



## Identifying solutions to psychological insulin resistance: An international study☆

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### ABSTRACT

**Aims:** To identify actions of healthcare professionals (HCPs) that facilitate the transition to insulin therapy (IT) in type 2 diabetes (T2D) adults.

**Methods:** Included were T2Ds in seven countries ( $n = 594$ ) who reported initial IT reluctance but eventually began IT. An online survey included 38 possible HCP actions: T2Ds indicated which may have occurred and their helpfulness. Also reported were delays in IT start after initial recommendation and any period of IT discontinuation.

**Results:** Exploratory factor analysis of HCP actions yielded five factors: “Explained Insulin Benefits” (EIB), “Dispelled Insulin Myths” (DIM), “Demonstrated the Injection Process” (DIP), “Collaborative Style” (CS) and “Authoritarian Style” (AS). Highest levels of helpfulness occurred for DIP, EIB and CS; lowest for AS. Participants who rated DIP as helpful were less likely to delay IT than those who rated DIP as less helpful ( $OR = 0.75$ ,  $p = 0.01$ ); participants who rated CS and EIB as helpful were less likely to interrupt IT than those who rated these as less helpful ( $OR = 0.55$ ,  $p < 0.01$ ;  $OR = 0.51$ ,  $p = 0.01$ , respectively).

**Conclusions:** Three key HCP actions to facilitate IT initiation were identified as helpful and were associated with more successful initiation and persistence. These findings may aid the development of interventions to address reluctance to initiating IT.

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## 1. Introduction

Many people with type 2 diabetes (T2D) are reluctant to initiate basal insulin. This phenomenon, referred to as “psychological insulin resistance” (PIR), has been observed in a range of T2D populations around the world, with data indicating that approximately 30% or more of insulin-naïve T2Ds report PIR.<sup>1–8</sup> Indeed, one recent study found that 29.9% of T2Ds who were encouraged to initiate basal insulin by their healthcare care provider (HCP) at first declined, with 790 days as the mean time until insulin was finally initiated.<sup>9</sup>

There is now a sizeable body of data pointing to the critical factors that underlie PIR, including injection anxiety, concerns about

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hypoglycemia, and misconceptions about insulin,<sup>1,10–12</sup> but little is known about how PIR can be overcome. Though several groups have put forward recommendations, including the need to address T2Ds' injection-related fears, their misbeliefs about insulin, and their concerns about hypoglycemia,<sup>13–16</sup> it is not known which of these strategies, if any, are critical and no intervention study has ever been conducted to reduce PIR.

Even though there may be an extended delay between when insulin is first recommended by an HCP and when an individual with PIR actually begins using insulin, it is apparent that the majority of those who are reluctant eventually acquiesce. It remains unclear, however, which specific events or circumstances led to a shift in individuals' willingness to try insulin. Identification of these events, and their underlying common themes, could be of value to HCPs when working with individuals with PIR. Also, reducing the time interval between when insulin is first recommended and when it is actually begun is crucial, since findings from several studies suggest that the absence of insulin therapy during this period is associated with prolonged periods of hyperglycemia. Furthermore, the negative effects of such long delays can remain even after insulin is eventually begun.<sup>17</sup>

To address these issues, a multinational study was undertaken to survey current insulin-using adults with T2D in Brazil, Canada, Germany, Japan, Spain, United Kingdom, and United States who indicated that they were initially unwilling to begin insulin therapy. The key objective of EMOTION (Accepting Insulin Treatment for Reluctant People with Type 2 Diabetes Mellitus – A Global Study to Identify Effective Strategies) was to evaluate the reported helpfulness of HCP statements and actions (from the T2D individual's perspective) in facilitating the transition to insulin in this reluctant population. By including T2D adults across multiple nations, we hoped to enhance the generalizability of any common themes in helpful actions that might emerge. In addition, the study aimed to determine how these reported HCP actions were associated with: 1) significant delay before insulin was initiated and 2) subsequent adherence to insulin during the first year after initiation.

## 2. Materials and methods

### 2.1. Study design and participants

EMOTION involved three phases. First, qualitative interviews with a total of 29 insulin-using T2D participants and 29 HCPs across 6 countries (Brazil, Canada, Germany, Spain, United Kingdom, and United States) were conducted to inform survey content and design. The second phase involved an online, 30-minute survey, derived from the qualitative interviews, with T2D participants from these same nations, plus Japan. This report briefly describes the methods employed during the initial interviews, but focuses primarily on the findings of the online survey. The third phase of EMOTION involved comprehensive qualitative interviews of a subset of participants, which will be published in a subsequent report.

Eligible participants were adults ( $\geq 21$  years old), diagnosed with T2D  $\geq 1$  year before initiating basal insulin, currently using a basal insulin (analog or NPH) for  $\geq 30$  days and  $< 3$  years before the survey, and who reported at screening that they were initially “not willing” or only “slightly willing” to start insulin treatment after the first HCP recommendation. Individuals were considered to be ineligible if they had type 1 diabetes or gestational diabetes, had previous experience with insulin therapy before initiation of basal insulin therapy, had initiated insulin using a pre-mix product or basal bolus therapy, or if they had initiated insulin after surgical procedures involving the pancreas. Of note, we excluded individuals who had commenced treatment with a pre-mix product or basal-bolus regimen due to concerns that they might represent a markedly different group of patients and/or that the strategies employed to overcome initial reluctance in this group might be substantially different.

Participants were recruited from four primary sources: public diabetes website announcements (US, Canada and UK), endocrine clinic databases (Canada), market research panels (all seven countries), and the Taking Control of Your Diabetes (TCOYD) online research registry, a privacy-protected online platform that includes adults with diabetes recruited primarily from TCOYD's one-day diabetes education events conducted in multiple cities across the United States.

Once identified and recruited, all survey participants were sent a link to a privacy-protected, online survey, with survey language specific to each country. Participants who were recruited via provider referral or TCOYD registry were compensated \$25 USD for their time. Participants recruited from market research panels received compensation typically offered by the panels for surveys of similar duration (the cash value across countries varied from \$10–\$14 USD). Participants recruited through diabetes website announcements accessed a public link to the survey; they were not offered compensation for completing the survey, thereby reducing the incentive for completing multiple surveys.

Because this was an online survey based, in part, on email invitations, we employed a highly conservative approach to reduce the potential impact of automated bot responses and the effects of other fraudulent survey techniques. This included putting all completed surveys through a multi-layered screening process to identify and then omit surveys that were problematic (e.g., surveys which were completed in  $< 10$  min or had straight-line responses to all survey items pertaining to HCP messages and actions).

### 2.2. Measures

To assemble a representative group of items to assess what HCPs did or said that may have helped reluctant individuals to initiate insulin, we conducted brief qualitative interviews with 4 T2D adults and 4 HCPs in the United States. Each participant was asked to describe what they felt to be particularly helpful statements or actions by HCPs that facilitated the initiation of regular insulin use. The interviews were transcribed from audio recordings and respondent comments were extracted, reviewed and used to develop a preliminary list of survey items. Additional qualitative interviews with 25 T2D adults and 25 HCPs were then conducted in Canada, Germany, Spain, United Kingdom and Brazil (for logistical reasons, Japan was not included). T2D adults and HCPs were asked to review the preliminary survey items and comment on the clarity of the instructions, items, and response options and the completeness of the preliminary survey items. These comments were then incorporated into a final set of survey items. The survey battery was then forward translated to the local language by a single, professional translation service to ensure uniformity of the translation process across countries. The translated versions were then reviewed and modified by the respective country HCPs to clarify language further.

The final battery, dubbed the PIR Action Survey (PAS), assesses the perceived occurrence and helpfulness of 38 HCP statements and actions regarding insulin initiation that may have occurred during medical visits. Each item is rated on a 5-point Likert scale: 0 (did not occur), 1 (did occur, and didn't help at all), 2 (did occur, and helped a little), 3 (did occur, and helped moderately) and 4 (did occur, and helped a lot). The broad range of items includes such HCP actions as directly addressing common concerns about insulin therapy (e.g., “My HCP helped me to see that an insulin injection wasn't as painful as I thought it might be”) and negotiating the initiation of insulin in a flexible, collaborative fashion (e.g., “My HCP encouraged me to try it for a while and see if it might help me to feel better”).

In addition to the PAS, the survey collected demographic data and clinical characteristics of the T2D sample, including self-reported current HbA1c and reported prior use of any injectable antihyperglycemic medication (i.e., a GLP-1-RA product). The survey also examined two key behavioral topics: time to actual insulin initiation following the initial recommendation as well as insulin persistence since it was first initiated. Time to initiation was assessed with a single

question, “How much time passed between when your HCP first recommended that you start taking insulin and when you actually started taking it regularly?” Eight options were offered: “I started taking it right away”, “less than 1 week”, “about 1 or 2 weeks”, “about 1 month”, “2–3 months”, “4–6 months”, “7–12 months”, and “more than 1 year”. Any response other than “I started taking it right away” was considered a delay in initiation. To assess insulin persistence, a single yes/no question was asked: “Since first starting insulin, has there been a period of 7 or more days when you did not use any kind of insulin?”

The study protocol was approved by Western Institutional Review Board (IRB), Puyallup, WA, USA as well as Nagoya University IRB, Nagoya, Japan. All participants provided informed consent.

### 2.3. Statistical analyses

Frequency of PAS items listed as occurring was evaluated by dichotomizing the response options as 0 (“did not occur”) and 1 (“did occur”), while the degree of helpfulness was evaluated using a 4-point score for those items that occurred: 1 = not helpful to 4 = helped a lot. An exploratory factor analysis using Principal Component Analysis with Promax rotation was conducted to examine whether the perceived helpfulness of the 38 PAS items could be grouped into meaningful constructs. For the purpose of the factor analysis, items that did not occur were grouped with items identified as not helpful. In addition to rotated factor loadings (requiring items to load  $\geq 0.50$  on a given scale and cross load  $< 0.40$ ), eigenvalues and scree plots were evaluated to determine the acceptable factor solution. Cronbach's alpha was computed to test the degree of internal consistency between the items included within each PAS factor.

Generalized linear models examined associations between PAS factors (participant-reported HCP actions) with select participant characteristics and the two insulin use behaviors (i.e., a delay in insulin initiation, and an interruption of 7+ days subsequent to initiation). Normal distributions were used for continuous variables (i.e., perceived helpfulness of HCP actions, grouped by PAS factors), while a logit link and binomial distribution was used for binary outcomes (i.e., insulin use behaviors). In all models, country was included as a random effect and time since insulin initiation was included as a fixed effect. In addition, models evaluating the associations between PAS factors and insulin use behaviors controlled for the following participant characteristics: age, gender, years since T2D diagnosis, body mass index (BMI) category prior to insulin initiation, and injectable antihyperglycemic medication use (i.e., GLP-1 RA products) prior to insulin initiation. Of note, we did not examine between-country differences, focusing instead on overall findings that are more broadly generalizable.

## 3. Results

The online survey was administered between December 2016 and August 2017, with 594 T2D adults meeting eligibility criteria and passing the data screening process: Brazil ( $n = 35$ ), Canada ( $n = 74$ ), Germany ( $n = 75$ ), Japan ( $n = 99$ ), Spain ( $n = 66$ ), United Kingdom ( $n = 125$ ), and United States ( $n = 120$ ). As seen in Table 1, mean age was 53.3 ( $\pm 11.3$  SD) years, mean time since T2D diagnosis was 8.2 ( $\pm 7.4$  SD) years, and 57% were male. Mean self-reported HbA1c at time of insulin initiation was 9.8% ( $\pm 2.8$  SD) or 83.3 mmol ( $\pm 30.1$ ), while mean self-reported HbA1c at time of survey completion was 7.9% ( $\pm 2.2$  SD) or 62.8 mmol ( $\pm 23.5$ ). Of note, 22% reported prior use of a GLP-1 RA product.

About half of the T2D adults (48.5%) reported some delay in starting insulin after the initial HCP recommendation, though relatively few (6.4%) reported long delays ( $> 6$  months). Also, 11% of respondents indicated at least one episode of stopping insulin for  $\geq 7$  days.

**Table 1**

Participant characteristics.

| Participant characteristic                                            | Total N = 594 |
|-----------------------------------------------------------------------|---------------|
| Age, mean (SD)                                                        | 53.3 (11.3)   |
| Male gender, %                                                        | 56.7%         |
| Years with T2D, mean (SD)                                             | 8.2 (7.4)     |
| BMI ( $\text{kg}/\text{m}^2$ ) prior to insulin initiation, mean (SD) | 30.3 (8.1)    |
| <24.9                                                                 | 26.3%         |
| 25.0–29.9                                                             | 30.5%         |
| $\geq 30.0$                                                           | 41.9%         |
| Most recent HbA1c value; mean (SD)                                    |               |
| (%)                                                                   | 7.9 (2.2)     |
| (mmol)                                                                | 62.8 (23.5)   |
| HbA1c value prior to insulin initiation, mean (SD)                    |               |
| (%)                                                                   | 9.8 (2.8)     |
| (mmol)                                                                | 83.3 (30.1)   |
| Prior use of injectable antihyperglycemic medications, %              | 21.5%         |
| Year of insulin initiation, %                                         |               |
| 2015                                                                  | 38.4%         |
| 2016                                                                  | 46.0%         |
| 2017                                                                  | 13.6%         |
| Time between HCP recommended insulin and insulin initiation, %        |               |
| Started taking it right away                                          | 51.5%         |
| Less than one week                                                    | 5.9%          |
| 1–2 weeks                                                             | 13.1%         |
| 1 month                                                               | 12.5%         |
| 2–3 months                                                            | 7.4%          |
| 4–6 months                                                            | 3.2%          |
| $> 6$ months                                                          | 6.4%          |
| One or more periods of discontinuing insulin for $\geq 7$ days, %     | 11.3%         |

Note:  $n = 414$  for current HbA1c and  $n = 346$  for HbA1c immediately prior to insulin initiation due to participants' inability to remember their value or reported that an HbA1c test was not performed at those points in time.

### 3.1. PAS results

An exploratory factor analysis of the 38 PAS items yielded five meaningful factors (Table 2). The final factor analysis included 25 items with factor loadings  $> 0.5$  (all eigenvalues  $> 1.0$ ; 59.3% variance explained; see Appendix 1 for individual items details). Two of the five factors addressed the HCP's provision of critical information about insulin: “Explained Insulin Benefits” (4 items;  $\alpha = 0.79$ ) highlighted the gain likely to accrue from insulin use (e.g., “My HCP told me that starting insulin could help me to live a longer and healthier life”), while “Dispelled Insulin Myths” (7 items;  $\alpha = 0.71$ ) addressed the individual's likely misgivings or misinformation (e.g., “My HCP helped me to realize that insulin wasn't going to cost me as much money as I feared it would”). A third factor, labeled “Demonstrated the Injection Process” (6 items;  $\alpha = 0.84$ ), was directed towards reducing fears and discomfort about the injection procedure (e.g., “My HCP walked me through the whole process of exactly how to take insulin”). Finally, the remaining two factors represented broader styles of HCP-patient interaction: “Collaborative Style” (5 items;  $\alpha = 0.80$ ) reflected efforts by the HCP to include the person with T2D in the decision making process (“My HCP took time to answer all my questions and address my concerns about insulin”), while “Authoritarian Style” (3 items;  $\alpha = 0.43$ ) characterized a more demanding, paternalistic approach (e.g., “My HCP said that he/she could not continue to treat me if I refused to start insulin”).

Mean levels of helpfulness were highest for Demonstrated the Injection Process, Explained Insulin Benefits and Collaborative Style, while relatively lower level of helpfulness was observed for Dispelled Insulin Myths and the lowest levels for Authoritarian Style (Table 3). While most study participants ( $\sim 90\%$  or more) reported that  $\geq 1$  item from each of the first four factors had occurred (demonstrating the breadth of HCP actions taken to encourage insulin initiation), only 54% of participants reported that  $\geq 1$  of the Authoritarian Style items occurred.

**Table 2**

Exploratory factor analysis: Factor loadings of PAS items (participant-reported HCP actions).

| Description                                                                                                                                   | Demonstrated the Injection Process | Dispelled Insulin Myths | Explained Insulin Benefits | Collaborative Style | Authoritarian Style |
|-----------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|-------------------------|----------------------------|---------------------|---------------------|
| My HCP showed me how small the actual needle was                                                                                              | <b>0.80</b>                        | −0.01                   | −0.12                      | 0.11                | 0.12                |
| My HCP helped me to see that an insulin injection wasn't as painful as I thought it might be                                                  | <b>0.79</b>                        | 0.07                    | −0.12                      | 0.07                | 0.13                |
| My HCP walked me through the whole process of exactly how to take insulin                                                                     | <b>0.66</b>                        | −0.04                   | 0.28                       | −0.01               | −0.14               |
| My HCP showed me an insulin pen                                                                                                               | <b>0.68</b>                        | −0.12                   | 0.13                       | 0.10                | −0.10               |
| My HCP had me try an injection myself while I was there in the office                                                                         | <b>0.72</b>                        | 0.20                    | −0.09                      | −0.16               | 0.04                |
| My HCP helped me to see how simple it was to inject insulin                                                                                   | <b>0.78</b>                        | 0.02                    | 0.19                       | −0.10               | −0.03               |
| My HCP explained that I might not have to take insulin forever                                                                                | 0.01                               | <b>0.71</b>             | 0.11                       | −0.04               | −0.13               |
| My HCP helped me to realize that insulin wasn't going to cost me as much money as I feared it would                                           | 0.07                               | <b>0.80</b>             | 0.03                       | −0.11               | −0.09               |
| My HCP helped me to recognize that insulin was more natural than the pills I was taking                                                       | −0.05                              | <b>0.57</b>             | 0.34                       | 0.00                | −0.02               |
| My HCP told me that by going on insulin, I might soon be able to discontinue other diabetes medications                                       | −0.07                              | <b>0.56</b>             | 0.38                       | −0.07               | 0.05                |
| My HCP reassured me that he/she would help me to avoid or minimize any weight gain because of taking insulin                                  | 0.07                               | <b>0.57</b>             | 0.05                       | 0.19                | 0.01                |
| My HCP and I talked about the real costs of insulin and insulin supplies; and together we figured out a way to make it more affordable for me | −0.02                              | <b>0.69</b>             | −0.12                      | 0.15                | 0.05                |
| My HCP helped me to get over my fears that others would treat me differently because I was taking insulin                                     | 0.06                               | <b>0.60</b>             | −0.17                      | 0.17                | 0.10                |
| My HCP told me that my blood glucose numbers would improve after I started insulin                                                            | 0.06                               | −0.01                   | <b>0.69</b>                | 0.07                | −0.01               |
| My HCP explained that insulin was a natural substance that my body needed                                                                     | 0.05                               | 0.06                    | <b>0.67</b>                | 0.05                | 0.04                |
| My HCP told me that starting insulin would help me to feel better                                                                             | 0.01                               | −0.03                   | <b>0.73</b>                | 0.08                | 0.15                |
| My HCP told me that starting insulin could help me to live a longer and healthier life                                                        | −0.03                              | 0.12                    | <b>0.74</b>                | 0.05                | 0.09                |
| My HCP took the time to ask me about the reasons why I did not want to take insulin                                                           | −0.04                              | 0.15                    | −0.11                      | <b>0.77</b>         | 0.05                |
| My HCP encouraged me to try it for a while and see if it might help me to feel better                                                         | 0.03                               | 0.17                    | 0.07                       | <b>0.56</b>         | 0.13                |
| My HCP explained to me that the final decision to try insulin was mine, not his/hers                                                          | −0.07                              | 0.01                    | 0.09                       | <b>0.71</b>         | 0.05                |
| My HCP took time to answer all my questions and address my concerns about insulin                                                             | 0.01                               | 0.00                    | 0.24                       | <b>0.67</b>         | −0.10               |
| My HCP encouraged me to contact his/her office immediately if I ran into any problems or had questions after starting insulin                 | 0.13                               | −0.12                   | 0.19                       | <b>0.65</b>         | −0.19               |
| My HCP warned me that he/she could not be responsible for what might happen if I did not start insulin soon                                   | −0.03                              | 0.18                    | 0.02                       | −0.03               | <b>0.71</b>         |
| My HCP said that he/she could not continue to treat me if I refused to start insulin                                                          | 0.07                               | 0.01                    | 0.02                       | −0.07               | <b>0.81</b>         |
| Repeatedly over many visits, my HCP kept trying to convince me to get started on insulin                                                      | −0.01                              | −0.19                   | 0.16                       | 0.05                | <b>0.83</b>         |

Note: Principal component extraction method with Promax rotation. Factor loadings represent correlation between each item and the rotated factor pattern.

Bold items are those that load mostly highly on the individual factor.

### 3.2. Associations of PAS factors with participant characteristics and insulin use behaviors

The perceived helpfulness of HCP actions, as reflected by the five PAS factors, was differentially associated with T2D participant demographics and insulin use. Participants without previous injectable experience (i.e., GLP-1-RA) rated four of the five factors (Demonstrated the Injection Process, Explained Insulin Benefits, Collaborative Style and

**Table 3**

Occurrence and helpfulness of PAS factors (participant-reported HCP actions).

|                                    | Percent of patients with ≥1 item occurring (% of total n = 594) | Helpfulness Mean (SD) |
|------------------------------------|-----------------------------------------------------------------|-----------------------|
| Demonstrated the Injection Process | 94%                                                             | 3.07 (0.74)           |
| Explained Insulin Benefits         | 97%                                                             | 2.97 (0.74)           |
| Collaborative Style                | 95%                                                             | 2.92 (0.78)           |
| Dispelled Insulin Myths            | 89%                                                             | 2.77 (0.72)           |
| Authoritarian Style                | 54%                                                             | 2.63 (0.85)           |

1 = not helpful; 2 = helped a little; 3 = helped moderately; 4 = helped a lot.

Authoritarian Style) as more helpful than participants with previous experience (all model coefficients  $\geq 0.19$ ,  $p < 0.05$ ). Differences due to weight were apparent as well. For example, heavier participants ( $\text{BMI} \geq 30 \text{ kg/m}^2$ ) rated Demonstrated the Injection Process, Explained Insulin Benefits and Collaborative Style as more helpful than thinner participants ( $\text{BMI} < 25 \text{ kg/m}^2$ ) (all model coefficients  $\geq 0.13$ ,  $p < 0.05$ ). In addition, Authoritarian Style was rated as more helpful by men than by women (coefficient =  $-0.27$ ,  $p < 0.05$ ), and more helpful by participants with fewer years since diagnosis (coefficient =  $-0.02$ ,  $p < 0.05$ ) (Table 4).

Regarding insulin initiation and disruptions (Table 5), participants who rated Demonstrated the Injection Process as helpful were less likely to delay insulin initiation than patients who rated this style to be less helpful (OR = 0.75,  $p = 0.01$ ), while participants who rated Collaborative Style and Explained Insulin Benefits as helpful were significantly more likely to report no episodes of insulin discontinuation than those who rated these styles as less helpful (OR = 0.55,  $p < 0.01$ ; OR = 0.51,  $p = 0.01$ , respectively). Of note, ratings of helpfulness of Authoritarian Style and Dispelled Insulin Myths were not significantly associated with insulin initiation delay or periods of discontinuation.



**Table 4**

Association between participant characteristics and helpfulness of HCP strategies.

| Participant characteristic                                                                      | Demonstrated the Injection Process | Explained Insulin Benefits | Collaborative Style | Dispelled Insulin Myths | Authoritarian Style |
|-------------------------------------------------------------------------------------------------|------------------------------------|----------------------------|---------------------|-------------------------|---------------------|
| Age                                                                                             | 0.01*                              | 0.00                       | 0.00                | 0.00                    | 0.00                |
| Female (vs. male)                                                                               | 0.06                               | 0.03                       | 0.06                | −0.04                   | −0.27*              |
| Years from T2D diagnosis to insulin initiation                                                  | −0.01                              | −0.01                      | −0.01*              | 0.00                    | −0.02*              |
| BMI at the time of insulin initiation: 25.0–29.9 kg/m <sup>2</sup> (vs. <25 kg/m <sup>2</sup> ) | 0.13*                              | 0.16*                      | 0.18*               | −0.02                   | 0.08                |
| BMI at the time of insulin initiation: ≥30 kg/m <sup>2</sup> (vs. <25 kg/m <sup>2</sup> )       | 0.17*                              | 0.23*                      | 0.23*               | 0.10                    | 0.09                |
| No prior anti-diabetic injectable use (vs. injectable use)                                      | 0.21*                              | 0.20*                      | 0.19*               | 0.12                    | 0.22*               |

Estimates from generalized linear models with identity link and normal distribution.

\*  $p < 0.05$ .

Thus, perceived helpfulness of three of the five PAS factors (Collaborative Style, Demonstrated the Injection Process and Explained Insulin Benefits) were each significantly linked with different aspects of participants' use of insulin over time.

For participants where one or more items of an HCP Authoritarian Style occurred, both a delay in insulin initiation (OR = 3.06,  $p < 0.01$ ) and at least one period of insulin discontinuation ( $\geq 7$  days; OR = 2.58,  $p < 0.01$ ) were more likely to have occurred than for participants who reported that no Authoritarian Style actions occurred.

## 4. Discussion

### 4.1. Conclusions

To the best of our knowledge, this is the first study to identify potentially helpful strategies for addressing psychological insulin resistance (PIR) in adults with T2D. As such, these findings are a critical step towards designing evidence-based clinical recommendations for HCPs. Five broad sets of HCP actions were identified that were reported by participants to be useful in addressing PIR. Of the five, two focused on providing critical information about insulin (Explained Insulin Benefits and Dispelled Insulin Myths), one centered on reducing concerns about injections and the injection process (Demonstrated the Injection Process) and two highlighted approaches to HCP-patient communication (Collaborative Style and Authoritarian Style). It is noteworthy that most participants reported that their HCPs used a variety of these types of actions, though all were not equally helpful.

Demonstrated the Injection Process, Explained Insulin Benefits and Collaborative Style were rated as the most helpful types of actions, and elements of each were reported to have occurred by >90% of participants. Furthermore, it was the perceived helpfulness of these three types of actions that were significantly associated with the key insulin-related behavioral outcomes.

The sole set of actions associated with whether or not insulin initiation was delayed was Demonstrated the Injection Process. Those who rated this approach as more helpful had a significantly lower rate of insulin delay, suggesting that this HCP strategy may be a critically

important intervention. This is consistent with common clinical recommendations for addressing PIR<sup>13</sup> and with reported findings from TRIAD (The Translating Research Into Action for Diabetes Insulin Starts Project), where one of the most striking differences between those T2Ds who did vs. those who did not start over the ensuing 60 days (i.e., did or did not have insulin dispensed after receiving an initial prescription) was whether or not they had received insulin self-management training (be it from a physician, nurse, or group class) at baseline.<sup>10</sup> When some form of such training occurs—when individuals are given the opportunity to see the needle, take a practice injection, receive a demonstration of the injection process and have their questions and concerns addressed—and it is perceived as truly helpful, it seems likely that they will feel more comfortable and confident in getting started, thus resulting in a shorter delay in insulin initiation.

Subsequent to insulin initiation, participants who rated Collaborative Style and Explained Insulin Benefits as helpful were significantly less likely to report a period of insulin discontinuation ( $\geq 7$  days) than those who rated these HCP strategies as less helpful. Problematic insulin persistence is recognized as a common and serious issue,<sup>13</sup> though it is noteworthy that only 11% in the current sample reported one or more periods of discontinuation. Still, previous studies have similarly demonstrated that medication adherence over time is significantly better among individuals with T2D who report elements of a more trusting, collaborative relationship with their HCP than those who report a less trusting relationship.<sup>18–20</sup> This suggests that people with T2D are better able and willing to take their prescribed medications more consistently when they feel and appreciate that their HCP has made treatment decisions with them, not for them. Of interest, Authoritarian Style—which can be viewed in some ways as the opposite of the collaborative approach—was rated as the least helpful of the five types of actions, and the rated helpfulness of this tactic was unrelated to insulin continuation. However, it is noteworthy that the reported occurrence of the Authoritarian style ( $\geq 1$  item occurring), regardless of the level of perceived helpfulness, was significantly associated with negative outcomes—a delay in insulin initiation as well  $\geq 1$  episode of insulin discontinuation.

**Table 5**

Multivariate associations between perceived helpfulness of PAS Dimensions (participant-reported HCP actions) and insulin use behaviors.

| Perceived helpfulness of HCP actions | Delayed start of insulin |         | Discontinued insulin use (7+ days) |         |
|--------------------------------------|--------------------------|---------|------------------------------------|---------|
|                                      | OR [95% CI]              | p-Value | OR [95% CI]                        | p-Value |
| Demonstrated the Injection Process   | 0.75 [0.61, 0.94]        | 0.01    | 0.67 [0.38, 1.18]                  | 0.17    |
| Explained Insulin Benefits           | 0.77 [0.55, 1.07]        | 0.12    | 0.51 [0.30, 0.86]                  | 0.01    |
| Collaborative Style                  | 0.88 [0.63, 1.22]        | 0.44    | 0.55 [0.36, 0.84]                  | 0.01    |
| Dispelled Insulin Myths              | 0.92 [0.57, 1.48]        | 0.72    | 0.67 [0.44, 1.03]                  | 0.07    |
| Authoritarian Style                  | 0.92 [0.72, 1.16]        | 0.47    | 0.95 [0.58, 1.57]                  | 0.85    |

OR = odds ratio; CI = confidence interval.

Note: Odds ratios estimated relative to 'I started taking insulin right away' and not discontinuing insulin use for 7+ days. Estimates from generalized linear models with a logit link and binomial distribution. Models controlled for age, gender, years since T2D diagnosis, BMI category prior to insulin initiation, and injectable antidiabetic use prior to insulin initiation. Additionally, country was included as a random effect and time since insulin initiation was included as a fixed effect in all models.

Surprisingly, though a plethora of studies have documented the impact of negative beliefs about insulin on the willingness of T2D adults to initiate insulin therapy,<sup>1,10–12</sup> efforts to address those beliefs (i.e., Dispel Insulin Myths) was rated as less helpful than Injection Process, Explained Insulin Benefits and Collaborative Style, and was not associated with either of the two behavioral outcomes. A recent review of the Necessity–Concerns Framework across 94 studies of medication adherence concluded that the perceived necessity of treatment was more strongly associated with adherence than perceived concerns (i.e., negative beliefs) about treatment.<sup>21</sup> The current findings support this conclusion — though addressing common negative beliefs about insulin may often be important, it may be even more valuable to help reluctant T2D individuals learn and recognize the potential personal value of initiating insulin treatment.

In summary, these findings suggest that PIR may be more effectively resolved when HCPs are able to take the time to address injection concerns by showing and/or demonstrating the actual injection process, explaining the benefits of insulin, and adopting a collaborative, communication style. Elements of each of these three types of actions were reported to occur in approximately 90% or more of participants, were broadly perceived as helpful by the majority of participants, and were differentially associated with key behavioral outcomes. In contrast, an authoritarian communication style was rated as the least helpful approach, was reported to occur much less frequently than the other four types of actions, and—when it did occur—was associated with poorer outcomes.

#### 4.2. Limitations and strengths

One of the key strengths of this study is that it included adults with T2D from a diverse group of nations, thus highlighting the commonality of the identified types of PIR actions. Still, there were between-country differences in provided incentives (due to differing requirements of the various recruitment sources) as well as in the final number of participants. While country was included as control variable in all analyses, potentially offsetting some of these biases, we acknowledge that there may be important differences between countries.

Furthermore, the majority of survey respondents were recruited from online panels of individuals who volunteer to participate in studies and may, therefore, be more involved with their own T2D care than the typical individual with T2D. Indeed, those T2D adults who are most reluctant to initiate insulin may represent a more disengaged cohort who, assuming they continued to be disengaged after finally starting insulin, may have been less willing to participate in the study. Thus, the perceptions regarding helpful PIR actions as observed in the current study sample may not be reflective of that subset of the T2D population who are more profoundly reluctant. We hypothesize that in those patients who are more demonstrably reluctant to begin insulin (and especially among those who delayed initiation for months or even years), the need to address and dispel insulin myths may loom even larger and may prove to be the most helpful and important intervention strategy.

Also, the retrospective nature of the study should engender some caution. First, self-reported data for events that occurred several years previously may be subject to recall bias, although insulin initiation is likely to have been an important milestone in one's diabetes treatment. Furthermore, the observed associations between helpful actions and the two insulin use outcomes may not necessarily indicate a causal relationship.

#### 4.3. Summary

In this multinational retrospective survey of T2D adults who were initially reluctant to begin insulin therapy, we identified five broad types of actions reportedly used by HCPs to address PIR. Of those five, efforts to address injection concerns by demonstrating the actual

injection process, explaining the benefits of insulin and adopting a collaborative, communication style were rated as the most helpful. The perceived helpfulness of these actions was, in turn, linked with earlier insulin initiation and greater insulin persistence over time. In contrast, use of an authoritarian communication style was reported to be the least helpful and its occurrence was associated with negative behavioral outcomes. In total, these findings highlight the potential value of specific HCP actions to address PIR and points the way towards the development of testable, structured interventions that may reduce the long delays towards starting insulin that remain a frequent occurrence in clinical care.

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#### Author contributions

WHP, LF and DH were involved in the design of the survey, and DH, JL and UD provided the statistical analysis. All authors contributed to the interpretation of the data, and gave input on, reviewed, and approved the final manuscript.

#### Appendix 1. Healthcare provider actions that helped participants make the decision to give insulin a try

| Description                                                                                                                                                          | Patients with occurrence |           | Helpfulness among patients with occurrence |                              |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|-----------|--------------------------------------------|------------------------------|
|                                                                                                                                                                      | N                        | (N = 594) | Mean (1–4 scale of helpfulness)            | % helped moderately or a lot |
| HCP walked patient through the whole process of exactly how to take insulin                                                                                          | 519                      | (87.4%)   | 3.26                                       | (80.5%)                      |
| HCP encouraged the patient to contact his/her office immediately if the patient ran into any problems or had questions after starting insulin                        | 503                      | (84.7%)   | 3.16                                       | (77.3%)                      |
| HCP showed patient an insulin pen                                                                                                                                    | 500                      | (84.2%)   | 3.16                                       | (75.8%)                      |
| HCP helped patient to see how simple it was to inject insulin                                                                                                        | 508                      | (85.5%)   | 3.16                                       | (78.5%)                      |
| HCP told patient that blood glucose numbers would improve after patient started insulin                                                                              | 556                      | (93.6%)   | 3.10                                       | (75.5%)                      |
| HCP had patient try an injection himself/herself while patient was there in the office                                                                               | 352                      | (59.3%)   | 3.10                                       | (75.9%)                      |
| HCP showed patient how small the actual needle was                                                                                                                   | 451                      | (75.9%)   | 3.06                                       | (73.8%)                      |
| HCP reviewed patient's blood sugar numbers with the patient, showing the patient that his/her diabetes was not under control and that action was needed <sup>a</sup> | 523                      | (88.0%)   | 3.02                                       | (72.1%)                      |
| HCP helped patient to see that an insulin injection wasn't as painful as patient thought it might be                                                                 | 453                      | (76.3%)   | 3.00                                       | (69.5%)                      |
| HCP told patient that starting insulin could help the patient to live a longer and healthier life                                                                    | 464                      | (78.1%)   | 3.00                                       | (71.8%)                      |
| HCP told patient that starting insulin would help the patient to feel better                                                                                         | 476                      | (80.1%)   | 3.00                                       | (69.7%)                      |
| HCP gave an injection while patient was there in the office <sup>a</sup>                                                                                             | 267                      | (44.9%)   | 2.98                                       | (70.4%)                      |

## Appendix 1 (continued)

| Description                                                                                                                                                     | Patients with occurrence |           | Helpfulness among patients with occurrence |                              |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|-----------|--------------------------------------------|------------------------------|
|                                                                                                                                                                 | N                        | (N = 594) | Mean (1–4 scale of helpfulness)            | % helped moderately or a lot |
| HCP explained to the patient that the final decision to try insulin was patient's, not his/hers                                                                 | 397                      | (66.8%)   | 2.97                                       | (67.5%)                      |
| HCP took time to answer all the patient's questions and address his/her concerns about insulin                                                                  | 501                      | (84.3%)   | 2.96                                       | (68.5%)                      |
| HCP explained that insulin was a natural substance that the patient's body needed                                                                               | 498                      | (83.8%)   | 2.95                                       | (70.3%)                      |
| HCP helped patient to understand how insulin works in patient's body to lower blood sugars and improve patient's health <sup>a</sup>                            | 495                      | (83.3%)   | 2.93                                       | (70.3%)                      |
| HCP explained that the patient might not have to take insulin forever                                                                                           | 390                      | (65.7%)   | 2.92                                       | (68.5%)                      |
| HCP warned patient that he/she was likely to develop complications if the patient didn't get started soon with insulin to control his/her diabetes <sup>a</sup> | 439                      | (73.9%)   | 2.91                                       | (66.3%)                      |
| HCP helped patient to understand that taking insulin didn't have to be as much of a burden as the patient had feared <sup>a</sup>                               | 505                      | (85.0%)   | 2.91                                       | (69.3%)                      |
| HCP encouraged patient to try it for a while and see if it might help the patient feel better                                                                   | 417                      | (70.2%)   | 2.89                                       | (65.9%)                      |
| HCP reassured patient that taking insulin didn't mean that diabetes was now a more serious condition <sup>a</sup>                                               | 455                      | (76.6%)   | 2.89                                       | (65.1%)                      |
| HCP reassured patient that taking insulin wasn't going to cause complications, like blindness, kidney disease or a heart attack <sup>a</sup>                    | 418                      | (70.4%)   | 2.88                                       | (64.8%)                      |
| HCP reassured patient that the risk of having a serious problem with hypoglycemia while taking insulin was low <sup>a</sup>                                     | 469                      | (79.0%)   | 2.87                                       | (68.0%)                      |
| HCP told patient that by going on insulin, he/she might soon be able to discontinue other diabetes medications                                                  | 373                      | (62.8%)   | 2.87                                       | (66.5%)                      |
| HCP helped patient get over his/her fears that others would treat the patient differently because he/she were taking insulin                                    | 301                      | (50.7%)   | 2.86                                       | (69.1%)                      |
| HCP gave patient leaflets or other reading material about insulin <sup>a</sup>                                                                                  | 459                      | (77.3%)   | 2.86                                       | (64.1%)                      |
| HCP took the time to ask the patient about the reasons why the patient did not want to take insulin                                                             | 406                      | (68.4%)   | 2.85                                       | (64.8%)                      |
| HCP helped patient to recognize that insulin was more natural than the pills the patient was taking                                                             | 386                      | (65.0%)   | 2.82                                       | (63.5%)                      |
| HCP told patient about all of the positives and negatives of insulin, and explained how the positives outweighed the negatives <sup>a</sup>                     | 469                      | (79.0%)   | 2.79                                       | (62.3%)                      |
| HCP and patient talked about the real costs of insulin and insulin supplies and together figured out a way to make it more affordable                           | 318                      | (53.5%)   | 2.78                                       | (64.5%)                      |
| HCP said that the he/she could not continue to treat patient if the patient refused to start insulin                                                            | 162                      | (27.3%)   | 2.78                                       | (63.6%)                      |
| HCP warned patient that he/she could not be responsible for what might happen if the patient did not start insulin soon                                         | 231                      | (38.9%)   | 2.77                                       | (60.2%)                      |
| HCP reassured the patient that he/she would help the patient avoid or minimize any weight                                                                       | 352                      | (59.3%)   | 2.76                                       | (58.8%)                      |

## Appendix 1 (continued)

| Description                                                                                                                                             | Patients with occurrence |           | Helpfulness among patients with occurrence |                              |
|---------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|-----------|--------------------------------------------|------------------------------|
|                                                                                                                                                         | N                        | (N = 594) | Mean (1–4 scale of helpfulness)            | % helped moderately or a lot |
| gain because of taking insulin                                                                                                                          | 172                      | (29.0%)   | 2.75                                       | (62.2%)                      |
| HCP helped patient meet other people who had already been taking insulin for a while <sup>a</sup>                                                       | 366                      | (61.6%)   | 2.71                                       | (60.4%)                      |
| HCP helped patient to realize that insulin wasn't going to cost patient as much money as the patient feared it would                                    | 381                      | (64.1%)   | 2.71                                       | (58.8%)                      |
| HCP told patient that he/she just needed to trust that the HCP knew best and that getting started on insulin was the patient's best option <sup>a</sup> | 251                      | (42.3%)   | 2.61                                       | (53.4%)                      |
| HCP referred patient to a class to help learn more about insulin <sup>a</sup>                                                                           | 258                      | (43.4%)   | 2.58                                       | (52.7%)                      |
| Repeatedly over many visits, HCP kept trying to convince the patient to get started on insulin                                                          |                          |           |                                            |                              |

Note: Level of helpfulness was scored on a scale of 1 (it didn't help at all) to 4 (it helped a lot). Items that did not occur for patients were considered as missing.

<sup>a</sup> Items that did not load on any of the five PAS factors.

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