabetes education delivered in routine care in Australia reduces diabetes-related emergencies and severe diabetes-related distress: The OzDAFNE program. *Diabetes Res Clin Pract.* 2016;112:65-72.
- Tiv M, Viel JF, Mauny F, Eschwège E, Weill A, Fournier C, et al. Medication compliance in type 2 diabetes: The ENTRED study 2007, a French population-based study. *PLoS One.* 2012;7(3):e32412.
- Tuomilehto J. The emerging global epidemic of type 1 diabetes. *Curr Diab Rep.* 2013;13(6):795-804.
- World Health Organization. Global status report on noncommunicable diseases 2014. Geneva: WHO Library Cataloguing-in-Publication Data; 2014. 302 p.
- Zhu VJ, Tu W, Marrero DG, Rosenman MB, Overhage JM. Race and medication compliance and glycemic control: findings from an operational health information exchange. *AMIA Annu Symp Proc.* 2011;2011:1649-57.

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