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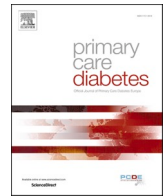Shingaki, Tomotaka

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Key factors for overcoming psychological insulin resistance: A qualitative study in Japanese people with type 2 diabetes

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ABSTRACT

Aims: We report the key factors that motivate reluctant Japanese people with type 2 diabetes (T2D) to initiate insulin treatment.
Methods: Participants were asked questions pertaining to 2 primary areas of exploration in a concurrent mixed methods approach: (a) understanding people's thoughts and perceptions before and after insulin initiation and any related factors; and (b) exploring the reasons behind people's responses. Data were analyzed using Steps for Coding and Theorization.
Results: Participant responses broadly related to 3 themes which influence insulin initiation; 1. Advice from a health care provider (HCP) that insulin is an appropriate treatment; 2. Demonstration by HCPs on how to use the insulin pen/needle and the injection process; and 3. Resignation/surrender/acceptance of insulin, where participants felt there was no other choice but to commence insulin.
Conclusions: Based on the 3 identified themes, it is important for HCPs to explain the benefits of insulin and demonstrate and explain the injection procedure to reluctant Japanese people with T2D. We also identified resignation/surrender/acceptance of insulin as a reason for treatment commencement. This study provides important information to assist HCPs in helping reluctant Japanese people with T2D to initiate basal insulin therapy.

1. Introduction

The prevalence of type 2 diabetes (T2D) in Japan is a major health concern and is predicted to further increase over coming decades due to an aging population [1]. In addition to lifestyle changes such as diet, exercise, and weight management, treatment for T2D comprises oral antidiabetic and/or injectable medications [2–5]. Due to its progressive nature, most people with T2D (PWT2D) will eventually require insulin to maintain glycemic control [6]. Although insulin treatment is associated with higher rates of adequate glycemic control [3,5], initiation of insulin therapy is often delayed. This delay, known as psychological insulin resistance (PIR), has been examined in several studies [7–11]. PIR is documented to be due to physician-related factors such as clinical inertia [12,13] and lack of knowledge concerning insulin [9], and

patient-related factors including fear of injections [11], fear of weight gain and hypoglycemia, misconceptions regarding the benefits of insulin, and feelings of personal failure [10,14,15].

Limited research exists regarding effective strategies that help PWT2D begin insulin treatment. Several groups [14,16–18] have put forward recommendations to address PIR, including the need to focus on injection-related fears and misconceptions concerning insulin, as well as interventions targeting health care providers (HCPs) [19]; however, interventional studies are currently lacking. Furthermore, there are limited studies describing PIR among Japanese PWT2D [20–22].

To further understand factors associated with reluctance to commence insulin, a multinational, non-interventional study was conducted with insulin-using PWT2D who were initially reluctant to commence insulin treatment [23]. The EMOTION (AccEpting Insulin

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TreatMent for Reluctant PeOple with Type 2 DIabetes Mellitus – A GlObal Study to IdeNtify Effective Strategies) study [23] was conducted in 3 phases: (1) qualitative interviews with PWT2D and HCPs (2) quantitative surveys, and (3) follow-up interviews. EMOTION identified certain HCP actions and life events that were helpful in initiating insulin among the total multinational population. These included efforts to address injection concerns by demonstrating the insulin injection process, explaining the benefits of insulin, and adopting a collaborative communication style [23]. The perceived helpfulness of these actions was linked with earlier insulin initiation and greater insulin persistence over time [23].

A subanalysis of Japanese participants from phase 2 of EMOTION has been previously described [24], outlining the frequency and level of helpfulness of HCP actions and life events that impact the decision to initiate insulin amongst Japanese PWT2D. Overall, practical demonstrations by HCPs on how to use insulin were rated by Japanese participants as most helpful. Examples of such practical demonstrations, reported as helping moderately or a lot, were 'HCP walked patient through the process of exactly how to take insulin', 'HCP showed an insulin pen', and 'HCP helped patient to see how simple it was to inject insulin' [23].

The present study builds on the current literature by describing the results of qualitative research on a subgroup of Japanese participants from phase 3 of EMOTION. We aim to identify key factors that motivated reluctant Japanese PWT2D to initiate insulin treatment in order to further elucidate potential clinical interventions for helping Japanese PWT2D overcome PIR, and to clarify actions/events from the phase 2 quantitative studies.

2. Methods

2.1. Study design and population

Data included in the study were derived from the EMOTION study. The study design and procedures have been described elsewhere [23]. Briefly, phase 1 of EMOTION involved qualitative interviews with a total of 29 insulin-using adults with T2D and 29 HCPs across 6 countries (Brazil, Canada, Germany, Spain, United Kingdom, and United States of America) to inform survey content and design. Phase 2 involved a 30-minute survey, derived from the qualitative interviews, with PWT2D from these same nations plus Japan. At the end of phase 2, participants were asked if they could be contacted for a follow-up qualitative phone interview (phase 3). This 45- to 60-minute interview involved an in-depth discussion about factors influencing the participants' decision to initiate insulin, and the effects of these factors on other outcomes such as satisfaction, diabetes distress, care management, and quality of life. This report focuses on phase 3 of EMOTION in Japanese PWT2D.

The EMOTION study was performed in accordance with principles of the Declaration of Helsinki. Regulatory approval was provided by the Western Institutional Review Board (Puyallup, WA, USA), Pennsylvania State University College of Medicine IRB (Hershey, PA, USA) as well as Nagoya University IRB (Nagoya, Japan). All participants provided informed consent.

PWT2D were selected from Survey Sampling International (SSI) and their local partners' market research panels or online communities. Eligible participants were adults ($\geq$ 21 years old), diagnosed with T2D $\geq$ 1 year before initiating basal insulin, used basal insulin for $\geq$ 30 days and $<$ 3 years before the survey, and who reported at screening that they were initially "not willing" to start insulin treatment after the first HCP recommendation. Individuals were ineligible if they had type 1 or gestational diabetes, had 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.

2.2. Interviews

The semi-structured participant interview guide was developed in accordance with findings from the first 2 phases of the EMOTION study, the current literature, and the experience of the experts and advisors leading the study. The open-ended questions were structured for a 45- to 60-min interview and designed to gain a deeper perspective relevant to the research questions (see Supplementary materials). Participants were asked questions pertaining to the following areas of exploration: a) participants' thoughts and perceptions about insulin before and after initiation and any related factors (e.g., through observation of other family members using insulin); b) reasons behind participants' responses to the individual PIR Action Survey questions (e.g., responses that were answered on a particular end of the spectrum such as, (1) not helpful or (2) little helpful and (4) moderately helpful or (5) helped a lot); c) other actions their HCP may have taken that convinced them to commence insulin treatment; and d) what advice, if any, they would give to other PWT2D facing a similar PIR. If all questions in a section were answered the same, the section was further analyzed by asking which action was the most or least helpful out of those checked. This approach aimed to give an in-depth summary of the survey questions and reasons behind responses.

Training sessions for interviewers were conducted by HS and KO. Data analysis was conducted by KO and NT. The informed consent documentation and the interview guide were translated into Japanese by SSI. Interviews were conducted and analyzed in Japanese, with the results translated into English. All translated materials were reviewed by advisors for appropriateness.

2.3. Data analysis

Demographics and clinical characteristics of participants were collected, including age, gender, educational level, HbA1c, and body mass index (self-reported).

Interviews were recorded, transcribed, and analyzed by Steps for Coding and Theorization (SCAT), a qualitative data analysis method [25–27]. SCAT is a 4-step coding process used to identify themes and constructs, and to develop a storyline by weaving these themes and constructs together. This method is applicable for analyzes of small-scale data, including open-ended questionnaire responses. SCAT is based on theory development from data that are collected and analyzed systematically and iteratively. In detail, data integration and analysis from each interview was performed to generate coding. Japanese interview data and the primary EMOTION analyses were reviewed and analyzes of data in line with the purpose of the study were performed followed by the development of a theoretical description. Data saturation was reached when no new findings were emerging [28,29]. Following this, Japanese interview data were checked and re-analyzed based on the theoretical description. Meanwhile, the theoretical description was revised by not only focusing on the sections that could be explained using the theory already generated, but also identifying those sections that did not correspond with the theoretical description. Thus, the theoretical description is modified to meet the research purpose.

The significance of the method is suggested in its explicit process of analysis, its smooth guidance towards the steps of analysis, the enhancement of the reflective quality of critique and falsifiability, and the integration of theoretical coding and qualitative data analysis [25]. Interviews were transcribed and coded as follows:

1. Noteworthy words and phrases from the text.
2. Paraphrases of 1.
3. Concepts that account for number 2.
4. Themes and constructs in consideration of context.

A storyline was described based on the themes and constructs, then a theory provided from the storyline.

3. Results

3.1. Participant characteristics

A total of 6 Japanese PWT2D participated in the interview. Baseline demographics are shown in Table 1. Most participants were male (83.3%), with a mean age of 60.5 years (SD 9.0). Mean time from initial T2D diagnosis to first insulin was 14.0 years (SD 9.3). Mean HbA1c reduced from the time of insulin initiation from 9.0% ($\pm$ 2.1%) to current reported levels of 7.6% ($\pm$ 1.7%). Baseline demographics and clinical characteristics of these 6 study participants were similar to those of the larger pool of Japanese participants in the EMOTION 2 study [24].

3.2. Actions that assisted with insulin initiation

Reluctant Japanese PWT2D cited a range of factors which initially assisted them to overcome their hesitancy. Participant responses broadly conformed to 3 themes (Table 2); 1. Receiving advice from an HCP that insulin was an appropriate treatment; 2. HCPs showing the patient the insulin pen/needle and demonstrating the injection process; and 3. Resignation/surrender/acceptance of insulin, where the participant felt there was no other choice but to commence insulin. Each theme is outlined in Table 2 and briefly described below.

3.2.1. Theme 1: advice from a health care provider that insulin was an appropriate treatmen

Advice from an HCP with whom the participant had rapport was considered important for Japanese participants in deciding to commence insulin. Participants reported that an explanation by the HCP of the benefits of insulin compared with the potential disadvantages contributed to the decision to initiate insulin therapy. A trusting relationship with the HCP was important to participants, as well as the HCP understanding the participants' circumstances and agreeing that insulin therapy was optimal for their current condition.

Three participants preferred a non-authoritarian approach on the part of the HCP, and a process where the participant and doctor collaborated from the outset in seeking solutions regarding insulin injection therapy. One participant had a short relationship with their doctor, a lack of communication, and consequently a lack of a trust or sense of security with the doctor. However, the participant decided to initiate insulin therapy, not only after the doctor's persuasion, but also after a nurse provided sufficient information and supplemented the doctor's advice. An HCP with good communication skills able to take an

Table 1

Participant characteristics.

Characteristic	Japan (N = 6)
Age, mean (SD)	60.5 (9.0)
Gender, male, n (%)	5 (83.3)
Education, years, mean (SD)	14.7 (2.1)
Years from T2D diagnosis to insulin use, mean (SD)	14.0 (9.3)
HbA1c before insulin initiation (%), mean (SD)[a]	9.0 (2.1)
Current HbA1c (%), mean (SD)[a]	7.6 (1.7)
BMI before insulin initiation / Current BMI (kg/m²)[b]	
Mean (SD)	26.7 (3.8)/26.1 (3.6)
< 18.5, n (%)	0 (0.0)/0 (0.0)
18.5–24.9, n (%)	3 (50.0)/2 (33.3)
25.0–29.9, n (%)	1 (16.7)/4 (66.7)
≥ 30, n (%)	2 (33.3)/0 (0.0)

BMI = body mass index, HbA1c = hemoglobin A1c, N/n = number of participants, T2D = type 2 diabetes, SD = standard deviation.

[a] Mean HbA1c was calculated among participants who had a test in the past year and knew the test result (self-reported). HbA1c mmol/mol were converted to % and vice versa according to New Zealand Society for the Study of Diabetes: 'HbA1c Conversion Tables', NZSSD. N.p., Sept.2011.

[b] BMI categories were defined using the World Health Organization's internal classification. BMI was self-reported.

Table 2

Key reasons for initiating insulin among Japanese people with type 2 diabetes.

Reasons for initiating insulin	Key factors
Advice from HCP that insulin is an appropriate treatment	• Advice that blood glucose/HbA1c will improve upon insulin initiation, ['I was convinced insulin was the only option to stabilize my blood sugar level'] • Explanation regarding risks and benefits of insulin, ['The doctor explained that taking insulin is far better than doing nothing, despite the low blood sugar risk'] • Explanation that insulin will decrease burden on body/organ complications, ['The impact on my organs could be reduced by changing the types of drugs. That was my doctor's advice. After such a discussion, I came to think I could try'] • Advice that insulin is suitable for the persons current medical condition and lifestyle, ['The doctor told me that insulin would suit my lifestyle and personality better'] • Recommendation of 'trying insulin', and that insulin may not need to be taken forever, ['The doctor told me that we would switch back to oral medication if I wanted to'] • A good patient-physician relationship and having trust in the physician, ['I wouldn't dream of leaving my health with a doctor I cannot trust. I value my current doctor highly'] and ['I started insulin because it was the doctor who recommended it to me, not because of insulin itself. It was because my current doctor suggested it that I started']
Demonstration by HCPs on how to use the insulin pen/needle and the injection process	• HCP explained the injection procedure, ['The nurse showed me how to use the pen and convinced me it is not difficult' and 'The nurse taught me well. I am confident to start this treatment by myself'] • HCP explanation changed the negative image of insulin ['My impression about insulin treatment is now good'] • Participant realized that administering insulin was not very painful, and the injection was easy to perform, ['The needle does not give me great pain'] and ['My biggest worry was the pain]. Experiencing little pain convinced me'] and ['The needle is extremely fine. I could visualize myself using the pen'] and ['I tried it and felt no pain. I was convinced what the nurse said was correct'] and ['It is more simple than I had imagined and it doesn't take time and effort'] • Participant realized that insulin helps them control their diabetes, ['What surprised me was that the glucose level came down quickly after a few days']
Resignation/surrender/acceptance of insulin	• Participant realized that there was no other choice other than to start insulin, ['Drug therapy isn't effective. I was thinking it (insulin) was the only option left for me'] and ['When I looked at my blood sugar level, I realized there was no other choice left. I profoundly decided to start insulin treatment'] and ['It was the figures in my test results'] • New life event contributed to participants decision to start insulin, ['As I had cancer, my blood sugar level became unstable. I was convinced insulin was the only option to stabilize my blood sugar level']

HCP = health care provider.

approach suited to the participants' character was deemed important to Japanese people.

3.2.2. Theme 2: demonstration by HCPs on how to use the insulin pen/ needle and the injection process

Japanese participants reported that the injection procedure itself, the stigma associated with insulin injections, and the fear of pain were obstacles in the decision to commence insulin therapy. Moreover, there are gaps between medical knowledge at the start of treatment, the recognition and acceptance of the disease condition, and a doctor's understanding of the situation. These gaps contribute to resistance to initiate insulin therapy. Education and a demonstration of how to use insulin was important to Japanese participants who reported that this experience was more convincing than just an explanation or images. Watching demonstrations of insulin-delivery devices, accompanied by an explanation by a HCP, helped to ease preconceptions and anxiety regarding insulin therapy. In addition, self-administering an insulin injection, with support from a nurse or doctor, was reported as being helpful. This process alleviated negative preconceptions regarding pain and ease of use.

3.2.3. Theme 3: resignation/surrender/acceptance of insulin

Four participants reported feeling that they had no choice but to commence insulin therapy due to other treatment options being unsuccessful, and that they were prepared to accept insulin injection therapy as unavoidable. This was particularly evident in cases where blood glucose levels and overall physical condition were declining. A change in lifestyle, including diagnosis of other serious conditions, may provide an opportunity to initiate insulin therapy. One participant reported feeling they had "no choice" regarding commencing insulin therapy yet had an expectation of future discontinuation of the therapy.

4. Discussion

We report the findings of exploratory interviews with Japanese participants from the global EMOTION study. Our study identified 3 major themes which influence Japanese PWT2D to commence insulin therapy. Our study findings add to the limited literature regarding PIR in Japanese PWT2D, providing a greater understanding of the factors which assist with the decision to commence insulin.

This study determined that HCP actions have significant influence on Japanese PWT2D in initiating insulin treatment. Reluctant Japanese participants valued the advice given by their primary physician regarding the benefits and risks of insulin. A good patient–HCP relationship and having trust in the HCP was also highly valued, with Japanese participants reporting that a collaborative approach between patient and HCP was preferred over an authoritarian relationship. This is supported by evidence that a patient's relationship with their HCP is closely related to self-management behavior [30,31]. Specifically, a positive patient–physician relationship has been shown to be associated with reduced diabetes-related distress and improved insulin adherence and glycemic control [19].

Demonstration of the insulin pen/needle and the injection process were important to Japanese participants, who valued practical demonstrations over explanations. This theme was also apparent in the global population of EMOTION [32], and is consistent with previous findings in Japanese participants from part 2 of the EMOTION study, where actions such as 'HCP walked participant through the process of exactly how to take insulin' and 'HCP showed an insulin pen' were rated as the most helpful factors in deciding to initiate insulin therapy [24]. Practical demonstrations are likely to dispel preconceived negative assumptions, such as the perceived large size of the needle and pain associated with the injection, the stigma attached to using insulin and people's anxiety

regarding the use of insulin, helping to build a strong and trusting relationship between patient and physician.

An interesting observation was the theme of resignation/surrender/ acceptance of insulin. The underlying concept of 'resignation' has cultural differences; implied to be a negative and weakened state of mind in Western culture but with more complex meaning in Eastern culture and generally regarded as a desired quality [33]. As explained by Meaders, surrender/resignation (called 'akirame' in Japan) is a specific form of defense with multilayered psychological and cultural meanings; a culture-specific adaptive defensive operation of the ego [33]. In the current study, Japanese participants reported that they felt there was no choice other than to commence insulin treatment, because alternative therapies were not effective at controlling blood glucose, or due to a new life event (such as the diagnosis of comorbid diseases). Once the participant initiated insulin treatment with their physician's support, they may have a positive experience relative to their expectations [23].

Overall, our findings are in alignment with previous studies that suggest a stepwise approach to diabetes and insulin education [14,17], although our findings should be interpreted with caution due to limited participants. In a recent UK subgroup analysis of the EMOTION study, the most helpful strategies for reluctant individuals were demonstration of the injection process, a collaborative approach with HCPs, explanation of the benefits of insulin, and addressing patients' concerns. Our current findings in Japanese participants are in alignment with the UK findings in terms of theme 1 (advice from HCP) and theme 2 (demonstration) [31]. There is consensus in the literature that assisting people get off to a 'good start' with insulin is critical, and that this should be complemented with appropriate clinical support and follow-up over the initial few months [14]. An optimal start to insulin treatment may have additional benefits such as an increased likelihood of people maintaining long-term treatment, thereby successfully reaching the recommended glycemic target. In terms of clinical practice recommendations for reluctant Japanese PWT2D, theme 1 (advice from HCP) and theme 2 (demonstration) are indicated as helpful for the initiation of insulin. It is inevitable that theme 1 precedes theme 2; however, theme 3 (resignation/surrender/acceptance of insulin) may occur independently. In some Japanese people, HCPs should consider that theme 3 may be necessary for the acceptance of insulin therapy, hence a level of patience and support from HCPs may be required.

The results of this study highlight the importance of understanding and addressing PWT2D perceptions regarding insulin therapy, and of providing a supportive environment to help facilitate insulin initiation. However, the study has some limitations. The number of Japanese participants was small, with the majority being male. Increased female participation may have resulted in varied perspectives, and this could be the subject of further investigation. Survey respondents were recruited from online panels of individuals who volunteer to participate in studies and may therefore be more involved in their T2D care compared with the broader population of reluctant PWT2D. In addition, self-reported data may not be accurate and may be subject to recall bias. The present study is exploratory in nature, providing a conceptual framework regarding key factors that motivate reluctant Japanese PWT2D to initiate insulin treatment. Further research is required, particularly regarding other factors that may influence PIR in Japanese PWT2D such as age, comorbid conditions, and mental health. A further area of study may relate to our findings regarding 'surrender/resignation', potentially applicable to Japanese people with other health conditions.

5. Conclusions

Our findings highlight the importance of the role of HCP during insulin initiation in reluctant Japanese PWT2D and indicate that it is important for HCPs to explain the benefits of insulin and demonstrate/ explain the injection procedure to their patients. We also identified surrender/resignation as a reason for treatment commencement. This study provides important information on HCP actions that can be used to

assist reluctant Japanese PWT2D in overcoming PIR to initiate basal insulin therapy. Identifying reasons for insulin initiation is a critical step towards designing broader clinical recommendations for HCPs treating Japanese PWT2D.

Declaration of Competing Interest

Kentaro Okazaki and Noriyuki Takahashi declare that their current affiliations were established by donations from Aichi prefecture and Nagoya city in Japan and Noriyuki Takahashi received a grant and personal fees from Novartis Pharmaceuticals K.K. Tomotaka Shingaki is a full time employee at Eli Lilly Japan K.K. and stockholder at Eli Lilly and Company. Magaly Perez-Nieves is a full time employee and stockholder at Eli Lilly and Company. Heather Stuckey is a consultant for Eli Lilly and Company.

Data Availability

Lilly provides access to all individual participant data collected during the trial, after anonymization, with the exception of pharmacokinetic or genetic data. Data are available to request 6 months after the indication studied has been approved in the US and EU and after primary publication acceptance, whichever is later. No expiration date of data requests is currently set once data are made available. Access is provided after a proposal has been approved by an independent review committee identified for this purpose and after receipt of a signed data sharing agreement. Data and documents, including the study protocol, statistical analysis plan, clinical study report, blank or annotated case report forms, will be provided in a secure data sharing environment. For details on submitting a request, see the instructions provided at www.vivli.org.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.pcd.2022.02.009.

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