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Predictor factors of glycemic control in children and adolescents with type 1 diabetes mellitus treated at a referral service in Rio de Janeiro, Brazil

Roberta Ferreira Fortins [a], *Elisa Maria de Aquino Lacerda* [a], *Raquel Nascimento Chanca Silverio* [a], *Cleber Nascimento do Carmo* [b], *Aline Alves Ferreira* [a], *Carolina Felizardo* [a], *Bárbara Folino do Nascimento* [a], *Jorge Luiz Luescher* [c], *Patrícia de Carvalho Padilha* [a,*]

[a] *Universidade Federal do Rio de Janeiro, Centro de Ciências da Saúde, Instituto de Nutrição Josué de Castro, Av. Carlos Chagas Filho, 373 – bloco J, Cidade Universitária, Rio de Janeiro, RJ, Brazil*

[b] *Fundação Oswaldo Cruz, Departamento de Epidemiologia e Métodos Quantitativos em Saúde, Escola Nacional de Saúde Pública, Fundação Oswaldo Cruz, Brazil*

[c] *Universidade Federal do Rio de Janeiro, Centro de Ciências da Saúde, Instituto de Puericultura e Pediatria Martagão Gesteira, Rua Bruno Lobo, 50, Cidade Universitária, Rio de Janeiro, RJ, Brazil*

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ABSTRACT

Aim: To evaluate the predictive factors of glycemic control in children and adolescents with type 1 diabetes mellitus (T1DM).

Methods: Cross-sectional study at a referral service in Rio de Janeiro, Brazil. Sociodemographic, anthropometric, clinical, and dietary factors were evaluated. Food consumption was evaluated by 24 h dietary recall and the NOVA system was adopted for classifying the foods according to the extent and purpose of industrial processing. The predictive factors were evaluated by multivariate linear regression, adopting $p < 0.05$.

Results: One hundred and twenty children and adolescents participated, with a mean age of 11.74 years (±2.88) and HbA1c of 8.13% (±1.26). The mean diabetes duration was 6.68 years (±3.33) and the insulin used was 1.05 units per kilogram of ideal weight (IU/kg of ideal weight; ±0.46) About 80% (n = 96) used carbohydrate counting and it was verified that 24.27% (±17.89) of the participants' total calories came from ultraprocessed foods. For each year of diagnosis with T1DM and for each IU/kg of weight used, HbA1c increased by 0.087% ($\beta = 0.087$, $p = 0.007$) and 0.651%, respectively ($\beta = 0.651$; $p = <0.001$). Use of carbohydrate counting was associated with a 1.058% reduction in HbA1c ($\beta = -1.058$; $p = 0.001$).

Conclusion: Disease duration and insulin dose were directly reflected in HbA1c concentrations, while carbohydrate counting showed an inverse association.

* Corresponding author.
E-mail addresses: elisalacerda@ufrj.br (Elisa Maria de Aquino Lacerda), cleber.carmo@ensp.fiocruz.br (C.N. do Carmo), alineaf@nutricao.ufrj.br (A.A. Ferreira), patricia@nutricao.ufrj.br (P.C. Padilha).

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1. Introduction

Type 1 diabetes mellitus (T1DM) is a chronic, multifactorial disease in which there is deficiency of insulin secretion caused by the progressive destruction of pancreatic β cells, leading to a hyperglycemic state [1,2]. It mainly affects the pediatric age group and its incidence is increasing worldwide. Brazil is the country with the third highest number of cases of T1DM, which affects 9600 individuals under 20 years of age per year [3].

The disease progresses when there is no effective glycemic control, resulting in damage to the growth and development of children and adolescents, acute complications such as episodes of hypoglycemia and ketoacidosis, and chronic complications such as neuropathy, nephropathy, retinopathy, and cardiovascular diseases [4,2].

The main guiding organizations for the care of diabetes mellitus (DM) recommend the use of glycated hemoglobin (HbA1c) as a parameter for the evaluation of glycemic control, setting the cut off at concentrations of less than 7.5% for all pediatric age groups, aiming at the prevention of future complications [5,1,2].

Setting a satisfactory glycemic target represents a major challenge. DM is a complex chronic disease in which innumerous social, dietary, emotional, economic, family, and clinical factors act as barriers or facilitators of care [6]. Previous studies point to some of these factors as predictors of glycemic control, such as parental schooling, family income, disease duration, age at diagnosis, insulin dose, diet, nutritional status, and others [7–11].

Among the modifiable factors involved, feeding represents one of the main barriers to treatment. Carbohydrate counting has an important role to play in adherence to prescribed diets and should be made an integral part of any regimen for adequate glycemic control and improved quality of life [12–14].

In recent decades, the food consumption of the Brazil population has deteriorated markedly, resulting in poorer quality of food intake. More ultraprocessed foods, manufactured products composed of innumerable ingredients with low nutritional value, to the detriment of unprocessed and minimally processed foods, which include traditional foods and home-cooked meals [15,16].

The increased consumption of ultraprocessed foods has been associated with an increased prevalence of obesity, poorer lipid profile, metabolic syndrome, higher systemic blood pressure, and micronutrient deficiencies [17–21]. However, there are few studies that have evaluated the quality of the diet of individuals with T1DM, including how much of their diet is made up of ultraprocessed foods and how this may affect their glycemic control [13].

In view of the above, the objective of this study was to evaluate the predictive factors of glycemic control in children and adolescents with T1DM who receive care at a referral service, including sociodemographic, clinical, anthropometric, and dietary data.

2. Methods

2.1. Study outline

This analytical, cross-sectional study was carried out with children and adolescents diagnosed with T1DM at a public referral service for the treatment of DM in Rio de Janeiro, Brazil. The service has a multidisciplinary team including endocrinologists, nutritionists, nurses, social workers, and psychologists, and provides an average of 200 consultations per month.

The sample of the present study was the same as that of the original study, "Quality of the Diet and its Association with the Nutritional Status and Glycemic Control of Children and Adolescents with Type 1 Diabetes Mellitus," which gathered data from 120 children attended at the same hospital between April and November 2016.

To calculate the sample size, it was considered that to detect a difference of 1.1% in HbA1c, with a standard deviation of 2.0%, an alpha error of 5%, and a test power of 80%, the sample size should be at least 41 children [22].

2.2. Study subjects

The studied population was composed of children and adolescents diagnosed with T1DM. Inclusion criteria were: age between 7 and 16 years, diagnosis of T1DM at least 1 year previously, absence of autoimmune disease, genetic syndromes, sickle cell anemia, and renal failure, and non-use of steroids or an insulin pump. Exclusion criteria were: incomplete information on glycemic control and food consumption, and refusal to participate in the study.

2.3. Recruitment and data collection

Participants were recruited and data were collected by previously trained staff who, during their outpatient care shifts, consulted the charts to identify any eligible patients. Subsequently, the individuals and their parent/guardian were told about the research, including its objectives and what would be required of participants. After the invitation was accepted, an Informed Assent Form and Informed Consent Form were read and signed in duplicate by the participants and researcher, each of whom kept one of the copies.

Sociodemographic, clinical, anthropometric, and dietary data were obtained by consulting the medical records or interviewing the participants, and recorded on a structured data collection form.

2.4. Study variables

The dependent variable of the study was glycemic control, which was evaluated continuously by taking the average of the two HbA1c values (%) measured by high performance liquid chromatography (HPLC) available in the previous six months.

The independent variables were sociodemographic, clinical, anthropometric, and dietary variables.

2.5. Sociodemographic information

The gender variables of the individuals (male/female), their age (years), place of residence (Greater Rio de Janeiro/other cities or states) were collected, along with their household size (number of residents), family structure (living with father and mother/living with father or mother/living with another responsible adult), parents' schooling (elementary/high/higher), and per capita income (reais).

2.6. Clinical information

Information was collected on age at diagnosis (months), diabetes duration (years), insulin dose (U/kg body weight), and medical nutrition therapy method (food by Exchange system/carbohydrate counting) [23,24].

2.7. Anthropometric evaluation

Weight and height were measured during a routine visit. Body mass index (BMI) was calculated by dividing body mass (kg) by the square of height (m). The z-scores for height/age and BMI/age were calculated using Anthro Plus, version 3.2.2 [25]. The growth reference standard proposed by WHO for children aged 5–19 years was used [26]. For classification of nutritional status, the cut-off points recommended by the Brazilian Ministry of Health were used: BMI z-score below −2 = underweight; BMI z-score between −2 and +1 = normal weight; BMI z-score between +1 and +2 = overweight; and BMI z-score of over +2 = obese [27].

2.8. Dietary assessment

Food consumption was evaluated by means of 24-hour dietary recall (24HR), which was taken in the waiting room before a routine consultation. In order to help the participants to remember the foods consumed the previous day, the five-step Multiple-Pass Method was used: (1) a quick list of foods consumed, (2) questions about forgotten foods; (3) questions about the timing of food consumption; (4) a detailed description of the food and its quantities, reviewing the information on time and consumption; (5) a review of the information and inquiries about foods potentially not reported [28].

To transform the home measures into units of mass or volume, the Table for Evaluation of Food Consumption in Domestic Measures was used [29]. The centesimal composition of the foods was determined with the aid of a Microsoft Office Excel® spreadsheet, in which foods and their nutrient content were included, based on the Brazilian Table of Food Composition [30] or, when the foods were not on this table, based on the nutritional information on the product labels.

The foods reported in the 24HR were classified according to the extent and purpose of industrial processing, based on the NOVA classification [31]. Three food groups were considered in the consumption assessment: (1) unprocessed and minimally processed foods: fruits, vegetables, tubers, rice, legumes, dried fruit, fruit juices without added sugar, spices in general, fresh or frozen meat, eggs, vegetables, coffee, water, and culinary preparations with one or more fresh or minimally processed ingredients, (2) processed foods: products in which manufacture involved the addition of salt or sugar, oil, vinegar or other substance to a food of the group unprocessed and minimally processed foods, being mostly products with two or three ingredients, and (3) ultraprocessed foods: including soft drinks, snack foods, candies and sweets in general, biscuits, cakes and cake mixes, chocolate drinks, flavored fruit beverages, nuggets, sausages, hamburgers, instant noodles, and other processed products made from five or more ingredients [31].

The foods were then quantified as to their energy value and percentage contribution to total daily energy intake.

2.9. Statistical analysis

After the analysis to verify the normality of the response variable (HbA1), the individual contribution of each independent variable to the outcome was evaluated through simple linear regression. The variables that presented p-values <0.20 were selected for the next step. In the multivariate analysis, amanual backward procedure was used, followed by an automatic procedure, to reach the final model. For the verification of the final model, the collinearity between the independent variables was determined by means of the variance inflation factor with a cutoff point of $\leq$10. To evaluate the contribution of the variables, the ANOVA test, the partial F statistic, and residue analysis were used. Data were analyzed using SPSS (21.0) and R (www.r-project.org), version 3.4.3. Statistical significance of results was set at 5%.

2.10. Ethical considerations

The original study was planned respecting the ethical considerations set forth in resolution 466/2012, and approved by the Research Ethics Committee of IPPMG/UFRJ, registered under CAAE 52560216.8.0000.5264. Participants and study researchers signed informed assent forms and informed consent forms, respectively.

3. Results

At the time of data collection, 134 patients met the eligibility criteria. Three of these did not agree to participate in the study and 11 supplied incomplete information on their food consumption, leaving 120 patients in the study (34 children and 86 adolescents).

The general characteristics of the sample are described in Table 1. The mean age of the participants was 11.74 years (standard deviation [SD] = 2.88) and 53.3% (n = 64) were female; 93.3% (n = 112) were residents of Greater Rio, 70.8% (n = 85) lived with their parents, and the average household size was 4.02 people (SD = 1.13).

The studied sample had been diagnosed with T1DM, on average, at 60.87 months (SD = 32.51) and the mean diabetes duration was 6.68 years (SD = 3.33). The mean HbA1c was 8.13% (SD = 1.26) and the mean insulin dose used was 1.05 IU/kg body weight (SD = 0.45). The mean BMI was

Table 1 – Sociodemographic, clinical, anthropometric, and dietary characteristics of children and adolescents with type 1 diabetes mellitus treated at a Rio de Janeiro reference service, 2016 (n = 120).

Continuous variables	Mean (SD)
Glycated hemoglobin, in% (n = 120)	8.13 (1.26)
Age, in years (n = 120)	11.74 (2.88)
Household size, in no. of residents (n = 120)	4.02 (1.13)
Per capita income, in reais (n = 115)	667.54 (264.83)
Diabetes duration, in years (n = 119)	6.68 (3.33)
Age at diagnosis, in months (n = 119)	60.87 (32.51)
Insulin dose (IU/kg) (n = 119)	1.05 (0.46)
BMI z-score (kg/m^2) (n = 120)	0.65 (0.89)
Protein in TEI, in% (n = 120)	21.44 (6.13)
Fat in TEI, in % (n = 120)	26.57 (9.98)
Carbohydrates in TEI, in % (n = 120)	51.99 (9.20)
UF and MPF in TEI, in % (n = 120)	58.22 (18.95)
Processed foods in TEI, in % (n = 120)	16.54 (13.78)
Ultraprocessed foods in TEI, in% (n = 120)	24.27 (17.89)
Categorical variables	**n (%)**
Sex	
Female	64 (53.3)
Male	56 (46.7)
Place of residence	
Greater Rio de Janeiro	112 (93.3)
Other regions and states	8 (6.7)
Household structure	
Lives with a parent	35 (29.20)
Lives with father and mother	85 (70.8)
Lives with another responsible adult	2 (1.7)
Schooling of the head of household	
Elementary school	17 (14.4)
High school	77 (65.3)
Higher education	24 (20.3)
Nutritional status	
Underweight	2 (1.7)
Normal weight	80 (66.7)
Overweight	27 (22.5)
Obese	11 (9.1)
Medical nutrition therapy method	
Exchange system	24 (20.0)
Carbohydrate counting	96 (80.0)

Ref: reference; SD: standard deviation; BMI: body mass index; UF: unprocessed foods; MPF: minimally processed foods; TEI: total energy intake.

19.74 kg/m^2 (SD = 3.71), 1.7% of the subjects (n = 2) were diagnosed as being underweight, 66.7% (n = 80) normal weight, 22.5% (n = 27) overweight, and 9.1% (n = 11) obese.

Most of the sample (80%; n = 96) used carbohydrate counting as a medical nutrition therapy method. According to their 24HR, the mean energy distribution of the sample was 52.99% (SD = 9.2) carbohydrates, 21.44% (SD = 6.13) proteins, and 26.58% (SD = 9.98) fats; 24.26% (SD = 17.89) of total energy intake (TEI) came from ultraprocessed foods.

In the bivariate linear regression (Table 2), the variables related to HbA1c concentration ($p < 0.20$) were: age ($p = 0.026$), lives with father and mother ($p = 0.056$), diagnosis time ($p = 0.017$), insulin dose ($p = 0.001$), BMI ($p = 0.039$), percentage of protein in TEI ($p = 0.127$), percentage of unprocessed and minimally processed foods in TEI ($p = 0.114$), and carbohydrate counting ($p = 0.001$).

Table 3 presents the best multivariate linear regression model for HbA1c. It is observed that for each year of diagnosis with T1DM and for each U/kg of ideal insulin weight used, there was an increase of 0.09% ($\beta = 0.087$, $p = 0.021$) and 0.65% ($\beta = 0.651$; $p = 0.007$) in HbA1c, respectively. However, increased use of carbohydrate counting as a medical nutrition therapy method was associated with a 1.0% reduction in HbA1c ($\beta = -1.058$, $p = 0.021$)

4. Discussion

The present study demonstrates the importance of carbohydrate counting for glycemic control, since its use has an inverse relationship with HbA1c concentrations, as observed by other authors [32–35]. Dalsgaard et al. [36], when evaluating the glycemic control of 93 children and adolescents12

Table 2 – Bivariate analyzes of the independent variables in relation to glycated hemoglobin of children and adolescents attended at a Rio de Janeiro reference service, 2016 (n = 120).

Variables	β	p-value
Age, in years	0.086	**0.026**
Sex		
Female	Ref (0)	
Male	−0.037	0.870
Place of residence		
Greater Rio de Janeiro	Ref (0)	
Other regions and states	0.267	0.549
Household size (no. of residents)	−0.031	0.756
Household structure		
Lives with one parent or a responsible adult	Ref (0)	
Lives with father and mother	−0.483	**0.056**
Schooling of the head of household		
Elementary school	Ref (0)	
High school	0.359	0.252
Higher education	−0.118	0.748
Per capita income, in reais	−0.001	0.271
Time sincediagnosis, in years	0.081	**0.017**
Age at diagnosis, in years	−0.021	0.619
Insulin dose (IU/kg)	0.909	**<0.001**
BMI (kg/m^2)	0.062	**0.039**
Protein in TEI, in %	−0.029	**0.127**
Fat in TEI, in %	0.012	0.309
Carbohydrates in TEI, in%	−0.001	0.915
Ultraprocessed foods in TEI, in %	0.006	0.313
Processed foods in TEI, in %	0.006	0.438
UF and MPF in TEI, in %	−0.009	**0.114**
Medical nutrition therapy method		
Exchange system	Ref (0)	
Carbohydrate counting	−0.883	**0.001**

Ref: reference; BMI: body mass index; UF: unprocessed foods; MPF: minimally processed foods; TEI: total energy intake.

Table 3 – Final multivariate analysis of significant independent variables in relation to glycated hemoglobin of children and adolescents attended at a referral service in Rio de Janeiro, 2016.

Variables	β	p-value	Test F (p-value)	R^2 adjusted
Diabetes duration, in years	0.087	0.007	12.5 (<0.001)	0.234
Insulin dose (IU/kg)	0.651	<0.001		
Medical nutrition therapy method				
Exchange system	Ref (0)			
Carbohydrate counting	−1.058	<0.001		

Ref: reference; IU: insulin unit; kg: kg of ideal weight.

months after introducing carbohydrate counting, noticed a 0.98% reduction in HbA1c values (p = 0.001). The 1% decrease in HbA1c reflects a 14% reduction in the risk of acute myocardial infarction, a 37% reduction in the risk of microvascular complications, and a 21% reduction in the risk of DM deaths [37].

Carbohydrate counting is currently the preferred nutritional guidance for T1DM [1,2]. Its use allows individuals greater integration between the administration of insulin and carbohydrates in meals by promoting an increase in their capacity to determine the quantities of carbohydrates consumed and better adjust the dose of insulin used, resulting in satisfactory glycemic control, flexibility and autonomy of food choices, better adherence and motivation to treatment [1,32–38], and enhanced quality of life [39,12].

In order to obtain the benefits promoted by carbohydrate counting, it is essential to adopt healthy eating habits [13,1]. Prioritizing the amount of carbohydrates ingested per meal may favor a preference for packaged foods [40] by individuals with T1DM, since this allows them to determine more easily the quantities of carbohydrates contained in the food from the label, which leads to an increased consumption of ultra-processed foods of low nutritional quality, high energy density, high trans and saturated fat content, with the addition of sugar and sodium, and low fiber and protein content [41,42]. In addition, highly processed foods may reflect a higher glycemic response, as evidenced by Fardet [43] when studying 98 ready-to-eat foods.

In the present study, a fourth of the individuals' energy intake came from ultraprocessed food. Elsewhere in Brazil,

other significant results have been observed in children and adolescents without the disease. In a study conducted at a primary health clinic in southern Brazil, Sparrenberger et al. [44] found that 47% of the daily energy intake of children aged 2 to 10 came from ultraprocessed foods. This figure was found to be 49% amongst adolescent Brazilian by D'Avila and Kirsten [45]. Meanwhile, Rauber et al. [46] found that ultraprocessed foods accounted for 34% and 38% of the energy intake of preschool and school-age children, respectively.

Also in Brazil, Louzada et al. [42] found the consumption of ultraprocessed foods amongst individuals older than 10 year to be 20.4% of total energy intake, which is consistent with our findings (24.45%). Although there is still no cut-off point for food classified according to the extent and purpose of industrial processing, it is agreed that ultraprocessed foods should be avoided by the entire population in order to promote health and prevent diseases [42,47], since the progressive increase in their consumption has been related to the growth of overweight and obesity, as well as other chronic non-communicable diseases [48].

The consumption of ultraprocessed foods in our study was lower than that found by most of the cited authors and was not directly related to HbA1c ($p = 0.31$). The results found may reflect the quality of the service provided at the health unit in question, where individuals have regular consultations with nutritionists with extensive experience in diabetes mellitus. They are given individual carbohydrate counting dietary plans based on the consumption of fresh foods, and every consultation includes nutritional education, with instructions in the reading of product labels in order to develop critical awareness of the quality of food chosen for consumption; the consumption of ultraprocessed foods is discouraged.

In the present study, besides carbohydrate counting, insulin dose and diabetes duration were identified as predictors of glycemic control. The direct relationship between insulin dose and concentrations of HbA1c evidenced in the multivariate linear regression demonstrates that the higher the insulin dose used, the worse the glycemic control. In the study of the Diabetes Complication Control Trial (DCCT), the evaluated adolescents received more units of insulin/kg than adults, yet their HbA1c values were 1% higher [4].

At puberty, there is physiological resistance to the action of insulin by the increase of hormones against insulin, which favor higher doses of exogenous insulin. In a study of subjects aged 3–23 years, Weigand et al. [49] found that the maximum insulin dosage was at 12 years for girls (1.42 U/kg) and at 14 years for boys (1.41 U/kg), suggesting the important influence of puberty. In the present study, the mean insulin dose used by the individuals aged 8.68 to 14.62 years was 1.05U/kg of ideal weight, which is within the range recommended by the Brazilian Society of Diabetes [1] for treatment of children and adolescents with established T1DM (0.7–1 U/kg) and those in the pubertal stage (1–2 U/kg).

Higher insulin doses are related to excessive weight gain [50,51]. Because it is an anabolic hormone, insulin increases weight gain by stimulating lipogenesis and decelerating basal metabolism. Adiposity is itself capable of causing increased insulin resistance [52], aggravating glycemic control [10]. Costa et al. [53] showed that each unit of insulin/kg used increased the relative risk of overweight in children and adolescents with T1DM more than threefold (OR 3.38; $p = 0.002$).

Diabetes duration is a non-modifiable risk factor and was related to HbA1c concentrations in this study, as seen by other authors [22,54–56]. With the progression of disease time, there is an increase in the deterioration of pancreatic β cells and, as a consequence, greater hyperglycemia. Maffeis et al. [57], in their study with children and adolescents, demonstrated that each year of disease increased by 30% the chance of having HbA1C > 7.5% ($p = 0.02$). Osan et al. [56], when evaluating 93 young adults with T1DM, observed that the longer duration of the disease was related to an increase in HbA1c ($r = 0.247$, $p = 0.038$).

In addition, over the years, children and adolescents with T1DM become more independent and partially responsible for their treatment, receiving less supervision from responsible adults, who reduce their involvement in the care of the disease [58]. In addition, with the temporal advancement of DM, it becomes difficult to remain motivated to keep up the daily care requirement of this chronic disease [22]. It is also worth noting that in adolescence, emotional, social, and cognitive changes occur that may interfere with self-care, resulting in impaired treatment adherence [54].

One limitation of this study is its cross-sectional design, limiting the determination of causal relationships. Another limitation is the evaluation of food consumption by only one 24HR, which may not satisfactorily reflect the individual's habitual diet, as well as the potential inaccuracies in the quantification of consumption inherent to the use of food records. To ensure data quality, the team was periodically trained, the collection forms were frequently reviewed, and the Multiple Pass Method was used when taking 24HR data [28].

One strength of this study is its unprecedented evaluation of factors classically defined as predictors of glycemic control, concomitantly with the evaluation of the dietary and food quality method. It is also the only study to date to evaluate the frequency of food consumption by individuals with T1DMaccording to the extent and purpose of the industrial processing of the foods, which could contribute to the design of new nutritional interventions in this population.

5. Conclusion

The results indicate that the longer the diabetes duration and the higher the insulin dose used, the worse the glycemic control of children and adolescents with T1DM. However, the greater the use of carbohydrate counting, the better the glycemic control. This suggests that this method should be encouraged, with nutritionists providing ongoing nutritional education in order to ensure the satisfactory use of carbohydrate counting, including the adoption of healthy eating habits, and thus the efficiency of the method.

Since T1DM is a chronic disease that, when poorly controlled, predisposes the risk of future complications, knowledge of the predictive factors of glycemic control identified in this study reinforces the importance of a broad and integrated approach to person-centered care. The involvement of different professionals and family members is therefore a prerequisite for achieving satisfactory glycemic control.

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Declaration of Competing Interest

The authors declare no conflict of interest in relation to the publication of this article.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2019.05.027.

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