A cross-sectional study of quality of life among Brazilian adults with type 1 diabetes treated with insulin glargine: Findings and implications

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ABSTRACT

We conducted a cross-sectional study with 401 patients of type 1 diabetes mellitus treated with insulin glargine in Minas Gerais, Brazil. Health-related quality of life (HRQoL) was assessed using EQ-5D-3L and the Diabetes Quality of Life Measure. Our findings showed that a worse HRQoL was associated with a low level of education, self-perceived health reported as poor/very poor, being bedridden and not physically exercised, had seen a doctor more than four times in the past year before the interview, and had reported comorbidities and episodes of hypoglycemia.

KEYWORDS: Brazil**,** Type 1 Diabetes Mellitus, Insulin Glargine, Health-Related Quality of Life, EQ-5D-3L.

INTRODUCTION

Type 1 Diabetes Mellitus (T1DM) is a chronic, costly disease, both for people living with T1DM and for governments and society (1,2). The economic burden of T1DM is largely due to the costs of medicines and the complications of diabetes (3,4), with the different insulins differing in terms of their pharmacokinetic parameters as well as costs (5).

Long-acting human insulin analogues (insulin glargine [IGla], insulin degludec [IDeg] and insulin detemir [IDet]) were developed and introduced into clinical practice as an alternative to neutral protamine Hagedorn insulin (NPH). Studies have documented an improvement in glycemic control and consequently a smaller number of hypoglycemic episodes alongside improved, quality of health-related life (HRQoL) (6,7). However, long-acting human insulin analogs (IGla and IDet) and ultra-long-acting human insulin analogs (IDeg and IGla U300) are considerably more expensive than intermediate-acting insulins, such as NPH insulin (8,9). This is an especially important for Health Technology Assessment (HTA) authorities among low- and middle-income countries (LMICs) where insulin availability is a major concern, especially in patients with T1DM, as well as for the sustainability of the National Health System (NHS) (10–12). There is also ongoing controversy regarding the level of patient benefit seen. Hemmingsen et al (2021) (13) in their recent Cochrane review stated there were no clear differences comparing IGla with NPH insulin for death, HRQoL, severe hypoglycemia (nocturnal), serious undesirable events, non-fatal complications of Diabetes Mellitus (DM) (e.g., heart attacks and strokes) and glycated hemoglobin (HbA1c). However, Tricco et al (2021) (7) came to a different conclusion in their systematic review suggesting that both ultra-long-acting and long-acting insulins were superior to intermediate-acting insulins in reducing HbA1c, and weight gain as well as major, serious, or nocturnal hypoglycemia.

HTA authorities, which are independent recommendation agencies for the incorporation of health technologies into their respective national health services, have made recommendations for and against the incorporation of long-acting insulin analogues into healthcare systems given their considerably higher costs than NPH insulin or similar insulins as well as variable findings regarding the extent of clinical benefit in practice, e.g.: HbA1c, HRQoL and hypoglycemia episodes (6,7,12–16).HTA agencies that recommend the incorporation of IDeg, IGla and IDet into their NHS for funding include the National Institute for Health and Care Excellence in the UK (17), the Scottish Medicine Consortium (18–20) and the Canadian Agency for Drugs and Technologies in Health (21,22). Brazil's HTA authority, the National Committee for Health Technology Incorporation into the Unified Health System (Conitec), in 2019 recommended the incorporation of IGla, IDet and IDeg into the Brazilian Unified Health System (SUS) (23,24). This is important as medicines indicated for incorporation by Conitec are provided free of charge to patients in Brazil (25). In addition, the different States of Brazil (Regions) can develop their own medicines lists and make accepted technologies available free to patients (12). For instance, the State of Minas Gerais listed IGla in 2005 (25). IGla is the most prescribed long-acting insulin analogue in Brazil and was incorporated in other Brazilian States (Regions) before the Conitec decision in 2019 (23). In contrast to other HTA authorities, the National Commission of Medicines and Supplies, Ecuador's HTA authority, requested the exclusion of IGla in March 2013 (26). The German Institute for Quality and Efficiency in Healthcare also recommended the exclusion of long-acting human insulin analogues in 2010 as there appeared to be no studies demonstrating their superiority over NPH insulin (27). However, the situation has changed since then (6,15,28). As a result, long-acting insulin analogues have become the most prescribed insulins in high-medium and high-income countries (8,12). We are also seeing growing use in LMICs (9,12,29).

After Conitec's recommendation to incorporate IGla, IDeg and IDet into SUS (23,24), the Brazilian Ministry of Health (MoH) created the Clinical Protocol and Therapeutic Guidelines (PCDTs) for T1DM (30). The PCDTs establish that there is no preferred analogue among the three analogues; however, the protocol makes a consideration about the modest clinical benefit of long-acting insulin analogues in patients with recurrent episodes of hypoglycemia (30). Interestingly, even with the introduction of biosimilars Abasaglar® by Eli Lilly, and Glargilin® by Biomm (31), the prices charged for IGla in public procurements, in 2020, remain high in Brazil compared to NPH insulin (US$ 16.38 and US$ 5.31, respectively) (32,33). This is a continuing concern versus lower prices for biosimilar IGla in countries such as Bangladesh (29). It is worth noting that the PCDTs for T1DM recommends that Brazil's MoH should procure treatments with the best cost-minimization profile (30). However, the MoH has not yet taken a position on biosimilars in SUS, which may explain the lack of price reductions to date (34). It is also noteworthy that, even after the incorporation of IGla, IDet and IDeg in March 2019, MoH of Brazil was still unable to acquire any medicines in August 2021 (24,35). This is probably for cost reasons since incorporation was conditional on the cost (general administration) of long-acting insulin analogues being equivalent to an NPH insulin pen, i.e., equivalent to $5.31 (100IU/ml 3ml) on a similar patient-day basis (23,24).

Adequate glycemic control minimizes episodes of hypoglycemia (whether nocturnal or severe) and improves the HRQoL of patients with T1DM (36). Alongside this, approximately 10% of deaths of young people with T1DM are attributable to hypoglycemia (37). Fear of hypoglycemia increases the psychosocial burden of T1DM and affects self-care behaviors, with a direct impact on glycemic control, increasing the risk of long-term macro- and microvascular complications and contributing to worsening HRQoL among patients with T1DM (14,38,39). In addition to hypoglycemic episodes, various factors are associated with the HRQoL of patients living with DM. These includes, but not limited to, prescribed antidiabetic treatments, overall glycemic control (i.e., HbA1c), the extent of comorbidities and diabetes-related complications as well as psychological and family factors (38,40,41).

However, studies that have assessed the HRQoL of patients with T1DM prescribed long-acting insulin analogs are generally limited to the assessment of HRQoL scores of the different analogs, and do not assess factors associated with individual treatment outcomes or assess the HRQoL of patients with T1DM without mentioning the treatment used by individual patients (14,38,42,43). There also appears to be no studies in Brazil that correlate HRQoL and HbA1c in patients treated with IGla. Having said this, there are still uncertainties regarding HRQoL in patients treated with IGla and with adequate control of HbA1c (14).

In view of the uncertainties regarding the role and value of long-acting human insulin analogs in T1DM patients in terms of HRQoL, especially in LMICs, and currently no studies exclusively evaluating the outcomes of T1DM patients treated with IGla in Brazil in terms of their HRQoL, we sought to address this. Consequently, this study aimed to examine the factors associated with the HRQoL of patients living with T1DM treated with IGla in Brazil.

METHOD

Study design, setting, and patient recruitment

Using convenience sampling methods, a cross-sectional study was conducted in March 2017 with 401 patients living with T1DM treated exclusively with IGla, identified via the SUS database from the SES-MG, Brazil. Patients with T1DM with a prescription for IGla in Minas Gerais State are dispensed their insulin only by public pharmacies in the State. This means that the public system only authorizes access to IGla after an assessment has been undertaken to appraise the conformity of the prescription with a Clinical Protocol specific for IGla in the State of Minas Gerais (44). If approved, insulins are provided free-of-charge. However, patients are subject to 100% co-payment if the prescribing criteria are not met (12). The other long-acting human insulin analogs were not evaluated in this study (IDet and IDeg), as most patients with T1DM in Brazil are treated with IGla, i.e.,IDet and IDeg do not have a large volume of prescriptions in Brazil currently and other insulins are subject to 100% co-payment.

The following inclusion criteria were adopted: patients with T1DM, aged ≥ 18 years, treated with IGla for a period of 6 months or more, with or without other insulins. The following exclusion criteria were applied: patients diagnosed with mental disorders (except for depression and bipolar disorder),

bedridden, with cognitive impairment, pregnant or lactating women, and patients diagnosed with latent autoimmune diabetes in adults.

The patients, selected based on the successful for treatment of their T1DM with IGla submitted to the Minas Gerais Sanitary Authority of the SES-MG (44), were interviewed by telephone. Patients answered a structured questionnaire administered by a trained interviewer. Up to five attempts were made to contact patients at different times. If telephone contact was unsuccessful, patients were excluded from the study. Overall, only eight patients were not reached in this way. The eight patients who were not reached are not part of the 401 patients evaluated in this study.

Structured survey questionnaire, measurements and definition
A structured survey questionnaire was specially developed for this study to collect data from T1DM patients treated with IGla. The structured survey questionnaire included the following information: 1) sociodemographic and occupational aspects data; 2) clinical aspects and access to health services data; and 3) HRQoL (EQ-5D-3L). In more details:

Sociodemographic and occupational aspects, i.e., age, gender, race, marital status, education, housing, number of residents in the household, occupation, weekly workload, employment status, stress, energy after work. We developed this structured survey questionnaire especially for this study based on previous questionnaires and the considerable experience of the co-authors in researching the management of patients with diabetes in Brazil and wider. However, it has not been validated.

The validated questionnaire with the Brazilian Economic Classification Criteria by the Brazilian Market Research Association (ABEP) was used to collect data on the economic status of the study patients(45). The ABEP questionnaire takes into account the consumption pattern of families, public utility services and householder's education. The questionnaire provides scores for the extent of appliances, bathroom and domestic servants being scored with values between 0 and 4 or more. The householder’s education level is scored 0 for no schooling/incomplete elementary school up to 7 for higher education degree. Public utility services (e.g., piped water and paved street) are scored as "yes" equal to 4 points and "no" equal to 0. At the end, a score between 0 and 100 is generated. A score between 45 - 100 is classified as A1-A2 classes = best social conditions; and a score between 0 -16 is classified as D-E classes = worst social conditions (45).

Clinical aspects and access to health services, i.e., self-perceived health, physical exercise and being bedridden in the last 15 days prior to the interview, doctor’s visits and hospitalizations in the past year, health insurance plan, comorbidities, alcohol consumption, tobacco use, problems accessing health services, body mass index – BMI, time since diagnosis (in years), HbA1c, hypoglycemic episodes in the last 6 months prior to the interview, type of hypoglycemia – severe or nocturnal, use of other insulins and whether injected with a syringe or a pen, and the number of medicines used. We again developed this structured survey questionnaire especially for this study. However, it has not been validated to collect these variables.

BMI was assessed according to the recommendations by the World Health Organization, which lists the following cutoff points: 18.5 kg/m², thin or underweight; 18.5 to 24.9 kg/m², eutrophic or normal weight; 25 to 29.9 kg/m², overweight; and ≥30 kg/m², obesity (46).

HbA1c was classified with reference values recommended by the American Diabetes Association: patients between 18 and 59 years old with HbA1c ≤7.0% and over 60 years old with HbA1c ≤8.0% were considered controlled, and patients who were outside this range of reference were considered uncontrolled (47,48).

HRQoL. The EQ-5D-3L, a generic instrument, translated and validated in Brazil, was used to measure HRQoL (49,50). This instrument comprises five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and three levels of severity (no problems, some problems, and extreme problems). The combination of these dimensions and levels identifies 243 health states, with respective utility scores for the Brazilian population (51,52).

Statistical analysis

Categorical variables were presented as absolute frequency and as relative frequency, and continuous variables as mean and standard deviation (SD). To compare EQ-5D-3L mean utility scores, by variable, an independent samples T test was used – either the Student's t test or analysis of variance (ANOVA). Normality parameters were verified using the Kolmogorov-Smirnov test for the EQ-5D-3L utility values.

Multiple linear regression analysis was performed using the forward stepwise method with the EQ-5D-3L utility scores of patients treated with IGla as the dependent variable and all other variables as explanatory variables. The explanatory variables that yielded p-values <0.05 remained in the final model. Model adequacy was checked by means of residual analysis.

We used IBM Statistical Package for the Social Sciences software, version 26.0, 2019 (IBM Corp., Armonk, United States of America) for the statistical, and a 95% confidence interval (95% CI) was adopted.

Ethical approval

The study was approved by the Ethics and Research Committee of the Federal University of Minas Gerais, Brazil, under protocol No. 55876816.0.0000.519 and Opinion No. 1.572.257, observing the principles of confidentiality of patient information, according to the Declaration of Helsinki.

We declare that patients did not receive any monetary or other incentives to participate in the study, i.e., patient participation in the study was entirely voluntary.

RESULTS

The study comprised 401 individuals with T1DM treated with IGla. There was a statistically significant difference in the mean utility scores treated with IGla regarding gender, age, education, occupation, employment status, weekly workload, stress, and energy after work (Table 1).

Insert Table 1

There was also a statistically significant difference in the mean utility scores of patients treated with IGla (n = 401) as regards self-perceived health; bedridden or engaged in physical activity in the last 15 days before the interview; doctor's visits and hospitalizations in the last year before the interview; problems in accessing health services; number of comorbidities; systemic arterial hypertension; cardiovascular disease ; stroke; kidney disease; diabetic retinopathy; dyslipidemia; diabetic neuropathy; chronic obstructive pulmonary disease (COPD); hearing problems; depression; cancer; BMI; time since diagnosis; hypoglycemic episodes in the last six months before the interview; type of hypoglycemia; alcohol consumption; and the number of medicines used (Table 2).

Insert Table 2

Regarding the HRQoL of patients treated with IGla (n = 401), the EQ-5D-3L analysis showed that 23% of patients with T1DM had the health state 11111, followed by 11112 (11%) and 11122 (7%). Other health conditions are described below (Table 3).

Moderate problems that have an impact on HRQoL have been reported by patients treated with IGla (n = 401) in the dimensions anxiety/depression (36%), pain/discomfort (31%), mobility (13.8%), usual activities – for example, work, study, household chores, family or leisure activities (13%), and self-care (5.8%) (Table 3).

Patients with T1DM treated with IGla (n = 401) obtained a mean utility value of 0.796 (0.181) with 95% CI (0.778; 0.813).

Insert Table 3

The multiple regression analysis showed that a level of education greater than nine years; self-perceived health reported as very good/good; not being bedridden and having exercised in the last 15 days before interview; having had a maximum of three doctor's visits in the past year; not having other comorbidities such as, diabetic neuropathy, COPD and not having reported episodes of hypoglycemia in the last 6 months, all contributed to the optimal HRQoL in individuals living with T1DM treated with IGla (Table 4). The variables that remained in the final model explained 39.7% of the variability of the EQ-5D-3L's utility scores.

Insert Table 4

DISCUSSION

We believe this is the first study in Brazil examining the factors associated with the HRQoL of patients living with T1DM treated with IGla. In the current study, most participants were young, white, from the highest social classes, and highly educated. Our findings are not surprising since in Brazil there is a great barrier to access to medicines provided in the Specialized Component of Pharmaceutical Assistance of SUS (CEAF/SUS) among the lower economic strata (25).

Barriers that contribute to insulin access for T1DM Brazilians are numerous and complex (25). Among the various barriers to access encountered, for maintain continuous insulin access, we can highlight that: patients in Minas Gerais must present at the clinic and receive a new medical prescription every 6 months (53), which includes current HbA1c levels every 6 months (30). However, these barriers are easily overcome by patients from higher socioeconomic strata who have regular access to health services including private medical offices, private clinics and periodic diagnostic tests compared to patients belonging to the lowest economic strata in Brazil (54,55). These equity differences need to be addressed in Brazil going forwards as they occur with other technologies in other chronic diseases, e.g., monoclonal antibodies and access to early diagnosis (58,59). This requires medium and long-term planning by the MoH in Brazil, mainly to improve access to CEAF/SUS medicines among the population from the lower social strata (61), and we will be monitoring this.

Individuals who were professionally active in our study reported stress resulting in worse HRQoL, which is similar to the findings from other studies that have assessed HRQoL, occupational status, and level of education in patients with DM (59). The results are a warning because, in addition to having a direct impact on HRQoL, stress may increase the psychosocial burden of T1DM and decrease self-care behavior, and may even affect glycemic control leading to increased macro- and microvascular complications over time (60). Consequently, patients with T1DM should be regularly monitored for their mental health status.

Regarding the participants' HRQoL data, low EQ-5D-3L scores were evident in patients with: poor/ very poor self-perceived health, who had been bedridden and who had not exercised in the last 15 days before the interview. In addition, in those who had had 2-4 doctor's visits in the past year, and who had been hospitalized twice or more in the past year prior to the interview. These findings are similar to those found in a case-control study with 1,074 participants, which compared individuals with DM and without DM (at the 1:2 ratio). The results demonstrated worse HRQoL and poor/very poor self-perceived health in patients with DM (61). T1DM patients' negative perspective regarding their life and living with the disease may also affect adherence to prescribed insulins which, needs to be avoided (62). Consequently, adherence to insulin needs to be carefully monitored alongside measures to help improve HRQoL. We recognize this is more difficult in LMICs where there can be affordability issues with monitoring equipment including glucose strips, especially if these are not provided free-of-charge by the health service (8,10); however, hopefully the situation is changing through donor and other support mechanisms.

Our findings suggest a worse HRQoL in patients with a greater number of comorbidities, including both microvascular and macrovascular complications, which is, similar to previous Brazilian studies (43,63). In addition, in a previous study conducted among patients from Minas Gerais (40). These results suggest an association with the age profile of patients with T1DM since in our study most of the patients were young, i.e., between the ages of 18 and 40. Young individuals appear to have greater difficulty in accepting complications and comorbidities with T1DM, that is to say, health conditions that may cause social stigmas, as well as increase their psychosocial burden or decrease

in their freedom. All of which should be considered by health professionals when reviewing treatment options with younger patients (64,65).

Our patients reported a number of hypoglycemic episodes, with nocturnal episodes being the second most frequent one. In addition, hypoglycemic episodes were responsible for a worse HRQoL score. Our findings though appear different from those of other studies (66,67) that demonstrated a lower number of hypoglycemic episodes with IGla. On the other hand, Raskin et al (2000) (68) and Yamamoto-Honda et al (69) did not find lower numbers of hypoglycemic episodes with IGla. In addition, 71% of patients in our study were treated with rapid-acting insulins (lispro, aspart, and glulisine). A recent systematic review indicated that rapid-acting insulins were associated with fewer hypoglycemic episodes (total, nocturnal and severe) when compared to regular insulins (70).We are not sure why our results are conflicting and we will explore this in other future studies. It is worth pointing out that the number of hypoglycemic episodes is directly related to a worse HRQoL due to an increase in fear, anxiety, and the emotional burden of the disease in patients with T1DM. For this reason, patients may reduce the amount of insulin they administer as a response to the fear of hypoglycemic episodes. Consequently, the levels of glycemic control will be lower, and the results of our study further demonstrate this (71).

Patients treated with IGla in our study did not have adequate HbA1c control. Our findings are similar to those found by Marra et al (2017) (72) and Souza el al (2015) (43), with more than 60% of patients with poor control of HbA1c which again can be different from other published studies. Two other Brazilian studies (73,74) also found poor glycemic control in DM patients, which needs to be addressed going forward. Having said this, Machado-Alba et al (2016) reported that patients with T1DM treated with long-acting insulin analogues reported better HRQoL versus those treated with human insulin; however, this was not statistically significant (42). Overall, it does seem that IGla yields better results in controlled environments since when IGla is subjected to real-world scenarios (effectiveness), the results appear less positive (14,25,72,75–77). This may be due to greater monitoring of patients in formal studies encouraging greater adherence to treatments such as IGla; however, this remains to be seen. In any event, we are seeing greater use of long-acting insulin analogues across a range of countries in view of their perceived benefits (8,12,29,78). Consequently, more studies are needed in LMICs in the real-world situation to fully assess the role and value of long-acting insulin analogues if considerable price differences still remain. However, these can be potentially reduced with the advent of biosimilars (12,29,72).

The HRQoL results in this study, measured by the EQ-5D-3L instrument, were similar to those found in other studies with patients living with T1DM (40,41). Overall, patients reported good health and ‘some problems’ in the five domains of the EQ-5D-3L. The multiple regression analysis showed worse HRQoL in individuals with a lower level of education; with poor/very poor self-perceived health; who had been bedridden and who had not exercised in the last 15 days before interview; who had seen a doctor more than four times in the past year; with comorbidities (systemic arterial hypertension, diabetic neuropathy and COPD); and with more than seven episodes of hypoglycemia in the last six months prior to the interview. These findings are similar to those observed in BrazDiab1SG study (43) where HbA1c, physical activity, time since diagnosis, age, and micro- and macrovascular complications were identified as variables of worse HRQoL. Conversely, in BrazDiab1SG, the variables only managed to explain 7.1% of the HRQoL variability of patients with T1DM. This contrasts with our study, where the variables explained 39.7% of the variability of the EQ-5D-3L’s utilities. This can be partially explained by the differences between the investigated populations as the selection of patients in the present study took into account only those being treated with IGla, that is, a more homogeneous population. In addition, the variables involved in the HRQoL of individuals with T1DM are not fully known and the results may vary. On the other hand, it is known that people living with DM have worse HRQoL when compared to populations without DM (38).

A correlation was observed between the numbers of hypoglycemic episodes, especially in individuals who had more than seven episodes, and worse HRQoL scores in our study. However, Bahia et al (2017) (79) found no statistical significance with the number of hypoglycemic episodes. We are again not sure why there were different findings. There is a consensus that patients with a greater number of hypoglycemic episodes have worse HRQoL scores when compared to patients who reported no hypoglycemic episodes (80). Furthermore, two studies found an association between worse HRQoL and the presence of hypoglycemic episodes in patients with DM. Consequently, the results of our regression model were confirmed (39,81).

There are a number of limitations with our study. Firstly, this is a cross-sectional study and cannot be used to analyze behavior over a longer period of time. Secondly, the results drew on individuals' self-reports from cross-sectional study. Consequently, clinical data on treatment with other insulins and time since diagnosis were self-reported by the participants, and medical records were not available for checking. This compromises the accuracy of the data. Thirdly, the T1DM diagnostic data were obtained from the SUS database from the entire state of Minas Gerais and were confirmed by patients' self-reports; however, there may be outliers. Furthermore, we used some non-validated questionnaires to collect sociodemographic, occupational, clinical and access to health services variables.

CONCLUSION

Our results suggest a barrier to access to medicines in the SUS. Consequently, the Brazilian MoH needs to reassess the CEAF/SUS medicines access policy, especially for the population from the lower economic strata. Another important aspect of our findings was the number of factors associated with the HRQoL of individuals living with T1DM treated with IGla, especially episodes of hypoglycemia and other comorbidities. We believe that our results can provide useful information to help guide future policy making and planning for the treatment of patients with T1DM in Brazil, particularly in prioritizing the follow-up of patients with low HRQoL scores, and we will be monitoring this. Finally, we recommend continuous monitoring by the MoH of IGla and the other long-acting human insulin analogues (IDet and IDeg) in the SUS and carrying out comparative post-incorporation analysis studies (real-world data). These are considerations for the future.

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Author Contributions: P.H.R.F.A. contributed to the conceptualization, literature review, data curation, formal analysis, methodology, writing – original draft, writing – review & editing and final approval of the submitted article. J.A-T. and B.G. contributed to conceptualization, literature review, writing – original draft, writing – review & editing and final approval of the submitted article. V.S.N.N., L.L.P.L., F.A.A., A.A.G-J., V.E.A. and A.M.A. contributed to writing – review & editing and final approval of the submitted article. P.H.R.F.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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List of Tables

Table 1. Sociodemographic, occupational characteristics and mean utility scores of individuals with type 1 diabetes mellitus treated with insulin glargine (N = 401). Minas Gerais, Brazil, 2017.

Variables		IGla = 401 *n*, %	Mean Utility (SD)	95 % CI	p-value*
Gender	Male	202 (51)	0.826 (0.012)	0.801; 0.852	0.001
	Female	199 (49)	0.764 (0.012)	0.740; 0.789	
Age (in years)	Mean (SD) = 40.76 (0.841)				
	18-40	223 (56)	0.841 (0.010)	0.821; 0.861	
	41-60	117 (30)	0.763 (0.015)	0.731; 0.794	<0.001
	61-90	61 (14)	0.695 (0.030)	0.634; 0.756	
Ethnicity	Nonblack	233 (58)	0.805 (0.011)	0.783; 0.827	0.274
	Black	168 (42)	0.783 (0.014)	0.753; 0.812	
Marital status	Has a partner	187 (47)	0.785 (0.014)	0.757; 0.814	0.295
	No partner	214 (53)	0.804 (0.011)	0.782; 0.827	
Education	≥ 9 years	324 (81)	0.815 (0.009)	0.797; 0.832	<0.001
	≤ 9 years	77 (19)	0.716 (0.026)	0.664; 0.768	
Housing	Owner	326 (81)	0.797 (0.010)	0.777; 0.817	0.790
	Nonowner	75 (19)	0.791 (0.018)	0.753; 0.828	
Residents in the household	With other people	374 (93)	0.796 (0.009)	0.778; 0.815	0.734
	Alone	27 (7)	0.784 (0.037)	0.708; 0.860	
Social class	A1-A2	199 (50)	0.784 (0.012)	0.759; 0.809	
	B1	194 (48)	0.808 (0.013)	0.782; 0.833	0.435
	B2	8 (2)	0.797 (0.052)	0.674; 0.920	
Occupation	Nonworkers**	193 (48)	0.763 (0.014)	0.735; 0.792	0.001
	Worker	208 (52)	0.826 (0.010)	0.804;0.847	
Employment status	Nonworkers**	193 (51)	0.764 (0.014)	0.735; 0.792	
	Formal employment	132 (30)	0.836 (0.013)	0.810; 0.863	0.001
	Informal employment	76 (19)	0.807 (0.018)	0.771; 0.844	
Weekly workload	Nonworkers**	193 (48)	0.764 (0.014)	0.735; 0.792	
	> 40 hours	120 (30)	0.840 (0.013)	0.814; 0.867	
	40 hours	58 (15)	0.807 (0.021)	0.763; 0.851	0.001
	30 hours	20 (5)	0.834 (0.034)	0.760; 0.907	
	20 hours	5 (1)	0.840 (0.070)	0.646; 0.999	

	10 hours	5 (1)	0.717 (0.088)	0.471; 0.962	
Stress	Nonworkers**	193 (48)	0.764 (0.014)	0.735; 0.792	<0.001
	Yes	107 (27)	0.805 (0.015)	0.775; 0.836	
	No	101 (25)	0.851 (0.014)	0.821; 0.880	
Energy after work	Nonworkers**	193 (48)	0.764 (0.014)	0.735; 0.792	<0.001
	Yes	151 (38)	0.841 (0.012)	0.816; 0.866	
	No	57 (14)	0.792 (0.020)	0.751; 0.833	

95% CI = 95% Confidence Interval; *p-value <0.05 Statistically Significant; **Nonworkers = Students, Retirees, Pensioners, Retired or Unemployed; A1-A2 classes = Best Social Conditions; and D-E classes = Worst Social Conditions (45); SD = Standard Deviation.

Table 2. Clinical data, lifestyle, access to health services, and mean utility scores of patients with type 1 diabetes mellitus treated with insulin glargine (n = 401). Minas Gerais, Brazil, 2017.

Variables		IGla = 401 *n*, %	Mean Utility (SD)	95 % CI	p-value*
Self-perceived health	Very Good/Good	227 (57)	0.856 (0.010)	0.836; 0.876	<0.001
	Fair	155 (39)	0.735 (0.014)	0.706; 0.764	
	Poor/Very poor	19 (4)	0.569 (0.032)	0.501; 0.638	
Bedridden in the last 15 days	Yes	40 (10)	0.666 (0.033)	0.599; 0.734	<0.001
	No	361 (90)	0.810 (0.009)	0.792; 0.828	
Physical exercise in the last 15 days	Yes	257 (64)	0.827 (0.010)	0.807; 0.847	<0.001
	No	144 (36)	0.739 (0.016)	0.707; 0.772	
Doctor's visits in the past year	DK/NR	8 (2)	0.768 (0.063)	0.617; 0.919	<0.001
	Zero to three	250 (63)	0.840 (0.010)	0.820; 0.861	
	Four or more	143 (35)	0.719 (0.015)	0.689; 0.750	
Hospitalizations in the past year	None	312 (78)	0.840 (0.009)	0.801; 0.839	<0.001
	One	72 (18)	0.729 (0.023)	0.682; 0.775	
	Two or more	17 (4)	0.626 (0.043)	0.534; 0.718	
Medical insurance	Yes	224 (56)	0.796 (0.011)	0.773; 0.819	0.937
	No	177 (44)	0.795 (0.014)	0.766; 0.823	
Problems to access health services	Scheduling a doctor's appointment	143 (36)	0.787 (0.015)	0.785; 0.817	0.025
	None	110 (28)	0.836 (0.014)	0.807; 0.864	
	Access to medicines	109 (26)	0.784 (0.017)	0.749; 0.820	
	Others	39 (10)	0.744 (0.037)	0.668; 0.820	
Number of comorbidities	Mean (SD) = 1.55 (0.064)				<0.001
	0-3	373 (93)	0.809 (0.008)	0.791; 0.826	
	4-6	22 (5)	0.649 (0.034)	0.577; 0.722	
	7 or more	6 (2)	0.521 (0.111)	0.234; 0.807	
Systemic arterial hypertension	Yes	62 (15)	0.676 (0.026)	0.623; 0.730	<0.001
	No	339 (85)	0.871 (0.009)	0.800, 0.835	
CVD	Yes	24 (6)	0.608 (0.042)	0.519; 0.697	<0.001
	No	377 (94)	0.808 (0.008)	0.790; 0.825	
Stroke	Yes	5 (1)	0.482 (0.058)	0.319; 0.645	<0.001
	No	396 (99)	0.800 (0.008)	0.782; 0.817	

Kidney disease	Yes	24 (6)	0.698 (0.042)	0.609; 0.786	0.006
	No	377 (94)	0.802 (0.009)	0.784; 0.820	
Diabetic retinopathy	Yes	41 (10)	0.646 (0.029)	0.587; 0.705	<0.001
	No	360 (90)	0.813 (0.009)	0.795; 0.831	
Dyslipidemia	Yes	10 (2)	0.623 (0.081)	0.439; 0.807	0.002
	No	391 (98)	0.800 (0.008)	0.782; 0.818	
Diabetic foot	Yes	4 (1)	0.670 (0.122)	0.281; 0.999	0.164
	No	397 (99)	0.797 (0.009)	; 0.779; 0.815	
Diabetic neuropathy	Yes	27 (7)	0.582 (0.032)	0.516; 0.649	<0.001
	No	374 (93)	0.811 (0.008)	0.793; 0.829	
COPD (e.g., emphysema, asthma, bronchitis)	Yes	11 (3)	0.614 (0.061)	0.477; 0.750	0.001
	No	390 (97)	0.801 (0.009)	0.783; 0.819	
Hearing problems	Yes	7 (2)	0.657 (0.081)	0.457; 0.857	0.041
	No	394 (98)	0.798 (0.009)	0.780; 0.816	
Depression	Yes	23 (6)	0.635 (0.038)	0.556; 0.715	<0.001
	No	378 (94)	0.805 (0.009)	0.787; 0.823	
Hyperthyroidism	Yes	68 (17)	0.776 (0.020)	0.734; 0.817	0.318
	No	333 (83)	0.800 (0.010)	0.780; 0.819	
Obesity	Yes	7 (2)	0.671 (0.076)	0.483; 0.859	0.067
	No	394 (98)	0.798 (0.009)	0.780; 0.816	
Any type of cancer	Yes	3 (1)	0.522 (0.028)	0.397; 0.646	0.008
	No	398 (99)	0.798 (0.009)	0.780; 0.815	
Time since diagnosis (in years)	Mean (SD) = 17.93 (0.519)				
	1-10	119 (30)	0823 (0.015)	0.792; 0.853	0.015
	11-20	147 (35)	0.808 (0.014)	0.780; 0.835	
	21-30	83 (21)	0.770 (0.023)	0.723; 0.816	
	31-40	42 (11)	0.759 (0.023)	0.713; 0.806	
	41 or more	10 (3)	0.661 (0.078)	0.484; 0.838	
HbA1c	Mean (SD) = 7.76 (0.059)				
	Uncontrolled	260 (65)	0.783. (0.016)	0.750; 0.816	0.306
	Controlled	141 (35)	0.802 (0.010)	0.781; 0.823	
Hypoglycemic episodes in the last 6 months	One to six	183 (46)	0.797 (0.012)	0.772; 0.822	<0.001
	More than seven	96 (24)	0.735 (0.019)	0.697; 0.772	
	None/DK	122 (30)	0.841 (0.016)	0.809; 0.874	

Type of hypoglycemia	None/NS	122 (30)	0.841 (0.016)	0.809; 0.874	<0.001
	Severe hypoglycemia (needed help or medical care)	56 (14)	0.723 (0.027)	0.668; 0.779	
	Nocturnal hypoglycemia	67 (17)	0.757 (0.022)	0.712; 0.801	
	Hypoglycemia (needed no help nor medical care)	156 (39)	0.802 (0.012)	0.777; 0.828	
Alcohol consumption	No	282 (70)	0.781 (0.011)	0.758; 0.803	0.012
	Yes	119 (30)	0.831 (0.013)	0.803; 0.858	
Tobacco use	No	373 (93)	0.796 (0.009)	0.778; 0.815	0.827
	Yes	28 (7)	0.788 (0.037)	0.711; 0.866	
Glargine injection	Syringe	220 (56)	0.778 (0.014)	0.787; 0.815	0.375
	Pen	181 (44)	0.803 (0.011)	0.780; 0.826	
Other insulins	NR	113 (28)	0.773 (0.019)	0.734; 0.811	0.071
	Lispro	140 (35)	0.815 (0.012)	0.790; 0.841	
	Aspart	86 (21)	0.816 (0.018)	0.779; 0.835	
	Glulisine	60 (15)	0.772 (0.024)	0.772; 0.822	
	Others	2 (1)	-	-	
Other insulins injection	NR	113 (28)	0.773 (0.019)	0.734; 0.811	0.078
	Syringe	76 (19)	0.777 (0.020)	0.735; 0.819	
	Pen	212 (53)	0.817 (0.011)	0.795; 0.839	
Number of medicines used	Mean (SD) = 2.36 (0.111)				
	No medicine	11 (3)	0.776 (0.055)	0.651; 0.900	<0.001
	1-4 medicines	337 (84)	0.818 (0.009)	0.800; 0.836	
	More than 5 medicines	53 (13)	0.656 (0.026)	0.603; 0.709	

95% CI = 95% Confidence Interval; *p-value <0.05 Statistically Significant; BMI = Body Mass Index; COPD = Chronic Obstructive Pulmonary Disease; CVD = Cardiovascular Disease; DK= Did Not Know; HbA1c = Glycated Hemoglobin; NR = Did Not Respond; SD = Standard Deviation.

Table 3. Descriptive states of EQ-5D-3L in patients with type 1 diabetes mellitus treated with insulin glargine (n = 401). Minas Gerais, Brazil, 2017.

EQ-5D-3L Dimensions	Severity*	N	%
Mobility	1	350	86
	2	50	13,8
	3	1	0,2
Self-care	1	375	94
	2	25	5,8
	3	1	0,2
Usual Activities	1	344	86
	2	52	13
	3	5	1
Pain/Discomfort	1	244	61
	2	124	31
	3	33	8
Anxiety/Depression	1	200	50
	2	143	36
	3	58	14

*Severity = Level 1: No Problem; Level 2: Some Problems; Level 3: Extreme Problems.

Table 4. Multiple regression analysis using the forward stepwise method of factors associated with health-related quality of life in patients with type 1 diabetes mellitus treated with insulin glargine (n = 401). Minas Gerais, Brazil, 2017.

Variables		Utility		
		Coefficient	SE (95 % CI)	p-value*
Education	≤ 9 years	-0.099	0.022 (-0.143; -0.055)	<0.001
	≥ 9 years	0		
Self-perceived health	Fair	-0.121	0.017 (-0.154; -0.087)	<0.001
	Poor/Very poor	-0.286	0.039 (-0.364; -0.209)	<0.001
	Very Good/Good	0		
Bedridden in the last 15 days	Yes	-0.144	0.029 (-0.201; -0,086)	<0.001
	No	0		
Physical exercise in the last 15 days	No	-0.088	0.018 (-0.124; 0.052)	<0.001
	Yes	0		
Doctor's visits in the past year	Four or more	-0.011	0.018 (-0.154; -0.083)	<0.001
	One to three	0		
Systemic arterial hypertension	Yes	-0.141	0.024 (-0.188; -0.094)	<0.001
	No	0		
Diabetic neuropathy	Yes	-0.229	0.034 (-0.296; -0.161)	<0.001
	No	0		
COPD (e.g., emphysema, asthma, bronchitis)	Yes	-0.187	0.055 (-0.295; -0.080)	<0.001
	No	0		
Hypoglycemic episodes in the last six months	One to six	-0.044	0.021 (-0.085; -0.004)	0.033
	More than seven	-0.107	0.024 (-0.154; -0.059)	<0.001
	None	0		

95 % CI = 95% Confidence Interval; *p-value <0.05 Statistically Significant; COPD = Chronic Obstructive Pulmonary Disease; SE = Standard Error.