Title:

Exploring the role of the patient-physician relationship on insulin adherence and clinical outcomes in type 2 diabetes: insights from the MOSAIc study

Running head:

MOSAIc patient-physician study

Authors:

Bruno LINETZKY,[1]* Dingfeng JIANG,[2] Martha M. FUNNELL,[3] Bradley H. CURTIS,[2] William H. POLONSKY[4,5]

[1]Eli Lilly and Company, Buenos Aires, Argentina; [2]Eli Lilly and Company, Indianapolis, USA; [3]University of Michigan Medical School, Ann Arbor, USA; [4]Behavioral Diabetes Institute, San Diego, USA; [5]University of California, San Diego, USA

***Corresponding author:**

Bruno Linetzky

Eli Lilly and Company

Tronador 4890, Piso 12

Buenos Aires C1430DNN

Argentina

Tel: +54 1145464049

Fax: +54 1145464172

Email: linetzky_bruno@lilly.com

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/1753-0407.12443

ABSTRACT

Background: MOSAIc is a 2-year, prospective, multi-national, observational study to determine if patient-, physician-, and health system-related factors impact outcomes in patients with T2D and to quantify these relationships. This sub-analysis of baseline data aims to investigate how aspects of the patient-physician relationship are associated with diabetes-related distress, insulin adherence and glycemic control.

Methods: Patients with T2D taking insulin for ≥3 months were recruited at primary care and specialty practice sites in 18 countries. Physicians provided usual care. Clinical history and most recent HbA1c values were collected; patients were surveyed regarding their perception of physician interactions, level of diabetes-related distress and insulin adherence.

Results: A total of 4341 patients were included in the analysis population. Four (of six) interpersonal processes of care domains showed a significant relationship with total diabetes-related distress ($p<0.01$). Poor insulin adherence was associated with greater diabetes-related distress (adjusted OR 1.14; 95% CI 1.06-1.22), higher *discrimination* (1.13; 1.02-1.27) and *hurried communication* scores (1.35; 1.20-1.53), and with lower *explained results* score (0.86; 0.77-0.97). Poor insulin adherence was associated with a 0.43% increase in HbA1c, and a one-unit increase in total diabetes-related distress, and *hurried communication* score was associated with a 0.171% and 0.145% increases in HbA1c, respectively.

Conclusions: We observed poor insulin adherence when patients feel distressed about living with T2D and when there are aspects of their physician interactions with which they are dissatisfied. Perceived physician inattention and lack of engagement, as well as diabetes-related distress, have a direct relationship with insulin adherence and glycemic control.

Word count: 249/250 words

Keywords: Medication Adherence; Physician-Patient Relations; Type 2 Diabetes Mellitus

Significant findings of the study:

- Patient perceptions of the quality of their interactions with their physicians have a significant association with total diabetes-related distress.
- Diabetes-related distress and patient-physician interactions have a significant independent association with insulin adherence and HbA1c level.

What this study adds:

- Delineation of the specific aspects of the patient-physician interaction that are linked to diabetes-related distress, insulin adherence behavior and glycemic control.

1. INTRODUCTION

A growing body of literature supports the positive impact of effective patient-provider communication in diabetes on patient outcomes. Evidence from a series of cross-sectional studies indicates that the patient's relationship with his or her healthcare provider is closely related to patient self-management behavior.[1-3] A multi-national survey of 2000 patients with diabetes found that patients' ratings of providers' communication effectiveness showed a positive relationship with self-management behavior.[1] Another large survey of adults with diabetes that examined general- and diabetes-specific communication found that patients' adherence to various self-management activities was positively associated with healthcare provider communication.[2] The cross-sectional Diabetes Attitudes, Wishes and Needs (DAWN) study assessed the relationship of self-reported well-being, self-management and diabetes control with factors related to patients' healthcare of patients with type 1 (T1D) and type 2 diabetes (T2D).[3] The study reported that better patient-provider collaboration was associated with more favorable ratings on all patient-reported outcome measures, including diabetes-related distress, general well-being, lifestyle and medical regimen adherence, perceived diabetes control and hyperglycemic symptoms.[3] The second DAWN study (DAWN2) highlighted the need for an improvement in patient-provider interactions. For instance, most providers (63%) agreed that there is a major need for better availability of resources for the provision of psychosocial support and that providers and patients differ considerably with regard to their perceptions about the support being given.[4] The global IntroDia™ study investigated the impact of early patient-physician conversations on patient self-care and self-reported outcomes. Better physician communication at the time of diagnosis, as recalled by patients, was linked to less diabetes distress, greater well-being and greater adherence to self-care behaviors.[5]

The importance of patient-provider communication and self-care behavior is reflected in the most recent ADA/EASD position statement, which advocates a patient-centered approach that takes into account the patient's attitude and expected treatment efforts.[6] In order to be able to guide improvements and

healthcare provider education to improve patient-provider communication, it would be valuable to understand which elements of the patient-provider interaction influence self-management behavior and ultimately, clinical outcomes.

One area of critical importance is medication adherence, and here there is specific evidence that patient-provider communication plays a key role.[5,7-10] In particular, adherence to prescribed insulin regimens is known to be a significant issue. For example, in a telephone survey of 1530 insulin-treated patients, one-third of patients reported missing shots at least one day in the past month, with an average of 3.3 days.[11] These results are consistent with prior findings that patients with T2D have insulin adherence rates in the range of 59% to 77%.[12] While we might presume that patient-physician communication plays an important role in adherence to insulin, we are not aware of any published research in this area.

MOSAIc (Multinational Observational Study assessing Insulin use: understanding the challenges associated with progression of therapy) is a 2-year prospective, multi-national observational study to determine if patient-, physician- and health system-related factors impact treatment progression in patients with T2D and to quantify relationships between these factors and long-term clinical outcomes. The primary aim of the current baseline analysis is to investigate how key aspects of the patient-physician relationship may be related to patients' levels of diabetes-related distress, insulin adherence and HbA1c level. Specifically, we aimed to test the hypothesis that the patient-physician interactions and diabetes-related distress may have independent and combined effects on both insulin adherence and glycemic control.

2. METHODS

2.2 Study design

A detailed description of the MOSAIc study methods, including design, data collection, data management and statistical analysis, has been published.[13] MOSAIc is a multi-national, prospective, observational cohort study of patients with T2D using insulin therapy for ≥3 months to collect real-world data, including demographic, clinical and psychosocial data, about patients' care and health outcomes at regular intervals during a 24-month follow-up period. Physicians provide usual care to their patients, reflecting characteristics and patterns of patients with T2D and their treatments in real-world settings.

The current analysis investigates cross-sectional associations between key psychosocial dimensions assessed at baseline (patients' perspective on their interactions with their physician and diabetes diabetes-related distress) and insulin adherence, as well as the potential impact of these factors on baseline HbA1c. The conceptual model tested builds on that investigated by Heisler and colleagues[1] and is shown in Figure 1.

2.3 Patient population

The MOSAIc study was conducted at primary care and specialty practice sites in 18 countries (Argentina; Brazil; Canada; China; Germany; India; Israel; Italy; Japan; Mexico; Russia; Saudi Arabia; South Korea; Spain; Turkey; United Arab Emirates; United Kingdom; United States, including Puerto Rico). Eligible patients are those ≥18 years diagnosed with T2D; taking any commercially-available insulin (except intensive basal-bolus insulin therapy, such as basal + 3 prandial injections) from any manufacturer for ≥3 months with or with no combination of approved non-insulin antidiabetic medications; not simultaneously participating in any study with an investigational drug or procedure; proficient in the country's primary language; and who provided written informed consent of study enrolment. Patients were recruited from both primary care practices and diabetes specialty clinics at sites in rural and urban locations and academic and non-academic settings. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and is consistent with the applicable laws and

regulations of the countries where the study is being conducted. All patients completed informed consent forms approved by their country-specific institutional review boards. The ClinicalTrials.gov study identifier is NCT01400971.

2.4 Data collection

Retrospective data collection occurred at the baseline visit (for the period beginning six months prior to baseline) and prospective collection occurs during four subsequent visit windows (within ± 3 months) at 6, 12, 18 and 24 months postbaseline. Baseline data relating to T2D clinical history, including diagnosis, treatment and complications and medication history, were collected from medical records. Most recently recorded laboratory values were recorded but limited to the period six months prior to the baseline visit. Information on patients' diabetes- and insulin-related attitudes and behaviors was collected using patient questionnaires administered at baseline. These included the Interpersonal Processes of Care (IPC) survey[14] and the Diabetes Distress Scale (DDS)[15] to assess patients' perceptions of their interactions with their physicians and their levels of diabetes-related distress, as well as additional questions to evaluate the current insulin regimen and insulin adherence behavior.

The IPC survey was used to assess the patients' perceptions of specific domains of the relationship with their physicians over the past 12 months.[14] The IPC survey is a validated questionnaire developed to evaluate physician-patient interpersonal process of care that is designed to be suitable for diverse population groups and languages.[14] However, one of the IPC dimensions, the 4-item *disrespectful office staff* domain, was not included in the final questionnaire battery; these results were not considered relevant or likely to provide accurate information given that the staff were entering the information into the electronic case report forms. From the 25 IPC items, six domains were assessed:[16] *hurried communication* (doctors spoke too fast, used complex words, ignored what I told them, appeared distracted, seemed bothered if I asked several questions); *elicited concerns* (doctors heard my concerns

and took them seriously); *explained results* (doctors explained results of tests/examinations and explained the possible side effects of and consequences of not taking prescribed medicines); *patient-centered decision-making* (doctors asked about preferences for helping to decide treatment and whether I would be able to follow the treatment); *compassionate/respectful* (doctors expressed concern about my feelings, were compassionate, supportive and respected me); *discrimination* (doctors made assumptions about my education and income status and I felt discrimination or inattentiveness due to my race/ethnicity). Each of the 25 items was rated by the patients on a 5-point scale, from 1 (never) to 5 (always). For the positive IPC domains (*elicited concerns*, *explained results*, *patient-centered decisions*, *compassionate/respectful*), higher scores indicated more satisfying interactions. For the negative IPC domains (*hurried communication* and *discrimination*), lower scores indicated more satisfying interactions.

The DDS is a 17-item scale for the assessment of diabetes-related emotional distress.[15] The DDS is a validated instrument with high reliability that has been shown to be applicable to different ethnic groups.[15] Patients were asked to rate the extent to which potential problems they may experience have bothered them during the past month. Responses are rated on a 6-point scale, from 1 (not a problem) to 6 (a very serious problem). Higher scores represent greater diabetes-related distress.

A series of questions were asked about the current insulin regimen and insulin adherence. The questions were the following: “How many times do you take your insulin a day?” with 4 response options, from once a day to more than three times a day, and “How often did you miss your insulin shot during the last seven days?” with the following response options: “I did not miss any shots,” “I missed “some, “about half,” “most” or “all” of my shots.”

2.5 Statistical analysis

Descriptive summary analyses (mean, standard deviation and frequency) were reported for baseline characteristics, clinical variables and laboratory values, and missing values were imputed by the multivariate imputation by chained equations method. Countries were divided into three income groupings according to The World Bank definitions using gross national income per capita (lower middle income: $1046 to $4125, upper middle income: $4126 to $12,735 and high income: $12,736 or more).

Insulin adherence was reported as complete adherence (patients who reported that missed no shots) or poor adherence (patients who reported missing "some," "about half," "most" or "all" of their insulin shots) during the past seven days. Due to the skewed distribution of responses, insulin adherence was analyzed as a binomial variable with responses split between complete and poor adherence. Unadjusted and adjusted regression estimates were calculated for the total distress results, insulin adherence (measured as frequency of missed shots) and HbA1c level. Linear regression was used for DDS and HbA1c, while logistic regression was used for adherence.

Structural equation modeling (SEM) was used to investigate the relationships between the IPC domains, total distress, insulin adherence and HbA1c level. Specifically, the maximum likelihood estimator with robust standard errors using a numerical integration algorithm was used in path analyses for this purpose. SEM has been advocated over regression methods for testing mediated effects because it allows measurement error to be controlled for.[17] Analysis-wide statistical significance was conducted at the 0.05 level. Regression analyses were performed using SAS 9.2 (SAS, Cary, NC, USA) and SEM was performed using Mplus 7.3 (Mplus, Los Angeles, CA, USA).

3. RESULTS

3.1 Patient characteristics

A total of 4341 patients met MOSAIc eligibility criteria and were included in the analysis population. Mean patient age was 61.8 years, 50% were female, mean T2D duration was 12.7 years and mean baseline HbA1c was 8.1%. Of note, 76% of the sample reported that they missed no insulin injections during the previous week. An overview of the baseline characteristics and pooled results for the IPC and DDS questionnaires are shown in Table 1. Further details about baseline characteristics for the MOSAIc study sample have been published elsewhere.[17]

3.2 The influence of patient-physician communication on diabetes-related distress

Higher scores in the two negative IPC domains (*hurried communication* and *discrimination*) were independently linked with greater diabetes-related distress (Table 2). In addition, higher scores in two of the positive IPC domains (*explained results* and *patient-centered decision-making*) were independently associated with lower levels of diabetes-related distress. *Hurried communication* showed a markedly stronger association with diabetes-related distress than any other IPC domain (adjusted regression estimate 0.40; $p<0.001$).

3.3 The influence of patient-physician communication and diabetes distress on insulin adherence

Greater likelihood of missed insulin injections was independently associated with higher scores on the two negative IPC domains (*hurried communication* [adjusted OR1.35; 95% CI 1.20-1.53] and *discrimination* [adjusted OR 1.13; 95% CI 1.02-1.27]), with lower scores on one of the positive IPC domains (less time spent having medical tests and results explained [adjusted OR 0.86; 95% CI 0.77-0.97] and with greater diabetes-related distress [adjusted OR 1.14; 95% CI 1.06-1.22]) (Table 3).

3.4 The influence of patient-physician communication, diabetes-related distress and insulin adherence on HbA1c

Higher HbA1c level was independently linked with diabetes-related distress (adjusted regression estimate 0.12; p<0.01), the *hurried communication* domain of the IPC scale (adjusted regression estimate 0.16; p<0.01) and poor insulin adherence (adjusted regression estimate 0.31; p<0.001) (Table 4).

3.5 Modeling the associations between HbA1c, insulin adherence and psychosocial factors

Structural equation modeling was performed to estimate the relationships between aspects of patient-physician communication, diabetes-related distress, insulin adherence and HbA1c level. The path analysis (Figure 2) shows the parameter coefficients for the interactions between these factors. Paths from four of the IPC domains (*patient-centered decision-making*, *discrimination*, *explained results* and *hurried communication*) to total diabetes-related distress were significant and in the predicted direction, with a particularly high proportion of diabetes-related distress explained by the *hurried communication* domain (parameter coefficient 0.414).

Variance in insulin adherence behavior was explained by three of the same IPC domains (*discrimination*, *explained results* and *hurried communication*) and by diabetes-related distress. A single-unit increase in the total distress score was associated with an 18% increase in the likelihood of poor insulin adherence (parameter coefficient 0.168; OR 1.18). Single-unit increases in the *hurried communication* and *discrimination* domain scores were associated with 29% and 19% increased odds of poor insulin adherence (parameter coefficients 0.254 and 0.176; ORs 1.29 and 1.19, respectively), while the same increase in the *explained results* domain was associated with a 15% reduction in the odds of poor insulin adherence (parameter coefficient -0.158; OR 1.15).

Insulin adherence behavior explained a substantial proportion of HbA1c level, with poor insulin adherence linked with a 0.43% increase in HbA1c. Diabetes-related distress and *hurried communication* were also

linked directly with HbA1c level, with a single-unit increase in each associated with a 0.171% and 0.145% increase in HbA1c, respectively.

4. DISCUSSION

This baseline analysis of cross-sectional data obtained as part of the global MOSAIc study demonstrated, through regression analyses and structural equation modeling, a significant relationship between aspects of the patient-physician relationship, insulin adherence and HbA1c level (Figure 2). We observed more problematic insulin adherence when patients were distressed about living with T2D and when there were aspects of their interactions with their physicians with which they were dissatisfied.

Problematic insulin adherence was associated with a 0.43% increase in HbA1c level, confirming the findings of other studies that have reported a significant relationship between medication adherence and HbA1c.[19] In terms of the factors that drive insulin adherence, various domains of the patient-physician relationship, as well as total distress, were shown to influence the likelihood of missing insulin shots. In particular, a patient's perception of *hurried communication* showed a substantial effect on insulin adherence, with a 29% increased likelihood of a patient missing at least some insulin shots associated with a single-unit increase in the score for *hurried communication* by their physician. The *hurried communication* domain provides a measure of not only how quickly the physician spoke, but also the patient's perception of whether the physician used complex words, appeared distracted, seemed bothered when the patient asked questions or ignored the patient's input. This could also be described as a measure of the physician's perceived lack of engagement or inattentiveness during consultations. The *explained results* domain assessed whether the physician explained the results of examinations and tests, and importantly, whether he or she informed the patient of the possible side effects of prescribed medicines and the consequences of not adhering to the prescribed treatment regimen.

Our study results build on prior research and demonstrate the importance of healthcare professionals' communication skills and style on patients' emotional response to their condition, insulin adherence behavior and HbA1c level. Mayberry and Osborn tested an information-motivation-behavioral skills (IMB) model, the elements of which explained 41% of the variability in medication adherence behavior. The elements of the IMB model were adherence information, adherence motivation and adherence behavior skills.[19] In this study, we investigated the impact of patient-physician communication on insulin adherence, rather than overall medication adherence. We also looked at specific aspects of the patient-physician interaction that allowed us to reveal the particularly important effect of the *hurried communication*, *explained results* and *discrimination* domains. The impact of these particular aspects of the patient-physician interaction is supported by findings from several other studies,[1,3] including the TRIAD study that investigated barriers to insulin initiation in patients with T2D.[7] In the TRIAD study, a significantly greater proportion of patients who failed to initiate prescribed insulin treatment reported the following about their physician interactions: compared with those who initiated, patients who did not initiate treatment more frequently reported that the risks and benefits of treatment were not well explained and a higher proportion had inadequate health literacy and reported having problems learning about their medical condition.[7] The importance of patient-physician interactions is further underscored by the Forum for Injection Technique recommendations, which include guidelines for patient-physician communication aimed at achieving optimal injection technique.[20]

Given the many competing priorities during time-limited patient consultations, the complexity of the disease and the factors that influence clinical outcomes, consideration for longer consultation times for the management of T2D is warranted by health policy makers. However, our findings suggest that identifying and implementing strategies to enhance physician engagement or attentiveness and the

quality of explanation regarding medical tests, their results and the pros and cons of the prescribed treatment regimen should be key focus areas in improving insulin adherence for patients with T2D.

The importance of the patient's experience interacting with their physician is further underscored by the direct association we reported between the patient-physician interaction and HbA1c level. The measure of physician inattentiveness showed a direct relationship with glycemic control that was separate from the impact on insulin adherence, lending support to the concept of patient empowerment. Perhaps having consultations with a physician who appears engaged, attentive and willing to answer questions is more likely to engage and support patients' interests and confidence in their own diabetes self-management, above and beyond careful attention to their insulin regimen. In support of this hypothesis, in one randomized, controlled trial, patients with diabetes who were coached to ask more questions and be more proactive in raising concerns during medical consultations, thereby prompting better engagement and attentiveness during the visit, had significantly better biomedical outcomes, including better glycemic control.[21]

One limitation of the current study was that insulin adherence was analyzed as a binomial outcome measure, with all responses indicating any degree of less-than-optimal adherence (≥1 missed shot/week) grouped together. This prevents us from distinguishing between patients with different degrees of poor adherence and the potential relationship that this may have on clinical outcomes. Also, given the cross-sectional nature of these findings, causal inferences cannot be made. Furthermore, patient-physician differences in gender and language, which can play important roles in medication adherence,[22,23] were not assessed. Still, a significant relationship was identified between aspects of the patient-physician relationship, diabetes-related distress, insulin adherence and HbA1c level. These data support the hypothesis that interactions between the patient and physician and diabetes-related distress may have a direct negative impact on insulin adherence and HbA1c level. Given the independent effect of patient-

physician interactions on HbA1c, we would expect to find that there are other mechanisms involved beyond adherence to insulin regimens. Further investigations are being conducted over a 2-year period and will explore the involvement of other factors, such as diabetes knowledge and increase in self-care activities, as well as a careful examination of the temporal relationship between these factors.

The findings of this study point to a clear relationship between diabetes-related distress and aspects of patient-physician interactions with insulin adherence in patients with T2D. Patients' perceptions of physician engagement and attentiveness, the quality of explanation about medical tests and results and discussion around the prescribed treatment regimen were directly associated with insulin adherence behavior. Diabetes-related distress and physician engagement and attentiveness were also shown to be independently linked to long-term glycemic control. Given the cross-sectional nature of this study, the direction of the relationships between patient-physician communication, level of diabetes-related distress and insulin adherence cannot be determined. However, the current findings are consistent with previous data suggesting that improving patient-physician interactions may help improve insulin adherence.[24] Our findings suggest that efforts to enhance physician engagement and attentiveness, explanation of medical tests and their results and discussion about the possible impact of the prescribed clinical management approach are warranted.

ACKNOWLEDGEMENTS

The MOSAIc study was sponsored by Eli Lilly and Company. Medical writing assistance was provided by Lucy Rutherford and Andrew Sakko, and editorial assistance by Jeanne Claypoole, of inVentiv Health Clinical, sponsored by Eli Lilly and Company.

DISCLOSURES

BL, DJ and BC are employees of Eli Lilly and Company. MF reports honoraria received from AstraZeneca and Bristol-Myers Squibb Diabetes Alliance, Eli Lilly, Novo Nordisk and Sanofi-Aventis, and a non-financial advisory relationship with Omada Health, outside the submitted work. WHP has served as a consultant for Eli Lilly, Novo Nordisk and Sanofi-Aventis.

REFERENCES

1. Heisler M, Bouknight RR, Hayward RA, Smith DM, Kerr EA. The relative importance of physician communication, participatory decision making, and patient understanding in diabetes self-management. *J Gen Intern Med* 2002; 17: 243-252.

2. Piette JD, Schillinger D, Potter MB, Heisler M. Dimensions of patient-provider communication and diabetes self-care in an ethnically diverse population. *J Gen Intern Med* 2003; 18: 624-633.

3. Rubin RR, Peyrot M, Siminerio LM. Health care and patient-reported outcomes: results of the cross-national Diabetes Attitudes, Wishes and Needs (DAWN) study. *Diabetes Care* 2006; 29: 1249-1255.

4. Holt RI, Nicolucci A, Kovacs Burns K et al. Diabetes Attitudes, Wishes and Needs second study (DAWN2^{TM}): cross-national comparisons on barriers and resources for optimal care—healthcare professional perspective. *Diabet Med* 2013; 30:789-798.

5. Polonsky WH, Belton A, Down S et al. Physician-patient communication at type 2 diabetes diagnosis and its links to physician empathy and patient outcomes: new results from the global IntroDia study. European Association for the Study of Diabetes Annual Meeting, Stockholm, Sweden, 14-18 September 2015. Available at: http://www.easdvirtualmeeting.org/resources/physician-patient-communication-at-type-2-diabetes-diagnosis-and-its-links-to-physician-empathy-and-patient-outcomes-new-results-from-the-global-introdia-study--2.

6. Inzucchi SE, Bergenstal RM, Buse JB et al. Management of hyperglycaemia in type 2 diabetes, 2015: a patient-centred approach. Update to a position statement of the American Diabetes

Association and the European Association for the Study of Diabetes. *Diabetologia* 2015; 58: 429-442.

7. Karter AJ, Subramanian U, Saha C et al. Barriers to insulin initiation: the translating research into action for diabetes insulin starts project. *Diabetes Care* 2010; 33: 733-735.

8. Kerse N, Buetow S, Mainous AG, III, Young G, Coster G, Arroll B. Physician-patient relationship and medication compliance: a primary care investigation. *Ann Fam Med* 2004; 2: 455-461.

9. Piette JD, Heisler M, Krein S, Kerr EA. The role of patient-physician trust in moderating medication nonadherence due to cost pressures. *Arch Intern Med* 2005; 165: 1749-1755.

10. Ratanawongsa N, Karter AJ, Parker MM et al. Communication and medication refill adherence: the Diabetes Study of Northern California. *JAMA Intern Med* 2013; 173: 210-218.

11. Peyrot M, Barnett AH, Meneghini LF, Schumm-Draeger PM. Insulin adherence behaviours and barriers in the multinational Global Attitudes of Patients and Physicians in Insulin Therapy study. *Diabet Med* 2012; 29: 682-689.

12. Weinger K, Beverly EA. Barriers to achieving glycemic targets: who omits insulin and why? *Diabetes Care* 2010; 33: 450-452.

13. Polinski JM, Curtis BH, Seeger JD, Choudhry NK, Zagar A, Shrank WH. Rationale and design of the multinational observational study assessing insulin use: the MOSAIc study. *BMC Endocr Disord* 2012; 12: 20.

14. Stewart AL, Napoles-Springer AM, Gregorich SE, Santoyo-Olsson J. Interpersonal processes of care survey: patient-reported measures for diverse groups. *Health Serv Res* 2007; 42: 1235-1256.

15. Polonsky WH, Fisher L, Earles J et al. Assessing psychosocial distress in diabetes: development of the diabetes distress scale. *Diabetes Care* 2005; 28: 626-631.

16. Napoles AM, Gregorich SE, Santoyo-Olsson J, O'Brien H, Stewart AL. Interpersonal processes of care and patient satisfaction: do associations differ by race, ethnicity, and language? *Health Serv Res* 2009; 44: 1326-1344.

17. Lee YY, Lin JL. The effects of trust in physician on self-efficacy, adherence and diabetes outcomes. *Soc Sci Med* 2009; 68: 1060-1068.

18. Polinski JM, Kim SC, Jiang D et al. Geographic patterns in patient demographics and insulin use in 18 countries, a global perspective from the multinational observational study assessing insulin use: understanding the challenges associated with progression of therapy (MOSAIc). *BMC Endocr Disord* 2015; 15: 46.

19. Mayberry LS, Osborn CY. Empirical validation of the information-motivation-behavioral skills model of diabetes medication adherence: a framework for intervention. *Diabetes Care* 2014; 37: 1246-1253.

20. Forum for Injection Technique (FIT). The UK Injection Technique Recommendations 3rd Edition. September 2015. Available at: http://www.fit4diabetes.com/files/6714/4293/6325/FIT_Injection_Technique_Recommendations_3rd_Edition_lo_res.pdf

21. Greenfield S, Kaplan SH, Ware JE, Jr., Yano EM, Frank HJ. Patients' participation in medical care: effects on blood sugar control and quality of life in diabetes. *J Gen Intern Med* 1988; 3: 448-457.

22. Schmittdiel JA, Traylor A, Uratsu CS, Mangione CM, Ferrara A, Subramanian U. The association of patient-physician gender concordance with cardiovascular disease risk factor control and treatment in diabetes. *J Womens Health (Larchmt)* 2009; 18: 2065-2070.

23. Traylor AH, Schmittdiel JA, Uratsu CS, Mangione CM, Subramanian U. Adherence to cardiovascular disease medications: does patient-provider race/ethnicity and language concordance matter? *J Gen Intern Med* 2010; 25: 1172-1177.

24. Nam S, Nam S, Song Y. Role of self-efficacy in the relationship between patient-provider relationships and psychological insulin resistance among patients with type 2 diabetes. *J Contemp Diabetes Res* 2014; 1: 1-15.

FIGURE LEGENDS

Figure 1. Conceptual model tested: hypothesis for how patient perception of care influences distress status, insulin adherence and the relationship with clinical outcomes.

Figure 2. Path analysis showing interaction between patient-physician interaction, diabetes-related distress, insulin adherence and HbA1c level. Model not adjusted for baseline covariates and showing only those factors with at least one significant interaction.

Table 1. Patient characteristics and Interpersonal Processes of Care, diabetes-related distress and insulin adherence results for patients enrolled in the MOSAIc study at baseline

Age, years	Mean (SD)	61.77 (11.02)
Gender, female	n (%)	2176 (50.13)
Duration of diabetes (years)	Mean (SD)	12.65 (7.98)
HbA1c,%	Mean (SD)	8.13 (1.75)
Country income level		
Low middle	n (%)	918 (21.15)
Upper middle	n (%)	1177 (27.11)
High	n (%)	2246 (51.74)
Education level		
Primary	n (%)	1291 (29.74)
High school	n (%)	1216 (28.01)
College	n (%)	1499 (34.53)
Insurance status		
Uninsured	n (%)	848 (19.53)
Private	n (%)	917 (21.12)
Public	n (%)	2229 (51.35)
Interpersonal Processes of Care		
Hurried communication	Mean (SD)	1.58 (0.70)
Elicited concerns	Mean (SD)	3.92 (1.04)
Explained results	Mean (SD)	3.92 (1.01)
Patient-centered decision making	Mean (SD)	3.36 (1.21)
Compassionate-respectful	Mean (SD)	4.10 (0.88)
Discrimination	Mean (SD)	1.51 (0.73)
Diabetes distress scale		
Total distress	Mean (SD)	2.27 (1.13)
Insulin treatment regimen		
Number of shots per day	Mean (SD)	1.63 (0.68)
Once per day	n (%)	1977 (45.54)
Twice per day	n (%)	1921 (44.25)
Three times per day	n (%)	244 (5.62)
More than three times per day	n (%)	77 (1.77)
Insulin adherence, missed insulin shots in last 7 days		
I did not miss any shots	n (%)	3290 (75.79)
I missed some / about half / most / all shots	n (%)	927 (21.35)

HbA1c, glycated hemoglobin; SD, standard deviation

Table 2. Unadjusted and adjusted regression estimates for the impact of patient characteristics and Interpersonal Processes of Care scores on diabetes-related distress.

	Diabetes-related distress			
	Unadjusted regression estimate (95% CI)		**Adjusted regression estimate (95% CI)**	
Age	-0.02***	(-0.02, -0.01)	-0.02***	(-0.02, -0.01)
Gender, female	0.14***	(0.07, 0.20)	0.11***	(0.04, 0.17)
Diabetes duration	-0.01***	(-0.01, -0.00)	0.00	(-0.00, 0.01)
Country income				
Upper middle	0.18***	(0.08, 0.28)	0.19**	(0.09, 0.30)
High	-0.00	(-0.09, 0.08)	0.06	(-0.03, 0.15)
Education level				
High school	-0.08	(-0.17, 0.01)	-0.02	(-0.11, 0.06)
College	0.05	(-0.03, 0.14)	0.06	(-0.03, 0.14)
Insurance status				
Public	0.13**	(0.04, 0.22)	0.09	(-0.00, 0.18)
Private	-0.01	(-0.11, 0.10)	0.04	(-0.06, 0.14)
Interpersonal Processes of Care				
Hurried communication	0.42***	(0.37, 0.47)	0.40***	(0.35, 0.46)
Elicited concerns	0.01	(-0.03, 0.05)	0.02	(-0.02, 0.06)
Explained results	-0.07**	(-0.12, -0.03)	-0.07**	(-0.12, -0.02)
Patient-centered decision making	-0.05**	(-0.09, -0.02)	-0.07***	(-0.10, -0.03)
Compassionate/respectful	-0.04	(-0.09, 0.01)	-0.03	(-0.08, 0.02)
Discrimination	0.17***	(0.12, 0.21)	0.16***	(0.11, 0.21)

CI, confidence interval. Significance levels are indicated as: * p<0.05; ** p<0.01; *** p<0.001. Adjusted regression model includes all parameters (age, gender, diabetes duration, country income, education level, insurance status, interpersonal processes of care domain results). Low middle country income, primary education level and uninsured insurance status served as reference groups for the regression analysis and are not shown in the table.

Table 3. Unadjusted and adjusted regression estimates for the impact of patient characteristics, Interpersonal Processes of Care scores and diabetes-related distress on adherence, measured as missed shots.

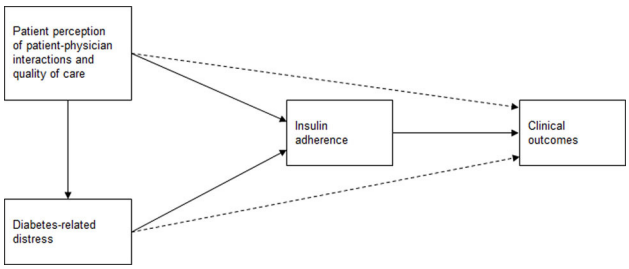
	Insulin adherence			
	Unadjusted OR (95% CI)		Adjusted OR (95% CI)	
Age	0.96***	(0.95, 0.97)	0.97***	(0.96, 0.98)
Gender, female	0.89	(0.77, 1.03)	0.90	(0.77, 1.06)
Diabetes duration	0.97***	(0.96, 0.98)	0.99*	(0.98, 1.00)
Country income				
Upper middle	0.83	(0.68, 1.01)	0.94	(0.74, 1.20)
High	0.60***	(0.50, 0.72)	0.77*	(0.62, 0.96)
Education level				
High school	1.22*	(1.00, 1.48)	1.12	(0.90, 1.38)
College	1.42***	(1.19, 1.71)	1.18	(0.97, 1.45)
Insurance status				
Public	0.84	(0.70, 1.02)	0.95	(0.76, 1.19)
Private	1.29*	(1.04, 1.60)	1.42**	(1.12, 1.79)
Interpersonal Processes of Care				
Hurried communication	1.36***	(1.21, 1.52)	1.35***	(1.20, 1.53)
Elicited concerns	0.95	(0.87, 1.04)	0.93	(0.85, 1.02)
Explained results	0.85**	(0.76, 0.94)	0.86*	(0.77, 0.97)
Patient-centered decision making	1.06	(0.97, 1.16)	1.03	(0.94, 1.13)
Compassionate/respectful	1.01	(0.90, 1.13)	1.08	(0.96, 1.22)
Discrimination	1.24***	(1.12, 1.38)	1.13	(1.02, 1.27)
Diabetes-related distress	1.29***	(1.21, 1.37)	1.14***	(1.06, 1.22)
Insulin treatment regimen				
Number of shots per day	1.25***	(1.12, 1.39)	1.23***	(1.10, 1.37)

CI, confidence interval; OR, odds ratio. Significance levels are indicated as: * p<0.05; ** p<0.01; *** p<0.001. Adjusted regression model includes all parameters (age, gender, diabetes duration, country income, education level, insurance status, interpersonal processes of care domain results). Low middle country income, primary education level and uninsured insurance status served as reference groups for the regression analysis and are not shown in the table.

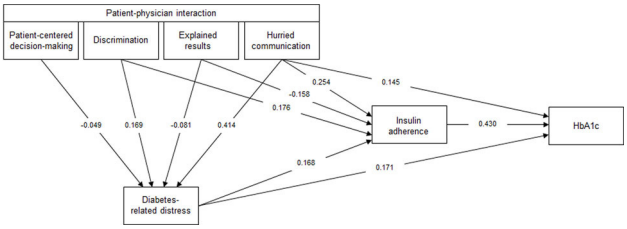
Table 4. Unadjusted and adjusted regression estimates of the impact of patient characteristics, Interpersonal Processes of Care, diabetes-related distress, and insulin adherence on HbA1c level.

	HbA1c			
	Unadjusted regression estimate (95% CI)		**Adjusted regression estimate (95% CI)**	
Age	-0.02***	(-0.03, -0.02)	-0.02***	(-0.02, -0.01)
Gender, female	0.11	(-0.01, 0.23)	0.08	(-0.04, 0.21)
Diabetes duration	-0.01	(-0.01, 0.00)	0.00	(-0.00, 0.01)
Country income				
Upper middle	-0.34***	(-0.53, -0.15)	-0.47***	(-0.70, -0.24)
High	-0.51***	(-0.69, -0.34)	-0.45***	(-0.66, -0.25)
Education level				
High school	-0.12	(-0.28, 0.04)	-0.20*	(-0.36, -0.03)
College	-0.19*	(-0.36, -0.03)	-0.30**	(-0.48, -0.12)
Insurance status				
Public	-0.28**	(-0.46, -0.09)	-0.05	(-0.27, 0.16)
Private	-0.22	(-0.48, 0.04)	-0.04	(-0.30, 0.23)
Interpersonal Processes of Care				
Hurried communication	0.18***	(0.08, 0.28)	0.16**	(0.05, 0.26)
Elicited concerns	0.01	(-0.08, 0.11)	0.01	(-0.08, 0.10)
Explained results	-0.04	(-0.15, 0.06)	-0.02	(-0.12, 0.09)
Patient-centered decision making	0.03	(-0.06, 0.11)	0.04	(-0.05, 0.12)
Compassionate/respectful	-0.03	(-0.14, 0.07)	-0.00	(-0.12, 0.11)
Discrimination	-0.00	(-0.11, 0.11)	-0.11	(-0.22, 0.00)
Diabetes-related distress	0.17***	(0.11, 0.23)	0.12**	(0.05, 0.19)
Insulin adherence				
Missed shots	0.46***	(0.32, 0.60)	0.31***	(0.17, 0.45)
Insulin treatment regimen				
Number of shots per day	0.20***	(0.10, 0.30)	0.15**	(0.05, 0.24)

CI, confidence interval; HbA1c, glycated hemoglobin. Significance levels are indicated as: * p<0.05; ** p<0.01; *** p<0.001. Adjusted regression model includes all parameters (age, gender, diabetes duration, country income, education level, insurance status, interpersonal processes of care domain results). Low middle country income, primary education level and uninsured insurance status served as reference groups for the regression analysis and are not shown in the table.



JDB_12443_F1.jpg



JDB_12443_F2.jpg