Challenges associated with insulin therapy progression among patients with type 2 diabetes: Latin American MOSAIc study baseline data

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Abstract

Background: Poor glycemic control in patients with type 2 diabetes is commonly recorded worldwide; Latin America (LA) is not an exception. Barriers to intensifying insulin therapy and which barriers are most likely to negatively impact outcomes are not completely known. The objective was to identify barriers to insulin progression in individuals with type 2 diabetes mellitus (T2DM) in LA countries (Mexico, Brazil, and Argentina).

Methods: MOSAIc is a multinational, non-interventional, prospective, observational study aiming to identify the patient-, physician-, and healthcare-based factors affecting insulin intensification. Eligible patients were ≥18 years, had T2DM, and were treated with insulin for ≥3 months with/without oral antidiabetic drugs (OADs). Demographic, clinical, and psychosocial data were collected at baseline and regular intervals during the 24-month follow-up period. This paper however, focuses on baseline data analysis. The association between glycated hemoglobin (HbA1c) and selected covariates was assessed.

Results: A trend toward a higher level of HbA1c was observed in the LA versus non-LA population (8.40 ± 2.79 versus 8.18 ± 2.28; p ≤ 0.069). Significant differences were observed in clinical parameters, treatment patterns, and patient-reported outcomes in LA compared with the rest of the cohorts and between Mexico, Brazil, and Argentina. Higher number of insulin injections and lower number of OADs were used, whereas a lower level of knowledge and a higher level of diabetes-related distress were reported in LA. Covariates associated with HbA1c levels included age (−0.0129; p < 0.0001), number of OADs (0.0835; p = 0.0264), higher education level (−0.2261; p = 0.0101), healthy diet (−0.0555; p = 0.0083), self-monitoring blood glucose (−0.0512; p = 0.0033), hurried communication style in the process of care (0.1295; p = 0.0208), number of insulin injections (0.1616; p = 0.0088), adherence (−0.1939; p ≤ 0.0104), and not filling insulin prescription due to associated cost (0.2651; p = 0.0198).

Conclusion: MOSAIc baseline data showed that insulin intensification in LA is not optimal and identified several conditions that significantly affect attaining appropriate HbA1c values. Tailored public health strategies, including education, should be developed to overcome such barriers.

Trial Registration NCT01400971

Keywords: Type 2 diabetes, Latin America, Observational study, Quality of care, Psychological impact, Diabetes knowledge, Diabetes self-care management, Insulin treatment, Diabetes education

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Background
Although it is widely accepted that tight glycemic control is associated with a decreased risk of diabetes-related complications [1–5], poor control (herein defined as HbA1c >7.0 %) is commonly recorded worldwide and the available data show that Latin America (LA) is not an exception [6–11]. Despite clear treatment algorithms established within international guidelines, insulin therapy is frequently delayed even after long periods of poor metabolic control [12, 13]. Furthermore, observational data and evidence provided by multiple clinical trials implemented in different countries demonstrate a lack of treatment goal achievement among insulin-treated patients [14–18].

Although insulin therapy has been shown to significantly reduce glycated hemoglobin (HbA1c) levels, patients and physicians are often reluctant to initiate insulin therapy. Studies suggest that the reasons for this inertia on behalf of patients include a perceived lack of efficacy, negative impact on lifestyle, injection phobia, and fear of weight gain or hypoglycemic events [19]. Physician barriers include fears for their patients’ safety (including weight gain and hypoglycemia), a perceived greater drain on physician’s resources (time and cost), and concern that insulin regimens are too complex for patients to understand and will result in poor adherence [20]. Health care system factors, such as limited access to medication, care, and out of pocket expenditures, represent additional barriers to insulin therapy initiation [21–23]. This multicomponent situation represents the major hurdles to overcome to achieve a successful initiation of, and persistence on, insulin therapy.

Despite these known barriers and their negative impact on the achievement of appropriate metabolic control, to the authors’ knowledge no longitudinal study is currently available that attempts to address this important issue. Moreover, considering the scarce achievement of treatment goals in patients under insulin treatment, it is necessary to identify the barriers to intensifying insulin therapy and which of these barriers are most likely to impact outcomes.

The Multinational Observational Study Assessing Insulin use (MOSAIc) study is a multinational observational cohort study aiming at identifying the patient-, physician-, and health care environment-based factors associated with insulin initiation and progression in patients with type 2 diabetes mellitus (T2DM) in real-world practice. Data collected include demographic, clinical, and psychosocial indicators at the patient and physician level and practice site characteristics recorded at baseline and regular intervals during a 24-month follow-up period [24]. This analysis attempts to identify particular challenges faced by patients treated with insulin in LA.

Methods
Study design
The rationale and design of the MOSAIc study have been reported elsewhere [24]. Briefly, MOSAIc is a multinational, non-interventional, prospective, observational cohort study due for completion in December 2015. Participants were recruited from July 2011 to July 2013 at 223 sites in 18 countries [United Arab Emirates (UAE), Argentina, Brazil, Canada, China, Germany, India, Israel, Italy, Japan, Mexico, Russia, Saudi Arabia, South Korea, Spain, Turkey, the UK, and the US (including Puerto Rico)].

Study sites represented a combination of specialist and general practice centers in urban and rural areas. Participants were followed for 2 years after study enrollment, with visit windows approximately 6, 12, 18, and 24 months after the baseline visit, with such visits being part of their usual care.

The study was conducted following the ethical principles of the Helsinki Declaration, in accordance with good clinical practices and the applicable laws and regulations of the participant countries. The MOSAIc study was registered under ClinTrials.gov (NCT01400971). All patients completed informed consent forms approved by their country-specific institutional review boards (can be provided on request). The study’s analytic plan has been approved by the Brigham and Women’s Hospital Institutional Review Board.

Study population
Inclusion criteria for participation in MOSAIc were age ≥18 years; diagnosis of T2DM; presentation to a study site as part of usual medical care; use of any commercially available initial insulin therapy for at least 3 months with or without any combination of approved non-insulin oral antidiabetic drugs (OADs) (e.g., metformin); and sufficient understanding of the primary language of the country to complete study surveys. Exclusion criteria were participation in another medical research study; use of intensive basal-bolus therapy (basal insulin in addition to three prandial doses); or initiation of insulin treatment with three daily injections of mixed insulin.

Baseline data collection and patient-reported outcomes
Patient data for demographic and clinical characteristics, comorbid conditions, and insulin regimen were retrospectively collected (limited to 6 months before the baseline visit) from medical records at the study site.
Extensive information on patient-reported diabetes- and insulin-related knowledge, attitudes, hypoglycemia, general health behaviors, patient-provider relationship, and perceived physical and psychological well-being were collected at baseline using self-report questionnaires.

The Brief Diabetes Knowledge Test was used to evaluate patients’ understanding of their disease, such as how to manage insulin administration and how to treat hypoglycemia, with a summary score ranging from 0 (no questions correct) to 9 (all correct) [25].

The 17-item Diabetes Distress Scale was used to measure patients’ degree of concern about different aspects of their type 2 diabetes care and treatment, using a six-point Likert scale ranging from “Not a problem” to “A very serious problem” [26]. Mean items score and standard deviation (SD) are reported.

The Insulin Specific Adherence Questionnaire was used to evaluate adherence to insulin therapy and included a question to assess patients’ willingness to increase the frequency of injections. This question asked the participant to indicate to what extent he/she agreed with the statement: “I am willing to add additional injections to control my diabetes”.

The 25-item Interpersonal Processes of Care (IPC) survey measured how patients’ perceived the quality of their relationship with their providers over the past 12 months. Five alternative responses were provided for each question: 1 (never), 2 (rarely), 3 (sometimes), 4 (usually), and 5 (always). There are four positive IPC domains (elicited concerns, explained results, patient-centered decisions, and compassionate/respectful) in which higher scores correspond to better perceived interactions. Two IPC domains (hurried communication and discrimination) that were negatively framed in a way that better perceived interactions are represented by a lower score [27].

The Summary of Diabetes Self-Care Activities questionnaire was also administered in the study, analyzing three questions: “On how many of the last 7 days did you test your blood sugar the number of times recommended by your health-care provider?”, “How many of the last 7 days have you followed a healthful eating plan?”, and “On how many of the last 7 days did you participate in at least 30 min of physical activity?”. Responses ranged from 0 to 7 [28].

Statistical analysis
Baseline participant characteristics were analyzed by region comparing LA participants with the rest of the cohort and by country comparing participants from Argentina, Brazil, and Mexico.

Categorical variables were described as the number and percentage of participants, and continuous variables were described using the mean and SD. Multiple imputation by Chained Equation was used to impute missing items [29]. Pooled analysis of variance (ANOVA) was used for continuous variables when comparing regional differences depending on whether the variables were imputed. Comparison of categorical variables was primarily undertaken using the Chi square test, except for insulin regimen where the Fisher’s exact test was used. The Cochran–Mantel–Haenszel test was used when comparing the number of oral agents. Pooled multivariate linear regression models were used to assess the association between HbA1c and selected covariates. For all statistical analyses, the significance level was set at ≤0.05. The imputation was done using Stata 13 (StataCorp LP; College Station, TX). All other analyses used SAS version 9.2 software (SAS Institute; Cary, NC).

Results
A total of 4341 patients met all MOSAic eligibility criteria and comprised the analyzed population; 521 were from LA (Argentina = 160; Brazil = 155; Mexico = 206). Demographic, clinical, and metabolic characteristics are listed in Table 1. Data were grouped as LA and non-LA participants, as well as by the three different LA countries. Comparable age values were recorded in all groups. Patients from Argentina were significantly older than those from the other two LA countries (p ≤ 0.0001).

The LA region had a higher percentage of female participants (56.2 %) compared to the global population, particularly in Brazil (64.5 %). Similarly, a significantly higher rate of participants with an education level of primary school or lower was also recorded in LA compared to non-LA countries (48.2 versus 27.2 %), particularly in Argentina (51.9 %) and Brazil (50.0 %). There was also a significant difference comparing the percentage of people with health insurance, with the lowest figures recorded in Mexico (25.2 %). The LA population had a longer duration of diabetes than the overall MOSAic cohort, with no significant difference among the three LA countries. Conversely, the rate of comorbidities (associated cardiovascular risk factors, microvascular complications, and macrovascular events) was lower in the LA population.

Baseline HbA1c levels were above the treatment targets recommended by international guidelines, with no significant differences among all the groups, although lower levels were recorded in the non-LA population (8.40 ± 2.79 versus 8.18 ± 2.28; p ≤ 0.069). Among LA countries, higher but not significantly different HbA1c values were recorded in Mexico (8.70 ± 3.55).

There were no significant differences between participants classified as overweight from LA or non-LA countries; conversely, there were significant differences among those classified as obese among countries, with
the highest and lowest rates recorded in Argentina and Mexico, respectively (p ≤ 0.0001).

Systolic blood pressure values were close to target values recommended by international guidelines, with Brazil and Mexico having the highest and lowest values, respectively (p = 0.0214).

Treatment patterns varied across countries included in the study (Table 2). A higher number of daily insulin injections were reported in LA compared to non-LA countries, with Argentina having significantly more reported insulin injections compared to Brazil and Mexico (p ≤ 0.0001 for both). Basal insulin alone was more frequently used in LA than in the rest of the MOSAic cohort, with the highest rate recorded in Brazil among LA countries (74.8 %; p ≤ 0.0001). A higher percentage of LA participants also required basal insulin more than once per day. Important differences were also recorded in the use of concomitant OADs agents between the LA and non-LA population, as well as within LA countries (p ≤ 0.0001 for both).

Metformin was the most commonly utilized therapy, with the highest and lowest figures recorded in Brazil and Mexico, respectively (p ≤ 0.0001).

Individual Diabetes Knowledge scores were low in the overall MOSAic population, with lower figures in the LA versus non-LA countries (4.16 ± 2.23 versus 4.89 ± 2.19; p < 0.0001). The lowest figures were recorded in Mexico (3.93 ± 2.10) and Brazil (3.88 ± 1.91) (p = 0.0002) (Table 3).

A small but statistically significant difference was observed in the patients’ Diabetes Distress Scale scores between LA and the rest of the study population (p ≤ 0.0001); an important and significant difference was also observed among LA countries, with highest level of distress recorded in Brazil (3.14 ± 1.36) and the lowest in Argentina (2.17 ± 1.19) (p ≤ 0.0001) (Table 3).

The summary of self-care activities questionnaire showed a lower number of days with at least 30 min of physical activity reported among study participants

Table 1  Demographic, clinical, and metabolic characteristics of the population by region and country

|                      | All Mosaic cohort | LA countries | Non-LA countries | p       | Argentina | Brazil | México | p       |
|----------------------|-------------------|--------------|------------------|---------|-----------|--------|--------|---------|
| Mean age, years (SD) | 61.77 (11.02)     | 61.99 (11.21)| 61.74 (10.99)    | 0.6326  | 65.48 (10.55)| 61.03  | 9.51  | 60.00  | <0.0001|
| Gender—females, n (%)| 2176 (50.1 %)     | 293 (56.2 %)| 1883 (49.3 %)    | 0.0029  | 76 (47.5 %) | 100    | 64.5 %| 117 (56.8 %)| 0.0095 |
| Education            |                   |              |                  |         |           |        |        |         |
| Primary school, n (%)| 1291 (29.7 %)     | 251 (48.2 %)| 1040 (27.2 %)    | <0.0001 | 83 (51.9 %)| 65     | 41.9 %| 103    | 0.0474 |
| High school or more, n (%)| 2715 (62.5 %)     | 235 (41.5 %)| 2480 (64.9 %)    |         | 69 (43.1 %)| 69     | 44.5 %| 97     |        |
| Insurance            |                   |              |                  |         |           |        |        |         |
| Private, n (%)       | 917 (21.1 %)      | 134 (25.7 %)| 783 (20.5 %)     | 0.0223  | 56 (35.0 %)| 48     | 31.0 %| 30     | <0.0001|
| Public, n (%)        | 2229 (51.3 %)     | 247 (47.4 %)| 1982 (51.9 %)    | 0.0584  | 65 (40.6 %)| 76     | 49.0 %| 106    | 0.5175 |
| Uninsured, n (%)     | 848 (19.5 %)      | 103 (19.8 %)| 745 (19.5 %)     | 0.0584  | 35 (21.9 %)| 16     | 10.3 %| 52     | 0.2524 |
| Mean diabetes duration, years (SD) | 12.65 (7.98)      | 13.52 (8.77)| 12.54 (7.87)     | 0.0083  | 13.71 (9.77)| 13.46 | 7.78  | 13.42  | 0.9492 |
| Comorbidities        |                   |              |                  |         |           |        |        |         |
| MI or CAD, n (%)     | 824 (19.0 %)      | 38 (7.3 %)  | 786 (20.6 %)     | <0.0001 | 16 (10.0 %)| 15     | 9.7 % | 7      | 3.4 %  |
| Stroke, n (%)        | 151 (3.5 %)       | 10 (1.9 %)  | 141 (3.7 %)      | 0.0384  | 4 (2.5 %)  | 5      | 3.2 % | 1      | 0.5 %  |
| Congestive heart failure, n (%)| 257 (5.5 %)      | 6 (1.2 %)  | 231 (60.0 %)     | <0.0001 | 0 (0.0 %)  | 3      | 1.9 % | 3      | 1.5 %  |
| Nephropathy, n (%)   | 665 (15.8 %)      | 48 (9.2 %)  | 637 (16.7 %)     | <0.0001 | 14 (8.8 %) | 17     | 11.0 %| 17     | 8.3 %  |
| Neuropathy, n (%)    | 1114 (27.5 %)     | 85 (16.3 %)| 1109 (29.0 %)    | <0.0001 | 14 (8.8 %) | 22     | 14.2 %| 40     | 23.8 % |
| Retinopathy, n (%)  | 954 (22.0 %)      | 78 (15.0 %)| 876 (22.9 %)     | <0.0001 | 24 (15.0 %)| 24     | 15.5 %| 30     | 14.6 % |
| Depression, n (%)    | 370 (8.5 %)       | 46 (8.8 %)  | 324 (8.5 %)      | 0.7899  | 4 (2.5 %)  | 16     | 10.3 %| 26     | 12.6 % |
| Hypertension, n (%)  | 2994 (69.0 %)     | 335 (64.3 %)| 2659 (69.6 %)    | 0.0140  | 112 (70.0 %)| 110    | 71.0 %| 113    | 54.9 % |
| Hyperlipidemia, n (%)| 2484 (57.2 %)     | 259 (49.7 %)| 2225 (58.2 %)    | 0.0002  | 81 (50.6 %)| 93     | 60.0 %| 85     | 41.3 % |
| HbA1c, mean (SD)     | 8.20 (2.47)       | 8.40 (2.79) | 8.18 (2.28)      | 0.0686  | 8.08 (2.05)| 8.34   | 2.38  | 8.70   | 3.55   |
| HbA1c physician reported goal (SD) | 7.02 (0.77)       | 7.10 (0.76)| 7.01 (0.73)      | 0.011   | 7.17 (0.65)| 7.11   | 0.89  | 7.04   | 0.79   |
| BMI, mean (SD)       | 29.58 (6.39)      | 29.78 (5.64)| 29.55 (6.49)     | 0.4437  | 31.24 (6.22)| 30.21  | 5.46  | 28.32  | 4.81   |
| Systolic blood pressure, mean (SD) | 132.42 (16.83)   | 132.94 (17.24)| 132.34 (16.72)  | 0.4395  | 133.64 (13.69)| 135.49 | 19.88 | 130.49 | 17.54  |

BMI body mass index, CAD coronary artery disease, LA = Latin America, MI myocardial infarction, SD standard deviation
in LA. Comparison of the number of days performing self-monitoring activities among the three LA countries showed higher values in Argentina, higher number of days following a healthy diet in Argentina and Brazil, and more days with physical activity practices in Mexico (Table 3).

A similar level of adherence was reported in LA compared to the rest of the MOSAiC participants, but a trend to a lower level of adherence was reported in Brazil (67.1 %). LA patients expressed more willingness to add additional injections to control their diabetes (67.4 versus 53.2 %; p < 0.0001).

Although no significant difference in the rate of not filling the prescription due to cost was observed between LA and the rest of the MOSAiC cohort, important variations were observed at the country level, with the lowest and highest rates in Argentina and Mexico, respectively (p = 0.0004).

Differences in the nature of the reported patient-health care provider relationship are depicted in Table 3. Lower levels of “hurried communication” were reported in Argentina, as well as higher scores in the domains of “elicited concerns”, “explained results”, “compassionate and respectful style”, and “patient centered decision making”, compared to the other LA countries.

Table 4 shows the analysis of variables associated with HbA1c levels. After the adjustment for potential confounders, patients in LA countries had similar levels of HbA1c compared to the rest of the MOSAiC cohort. The variables significantly associated with HbA1c levels were age (−0.0129; p < 0.0001), number of other OADs (0.0835; p = 0.0264), having higher education level (−0.2261; p = 0.0101), following a healthy diet (−0.0555; p = 0.0083), self-monitoring blood glucose (−0.0512; p = 0.0033), a hurried communication style in the interpersonal process of care questionnaire (0.1295;
The current analysis of MOSAIC study baseline data provides relevant information regarding the potential challenges that individuals with T2DM face when using insulin in LA countries. Although people from the three LA countries included in the study share some of these challenges with the whole cohort, others appear to be more specific for the region. These findings highlight, from a public health perspective, the importance of implementing more locally tailored solutions to optimize blood glucose control in individuals with T2DM treated with insulin.

A common problem recorded was the poor degree of metabolic control (HbA1c ≈ 8%), that coincides with data reported consistently in previous studies [7, 9, 10, 30].

This poor metabolic control was observed despite the wide variety of treatment patterns recorded in the studied population; in fact, patients in the three LA countries have a different treatment pattern compared to other regions, namely, a higher rate of basal insulin use and a lower rate of OADs agents used. Conversely, a comparable rate of metformin prescription was recorded in LA and non-LA countries. However, metformin was differently prescribed in LA countries, with a higher rate in Brazil (78.7%) and a lower rate in Mexico (37%). The recommendation of Asociación Latinoamericana de Diabetes (ALAD) guidelines regarding the use of metformin and precaution with the use of sulfonylureas may explain, at least partly, such a prescription pattern [31].

The low rate of incretin therapies use is also noteworthy, despite data showing that they are associated with a better HbA1c control and a lower risk of hypoglycemia and weight gain compared to insulin treated patients [32–34]. Clearly, none of the variety of treatment alternatives employed were effective in attaining the HbA1c target values recommended by international guidelines to prevent development and progression of chronic complications.

The linear regression analysis identified many variables associated with attainment of HbA1c treatment goals, with some of them unmodifiable (such as the age of the patients). Similar results have been reported in the ABCs of good management study in China [35, 36].

Other variables identified were the number of other associated OADs, the number of insulin injections, and adherence to insulin treatment, demonstrating once
Table 4 Variables associated with HBA1c levels (univariate and multivariate analysis)

|                        | Unadjusted regression | Adjusted regression |
|------------------------|-----------------------|---------------------|
|                        | Estimate   | 95 % CI  | p    | Estimate   | 95 % CI  | p value |
| Age                    | −0.0206    | (−0.03, −0.02) | <0.0001 | −0.0129    | (−0.02, −0.01) | 0.0001 |
| Gender—female          | 0.1085     | (0.01, 0.23) | 0.0735 | 0.0589     | (0.07, 0.19) | 0.3632 |
| Diabetes duration      | −0.0054    | (−0.01, 0.00) | 0.1866 | 0.0036     | (−0.01, 0.01) | 0.4219 |
| BMI                    | 0.0114     | (0.00, 0.02) | 0.0643 | 0.0075     | (0.00, 0.02) | 0.2243 |
| Number of OAD          | 0.0631     | (0.00, 0.13) | 0.0639 | 0.0835     | (0.01, 0.16) | 0.0264 |
| Insulin-mixed only     | 0.1715     | (0.03, 0.31) | 0.0143 | 0.0402     | (−0.14, 0.22) | 0.6625 |
| Short acting only      | 0.4457     | (0.11, 0.78) | 0.0098 | 0.3583     | (0.00, 0.72) | 0.0506 |
| Other                  | 0.2045     | (0.02, 0.39) | 0.0323 | 0.0892     | (−0.11, 0.29) | 0.3717 |
| Country group—LA       | 0.2248     | (−0.01, 0.46) | 0.0620 | 0.2129     | (−0.05, 0.48) | 0.1077 |
| Education level—high school | −0.1189 | (−0.28, 0.04) | 0.1496 | −0.1436    | (−0.32, 0.03) | 0.1010 |
| College                | −0.1936    | (−0.36, −0.03) | 0.0211 | −0.2261    | (−0.40, −0.06) | 0.0101 |
| Insurance status—public| −0.2764    | (−0.46, −0.09) | 0.0037 | −0.1834    | (−0.38, 0.02) | 0.0700 |
| Private                | −0.2186    | (−0.48, 0.04) | 0.0974 | −0.1407    | (−0.40, 0.12) | 0.2788 |
| SC—general diet        | −0.0758    | (−0.12, −0.04) | 0.0004 | −0.0555    | (−0.10, −0.02) | 0.0083 |
| Specific diet          | −0.0329    | (−0.08, 0.01) | 0.1451 | −0.0368    | (−0.08, 0.01) | 0.1025 |
| Exercise               | −0.0413    | (−0.07, −0.01) | 0.0035 | −0.0266    | (−0.06, 0.00) | 0.0798 |
| Blood Glucose testing  | −0.0658    | (−0.09, −0.04) | <0.0001 | −0.0512    | (−0.08, −0.02) | 0.0033 |
| IPC-hurried communication| 0.1800    | (0.08, 0.28) | 0.0004 | 0.1295     | (0.02, 0.24) | 0.0208 |
| Elicited concerns      | 0.0145     | (−0.08, 0.11) | 0.7506 | 0.0414     | (−0.05, 0.13) | 0.3745 |
| Explained results      | −0.0424    | (−0.15, 0.06) | 0.4186 | −0.0038    | (−0.11, 0.10) | 0.9422 |
| Patient-centered decision| 0.0251    | (−0.06, 0.11) | 0.5659 | 0.0513     | (−0.03, 0.14) | 0.2323 |
| Compassionate/respectful| −0.0346   | (−0.14, 0.07) | 0.5215 | −0.0109    | (−0.12, 0.10) | 0.8461 |
| Discriminated style    | −0.0039    | (−0.11, 0.11) | 0.9434 | −0.0818    | (−0.19, 0.03) | 0.1403 |
| DDS-total distress     | 0.1682     | (0.11, 0.23) | <0.0001 | 0.0660     | (−0.00, 0.14) | 0.0655 |
| Insulin injection frequency| 0.2001    | (0.10, 0.30) | 0.0002 | 0.1616     | (0.04, 0.28) | 0.0088 |
| Adherence (no missed shots) | −0.4575  | (−0.60, −0.32) | <0.0001 | −0.1939    | (−0.34, −0.05) | 0.0104 |

BMI: body mass index, CI: confidence interval, DDS: Diabetes Distress Scale, IPC: Interpersonal Process of Care, LA: Latin America, OADs: oral antidiabetic drugs, SC: self-care.
indicators, and quality of life were significantly better in the intervention group than in the control group [44].

Our study has several limitations, mainly associated with the nature of observational research (i.e., observational studies cannot provide causal evidence of an effect, in our case the real impact of conditioning factors on attainment of HbA1c target values). Baseline data were not available for all patients for all variables considered, thus we used multiple imputation with chained equations, a well-recognized method that accommodates both categorical and continuous variables, to impute missing values. Although this approach assumes that the missing values are missed at random, it is not possible to prove this assumption. Consequently, we also used a complete case analysis approach and results were quantitatively similar. Finally, the demographic, clinical, and psychosocial characteristics of the enrolled patients may be different from those individuals with T2DM in the general population of each country (24); this last bias could be of a lower magnitude because we recruited patients from both endocrinology and primary care practice sites with different practice locations (urban/rural), sizes, and practice types (academic/stand-alone) to maximize the data generalizability.

Conclusions

The MOSAIc baseline data showed that patients under an initial scheme of insulin treatment in LA and non-LA countries are not achieving appropriate glycemic control, and this analysis identified several conditions that significantly affect the attainment of HbA1c values suggested by international guidelines. Appropriate glycemic control can effectively prevent the development and progression of chronic complications that decrease quality of life and increase cost of care over time. Although some of these factors are not modifiable (e.g., age), most of them can be significantly removed by educational strategies. Therefore, policy makers, particularly in the LA region where health resources are frequently scarce, might seriously consider the wide implementation of educational activities to improve the metabolic control of individuals with diabetes. This strategy could effectively decrease the heavy burden of the disease on health budget, the society, and particularly on individuals with diabetes.

Abbreviations

ALAD: Asociación Latinoamericana de Diabetes; ANOVA: analysis of variance; HbA1c: glycated hemoglobin; IPC: Interpersonal Processes of Care; LA: Latin America; MOSAIc: Multinational Observational Study Assessing Insulin use; OADs: oral antidiabetic drug; PEDNID-LA: Programa de Educación de Diabéticos No Insulinodependientes en América Latina; Prodiacor: PROgrama Diabéticos CORrientes; SD: standard deviation; T2DM: type 2 diabetes mellitus; UAE: United Arab Emirates.

Authors’ contributions

BL is responsible for the concept and design the study the analysis and interpretation of data, the drafting the manuscript, and is the guarantor of this work. BC is responsible for concept and design of the study, the acquisition of data, the analysis and interpretation of data, and critical revision of the manuscript. GF, RM, MIE are responsible for data acquisition and critical revision of the manuscript. OS, JML are responsible of the critical revision of the manuscript. JGG is responsible for the data analysis and interpretation as well as drafting of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The results of this analysis are derived from baseline data from an ongoing study and at this stage the data will not be made available publicly until the conclusion of the study.

Competing interests

Drs. Linetzky, Curtis, Stempa and Martins de Lana are employees of and hold stock in Eli Lilly and Company. Dr. Frechtel has received speaker fees from Sanofi-Aventis, Lilly, Merck Sharp & Dohme (MSD), is an advisory board member for Sanofi and MSD and has received research funding from NovoNordisk, Sanofi-Aventis, Merck Sharp & Dohme, Lilly, and AstraZeneca. Dr. Renan received research funding from Eli Lilly, NovoNordisk, MSD, Merck Serono, Novartis, AstraZeneca, Boeringher, Sanofi, Aegerion, Amgen, and Jansen and is on advisory boards of Eli Lilly, NovoNordisk, MSD, Merck Serono, Novartis, AstraZeneca, Boeringher, Sanofi, Aegerion, Amgen, and Jansen. Dr. Escalante Pulido is an advisory board member for Eli Lilly, MSD, Boehringer, Jansen, Sanofi-Aventis, NovoNordisk, Bristol-Myers Squibb (BMS), AstraZeneca, and Abbott and has received research funding from BMS, AstraZeneca, Glaxo SmithKline, Eli Lilly, Sanofi-Aventis, and NovoNordisk. Dr. Gagliardino has received speaker fees from BMS, Eli Lilly, MSD, NovoNordisk, Roche, Sanofi-Aventis and Servier; is an advisory board member for BMS, Eli Lilly, MSD, and NovoNordisk; and received unrestricted research grants from Beta, BMS, Eli Lilly, MSD, NovoNordisk, Roche, and Sanofi-Aventis.

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