



Original Article

Factors associated with reluctance to initiate or continue oral antihyperglycemic agent (OAHA) treatments in type 2 diabetes mellitus patients in Japan: An observational patient-reported study



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ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is undertreated in Japan. We sought to understand the potential factors associated with reluctance to initiate/continue oral antihyperglycemic agents (OAHA) treatment in Japan.

Methods: A two-phase study was conducted which included cognitive interviews in the first phase (N = 12) to ensure retrieval from memory of relevant information to respond to questions. The second phase included recruitment of respondents from an internet re-contact survey (N = 560) using NHWS or other Lightspeed panels. Patients' self-reported measures were collected to identify the potential barriers to T2DM treatment initiation or continuation. All measured variables were summarized descriptively using means and standard deviations for continuous variables, and frequencies and percentages for categorical variables.

Results: A total of 560 respondents were assessed. Of those who were drug-naïve and ever been recommended prescription medication, only 17.3% were satisfied with how physicians presented the treatment options compared to current users or those who discontinued treatment (47.2% and 47.6% respectively). More than 50% of respondents did not realize neuropathic pain and end organ damage as potential consequences of untreated T2DM. 34.8% and 47.6% of drug-naïve and T2DM respondents who discontinued treatment were likely to start/restart treatment after realizing potential complications. Among those who discontinued treatment, 23.1% were extremely dissatisfied with their dosing frequency and less than 15% reported that their physicians discussed the importance of staying on medication long-term.

Conclusion: The potential barriers addressed in this study should be considered when planning intervention strategies targeted at T2DM patients to promote their treatment in Japan.

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1. Introduction

Prevalence of Type 2 Diabetes Mellitus (T2DM) has been increasing worldwide [1] with escalating prevalence in Asia [2,3]. In Japan it affects 3.2 million adults, with prevalence on the rise over the last decade [4]. Accompanied with an increase of T2DM prevalence, the number of “strongly suspected to have T2DM” (HbA1c>6.5%) population has also increased from approximately

6.9 million in 1997 to 10.0 million in 2016 [5]. In order to promote the nation's health, the Japanese government initiated a 10 year campaign named “Health Japan 21” in 2013 to improve patients' lifestyle, early discovery, and continued treatment promoting the primary prevention of diabetes [6].

Despite the government striving to control diabetes, a survey conducted among patients with “suspected T2DM” showed that approximately 23% of them were not visiting a medical institution even though they were recommended to do so, and although 16% of them were visiting medical institutions they remain untreated [7]. The issue of not receiving treatment applies also to those already diagnosed and on treatment. In Japan, different classes of

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antihyperglycemic agents are currently approved for T2DM treatment, including oral antihyperglycemic agents (OAHAs) and injectables like insulin and glucagon like peptide-1 (GLP-1) receptor agonists. Despite the availability of different treatment options, Japan Diabetes Outcome Intervention Trial, a national study conducted by the Ministry of Health, Labour and Welfare reported that as many as 8% of T2DM patients on treatment were estimated to discontinue their regular medical visits [8]. The main reasons raised for ceasing medical visits were time pressure (38%), objective hurdles like transportation barriers or economic burden (21%), but not a negligible number of patients gave subjective reasons including treatment burden (16%) [9].

To our knowledge no study has collectively addressed potential hurdles for initiating OAHA treatment in drug naïve T2DM patients and existing hurdles towards OAHAs in currently on-treatment or discontinued T2DM patients in Japan. Ergo, the primary objective of this study is to describe the barriers to T2DM treatment among both drug naïve and drug-treated patients while the secondary objective is to assess the motivations to start/restart new OAHA treatment among T2DM patients.

2. Materials and methods

2.1. Data source, sample and procedure

This study was conducted via a two-phase approach from 2017 to 2018. In the first phase, 1-h cognitive interviews were piloted for 12 participants in a qualitative research setting to ensure retrieval from memory of the relevant information to respond to questions and the survey instrument was concise so that we minimized respondents' burden to ensure high-quality data collection. Participants who met the eligibility criteria and consented for this study were recruited by convenience sampling via JMax's database. Inclusion criteria were as the followings: (a) Japanese aged 20 years old and above, (b) received healthcare in Japan, (c) self-reported being either (i) suspected/diagnosed with T2DM who have seen a physician in the past and were recommended diet and exercise (D&E), but did not start any drug treatment for T2DM (Group 1) or (ii) diagnosed with T2DM who have seen a physician in the past 6 months and were currently on OAHA monotherapy (Group 2) or (iii) diagnosed with T2DM who initiated OAHA treatment but then discontinued (Group 3), and (d) able to read and understand Japanese. The exclusion criteria were: diagnosed with type 1 diabetes mellitus, pregnant, had drug-induced T2DM, and respondents in Group 1 who were told by their physicians that they have already being well-controlled on their glycemic levels and do not have to engage in D&E therapies. Of the 12 consented participants, 6 were recruited for Group 1, and 3 were recruited for Group 2 and 3 each.

In the second phase, Japanese participants were recruited from an internet re-contact survey (N = 560). Participants who participated in the National Health and Wellness Survey (NHWS) or other Lightspeed studies were identified as the potential respondents. The NHWS is a self-reported, online cross-sectional health survey. More details on survey methodology and sample recruitment for NHWS were stated elsewhere [10–12]. To recruit enough samples, additional T2DM patients were recruited from the Lightspeed GMI global panel, one of the largest global online sample providers in the world, providing digital access to the most qualified panellists across 40 countries. All respondents were emailed an invitation to participate, administered informed consent and screened to ensure they meet the inclusion and exclusion criteria used in Phase 1. The protocol for this study received an approval from the Independent Ethics Committee (IEC).

2.2. Measures

This study collected patients' self-reported measures categorized into five different domains hypothesized to be the potential barriers to T2DM treatment initiation or continuation: social/economic factors, therapy-related factors, patient-related factors, health system-related factors and, condition-related factors. Details on the factors included in each of the five domains in appendix A (Supplementary Table 1). Additionally, motivations and influencers to initiate/continue/restart a T2DM treatment were also collected in this study.

2.3. Statistical analysis

All measured variables were summarized and presented descriptively using means and standard deviations for continuous variables, and frequencies and percentages for categorical variables. Stratified descriptive analyses were conducted by patient population that was composed of drug-naïve diagnosed/suspected T2DM (Group 1), T2DM on-treatment of an OAHA (Group 2) and T2DM discontinued OAHAs (Group 3). In Group 1, drug-naïve patients who have ever been recommended prescription medications by physician (named as Group 1.1 hereafter) were identified and analysed separately. No between groups comparison were conducted as this is primarily a descriptive study. All statistical analyses were performed using the statistical software IBM SPSS Statistics for Windows (version 23.0) [13].

3. Results

A total of 560 eligible respondents completed the survey and were included for analysis. Of which 231, 303 and 26 were classified into Group 1, 2, and 3, respectively. In Group 1, 23 respondents have ever been recommended for prescription medications accounting for 10% of the drug-naïve respondents.

The socio-economic characteristics of study participants by treatment status were summarized in Table 1. The mean age of the sample ranged from 56 to 63 years old, majority of them were male (>78%) and married/living with their partners (>65%). Drug-naïve respondents who have ever been recommended prescription medications (Group 1.1) were less likely to complete a university degree or above (52.2%), more likely to be employed (82.6%), less likely to live in urbans/cities and their sub-regions (43.5%), and more likely to have a household income of <¥3,000,000 (39.1%).

On an average, Group 1 respondents visited primary care physicians 6–7 times regarding their condition in the past year, but respondents who were currently on treatment (Group 2) visited primary physicians relatively more times (9 ± 5) in the past year (Table 2). Additionally, more than 40% of the respondents from Group 1 received printed information on the condition and lifestyle changes. More than 40% of the respondents from Group 2 and 3 received printed information on drug medications, while printed information on drug medication was received by less than 20% of the respondents from Group 1.1 (Table 2).

Approximately 47.2% and 47.6% of Group 2 and 3 respondents were satisfied with how the physicians presented the drug treatment options, compared to only 17.3% of Group 1.1 respondents (includes very satisfied and somewhat satisfied, Table 2). Also, more than half of the Group 2 and 3 respondents mentioned that their physician discussed the importance of taking medication along with Diet and Exercise (D&E), compared to only 26.1% of Group 1.1 respondents. Additionally, only 14.3% of Group 3 respondents reported that their physician discussed the importance of staying on the medication long-term. When asked about the clarity of explanation about prescription medications, 58.4% and

Table 1
Social/economic characteristics of study participants by treatment status.

		N (%)			
		Group 1		Group 2 (N = 303)	Group 3 (N = 26)
		Total (N = 231)	Group 1.1 (N = 23)		
Age (Mean [SD])		58 (9)	56 (8)	63 (10)	59 (14)
Gender	Male	190 (82.3%)	18 (78.3%)	264 (87.1%)	22 (84.6%)
Marital status	Married/living with partner	168 (72.7%)	15 (65.2%)	209 (69.0%)	17 (65.4%)
Education	Completed university degree or above	141 (61.0%)	12 (52.2%)	184 (60.7%)	15 (57.7%)
Employment	Employed	162 (70.1%)	19 (82.6%)	144 (47.5%)	14 (53.8%)
Living community	Urban/City and their sub-regions	139 (60.2%)	10 (43.5%)	199 (65.7%)	18 (69.2%)
Household income	<¥3,000,000	46 (19.9%)	9 (39.1%)	70 (23.1%)	4 (15.4%)
	¥3,000,000 - <¥5,000,000	50 (21.6%)	2 (8.7%)	79 (26.1%)	4 (15.4%)
	¥5,000,000 - <¥8,000,000	63 (27.3%)	5 (21.7%)	50 (16.5%)	12 (46.2%)
	¥8,000,000 or more	59 (25.5%)	5 (21.7%)	64 (21.1%)	4 (15.4%)
	Decline to answer	13 (5.6%)	2 (8.7%)	40 (13.2%)	2 (7.7%)

66.7% of Group 2 and 3 respondents respectively, found clarity in physician's explanation compared to only 34.8% of Group 1.1 respondents. (includes very clear and somewhat clear, [Table 2](#)). Nearly all respondents (>70%) reported that the reasons for their physician recommendations of prescription medications were: (1) D&E were not enough/effective in lowering my blood sugar, or (2) the drug would reduce the elevated blood sugar effectively.

DPP-4i was the top prescription medication currently used for patients who were on treatment of OAHAs (47.9%), while more than 90% of T2DM respondents who discontinued their treatment used fixed dose combination therapy (FDC; 96.2%) and Glinide (92.3%) previously ([Table 3](#)). A relatively lower proportion of Group 1.1 respondents adhered to the recommended D&E plan compared with other groups (Adherence to diet: 45.4% vs 63.8% vs. 72.8% vs 59.6% for Group 1.1 vs. 2 vs. 3 vs 1, respectively (Values from 5 to 7 used as adherence scale, [Table 3](#)). Adherence to exercise: 31.8% vs 54.3% vs 52.3% vs 51.7% for Group 1.1 vs 2 vs 3 vs 1 (Values from 5 to 7 used as adherence scale, [Table 3](#)). Efficacy (>50%), long-term safety (>40%), preventing/delaying from taking insulin (>38%), affordability (>37%), ease of administration (>30%) and less frequent dosing schedule (>20%) were top factors that all respondents valued when considering a prescription medication. Interestingly, >50% of patients did not realize neuropathic pain and end organ damage that could be potential complications of untreated T2DM and 34.8% and 47.6% Group 1 and 3 respondents (includes very likely and somewhat likely, [Table 3](#)), respectively, were likely to start/restart on treatment after knowing the potential complications.

Among Group 3 respondents, regarding their previous treatment, 26.9% of them had their treatments three times a day (11.9% for Group 2), 23.0% of them were dissatisfied with their current oral prescription medication (includes extremely dissatisfied, very dissatisfied and somewhat dissatisfied; 7.7% for Group 2) and 23.1% were extremely dissatisfied with the dosing frequency (only 0.3% for Group 2) ([Supplementary Table 2](#)).

Many drug naïve respondents (Group 1 and 1.1) felt worried (56.3% and 52.2%), embarrassed (29.4% and 34.8%), fearful (21.2% and 26.1%), and frustrated (16.5%) with T2DM diagnosis respectively. Similarly, many respondents who discontinued treatment (Group 3) also felt worried with the diagnosis (50.0%), being recommended for prescription medications (47.6%), and taking their last oral prescription medication to treat T2DM (23.1%). However, a substantial proportion of T2DM respondents currently on OAHA treatment (Group 2) felt hopeful (13.5% and 14.5%) and optimistic (12.9% and 19.1%) about their current treatment as well as when their physicians recommended prescription medications ([Supplementary Table 3](#)), even though they felt worried (51.5%), embarrassed (29.7%) and fearful (17.2%) when diagnosed with T2DM.

All respondent groups had similar BMI, smoking status and level of alcohol use. Approximately 80% of Group 2 respondents had blood glucose or HbA1c level measured since they started to follow the recommended D&E plan. Group 1.1, 2 and 3 respondents had higher HbA1c level at the diagnosis (7.9%, 7.8% and 8.0%, respectively) relative to all drug-naïve respondents i.e. Group 1 (7.3%). However, Group 2 and 3 respondents had a substantial decrease in HbA1c level at their most recent office visit (6.8% and 6.3%, respectively) relative to Group 1.1 respondents (7.3%). Also, Group 1.1 drug-naïve respondents were more likely to have medical conditions other than T2DM prior to the diagnosis of condition (73.9%) compared with other groups (66.0% and 61.5% for Group 2 and 3, respectively). Hypertension, Hay fever, Dyslipidemia and gout/hyperuricemia were top common medical conditions that respondents had prior to the diagnosis of condition ([Supplementary Table 4](#)).

Among the motivations to take prescription medicines, respondents from Group 1.1 and 2 respondents reported that they would be motivated to take prescription medication if D&E were not enough/effective in lowering their blood sugar (39.1% and 54.8%, respectively) and if the treatment was affordable (39.1% and 12.5%, respectively). Many Group 2 respondents also reported that they would be motivated if the drug was more convenient to take (21.5%) with less frequent dosing schedule (14.5%). Advice or recommendation of physicians (>60%) and other health care professional (>30%) were reported to be influential in respondents' final decision to start/continue/restart medication treatment for their conditions ([Supplementary Table 5](#)).

4. Discussion

The present analysis provides insights on the barriers to T2DM treatment initiation among drug naïve respondents and discontinuation among drug-treated respondents. Our survey results showed that drug naïve respondents who have ever been recommended treatment had relatively lower education level, lower household income, less than half of them lived in urban cities, relatively higher employment rate and lower adherence to recommended D&E plan. Lower health literacy could also be associated with lower adherence to D&E plan. In diabetes, health literacy is related to diabetes knowledge and understanding of the importance of self-care behaviours and glycemic control. Previous studies have shown that inappropriate glycemic control is associated with high risk of microvascular complications which could lead to an increased risk of morbidity and mortality [14–16] emphasizing the importance of appropriate glycemic control among T2DM respondents. Thus, there is a need to further increase health literacy among drug naïve T2DM respondents and create more awareness about the potential complications of not managing T2DM well. We

Table 2
Health-system related characteristics of respondents by treatment status.

		N (%)			
		Group 1		Group 2 (N = 303)	Group 3 (N = 26)
		Total (N = 231)	Group 1.1 (N = 23)		
No. of times visited primary physician regarding your condition in the past year (Mean [SD])		6 (4)	7 (4)	9 (5)	6 (3)
Printed information provided to you about your condition	Information on the medication	13 (5.6%)	4 (17.4%)	140 (46.2%)	11 (42.3%)
	Information about the diabetes condition	102 (44.2%)	10 (43.5%)	17 (5.6%)	1 (3.8%)
	Information about pre-diabetes	24 (10.4%)	1 (4.3%)	102 (33.7%)	7 (26.9%)
	Information about lifestyle changes	99 (42.9%)	6 (26.1%)	2 (0.7%)	0 (0.0%)
	Other	1 (0.4%)	0 (0.0%)	122 (40.3%)	11 (42.3%)
How the medication treatment options were presented to you by your physician	I wasn't given any printed information	89 (38.5%)	10 (43.5%)	140 (46.2%)	11 (42.3%)
	My physician explained all my treatment options and told me to think about it.	–	3 (13.0%)	9 (3.0%)	1 (4.8%)
	My physician explained all my treatment options and asked for my preference.	–	5 (21.7%)	26 (8.6%)	3 (14.3%)
	My physician explained all my treatment options and then made a recommendation.	–	2 (8.7%)	64 (21.1%)	2 (9.5%)
	My physician presented/recommended just one treatment option right away.	–	5 (21.7%)	198 (65.3%)	13 (61.9%)
Satisfaction with how physician presented treatment options	Other	–	3 (13.0%)	9 (3.0%)	1 (4.8%)
	Very Satisfied	–	1 (4.3%)	51 (16.8%)	4 (19.0%)
	Somewhat Satisfied	–	3 (13.0%)	92 (30.4%)	6 (28.6%)
	Neither Satisfied/Dissatisfied.	–	16 (69.6%)	150(49.5%)	8 (38.1%)
	Somewhat Dissatisfied	–	0 (0.0%)	4 (1.3%)	2 (9.5%)
Topics that physicians focus on during discussion regarding patient's potential treatment	Very Dissatisfied	–	1 (4.3%)	1 (0.3%)	0 (0.0%)
	Other	–	2 (8.7%)	5 (1.7%)	1 (4.8%)
	Medication dosing schedule	–	1 (4.3%)	95 (31.4%)	4 (19.0%)
	Potential risk of side effects	–	5 (21.7%)	94 (31.0%)	3 (14.3%)
	Patient support programs	–	2 (8.7%)	4 (1.3%)	0 (0.0%)
	Cost	–	2 (8.7%)	18 (5.9%)	0 (0.0%)
	The importance of staying on the medication long-term	–	7 (30.4%)	63 (20.8%)	3 (14.3%)
	Administration of the medication	–	2 (8.7%)	113(37.3%)	11(52.4%)
	Importance of taking this medication with D&E	–	6 (26.1%)	155(51.2%)	12(57.1%)
	Other	–	8 (34.8%)	12 (4.0%)	4 (19.0%)
How clear was the explanation about prescription treatments	Very Unclear	–	2 (8.7%)	5 (1.7%)	1 (4.8%)
	Somewhat Unclear	–	2 (8.7%)	23 (7.6%)	2 (9.5%)
	Neither Clear or Unclear	–	7 (30.4%)	91 (30.0%)	3 (14.3%)
	Somewhat Clear	–	6 (26.1%)	106 (35.0%)	9 (42.9%)
	Very Clear	–	2 (8.7%)	71 (23.4%)	5 (23.8%)
	Don't Know	–	4 (17.4%)	7 (2.3%)	1 (4.8%)
Reasons that your physician provided for recommending prescription medication	D&E were not enough/effective in lowering my blood sugar	–	15 (65.2%)	137 (45.2%)	9 (42.9%)
	Drug would reduce elevated blood sugar effectively	–	4 (17.4%)	140 (46.2%)	7 (33.3%)
	Drug would relieve symptoms quicker	–	0.0%	27 (8.9%)	5 (23.8%)
	Drug had fewer side effects than previous medication	–	3 (13.0%)	31 (10.2%)	0.0%
	Drug would improve daily lifestyle	–	0.0%	8 (2.6%)	0.0%
	Drug is more convenient to take	–	0.0%	31 (10.2%)	1 (4.8%)
	Drug would stop the progression/ complications associated with diabetes	–	5 (21.7%)	47 (15.5%)	1 (4.8%)
	Drug has a better dosing schedule	–	0.0%	30 (9.9%)	1 (4.8%)
	More affordable	–	1 (4.3%)	15 (5.0%)	2 (9.5%)
	Has been on the market for a long time	–	1 (4.3%)	6 (2.0%)	0.0%
	Safer than similar drugs	–	0.0%	10 (3.3%)	1 (4.8%)
	Wouldn't have to take as many medications	–	0.0%	16 (5.3%)	0.0%
	Physician had more experience with this drug than with similar drugs	–	0.0%	6 (2.0%)	0.0%
	Physician told it was the newest treatment option	–	0.0%	15 (5.0%)	1 (4.8%)
	Complications that result from untreated diabetes/high blood glucose	–	3 (13.0%)	38 (12.5%)	1 (4.8%)
	Other (specify)	–	0.0%	6 (2.0%)	1 (4.8%)
	Wasn't given a reason, and just followed physician's recommendation.	–	2 (8.7%)	48 (15.8%)	5 (23.8%)

Figure legend: '–' data was not available.

Table 3
Therapy-related characteristics of study participants by treatment status.

		N (%)				
		Group 1		Group 2 (N = 303)	Group 3 (N = 26)	
		Total (N = 231)	Group 1.1 (N = 23)			
Drug class of OAHA currently/ previously (discontinued) being used for T2DM treatment	Alpha-glucosidase inhibitors (AGI)	—	—	31 (10.2%)	7 (26.9%)	
	Biguanide	—	—	55 (18.2%)	8 (30.8%)	
	DPP-4i	—	—	145 (47.9%)	8 (30.8%)	
	Fixed dose combination (FDC)	—	—	27 (8.9%)	25 (96.2%)	
	Glinide	—	—	7 (2.3%)	24 (92.3%)	
	GLP-1	—	—	0 (0%)	0 (0%)	
	SGLT-2	—	—	15 (5%)	1 (3.8%)	
	Sulfonylurea	—	—	23 (7.6%)	4 (15.4%)	
	Thiazolidinedione	—	—	0 (0%)	0 (0%)	
	All other	—	—	0 (0%)	1 (3.8%)	
Level of Adherence to recommended diet plan	Insulin	—	—	0 (0%)	1 (3.8%)	
	1: I do not follow at all	8 (3.8%)	1 (4.5%)	5 (2.3%)	2 (9.1%)	
	2	14 (6.6%)	3 (13.6%)	8 (3.6%)	0 (0%)	
	3	26 (12.2%)	5 (22.7%)	33 (14.9%)	3 (13.6%)	
	4	37 (17.4%)	3 (13.6%)	33 (14.9%)	1 (4.5%)	
	5	62 (29.1%)	5 (22.7%)	80 (36.2%)	8 (36.4%)	
	6	50 (23.5%)	4 (18.2%)	50 (22.6%)	6 (27.3%)	
	7: I completely follow	15 (7%)	1 (4.5%)	11 (5%)	2 (9.1%)	
	Don't Know	1 (0.5%)	0 (0%)	1 (0.5%)	0 (0%)	
	Level of Adherence to recommended exercise plan	1: I do not follow at all	15 (7.2%)	1 (4.5%)	15 (5.9%)	1 (4.8%)
2		23 (11.1%)	4 (18.2%)	35 (13.7%)	2 (9.5%)	
3		28 (13.5%)	5 (22.7%)	27 (10.5%)	3 (14.3%)	
4		32 (15.5%)	5 (22.7%)	38 (14.8%)	4 (19%)	
5		39 (18.8%)	2 (9.1%)	31 (12.1%)	4 (19%)	
6		42 (20.3%)	3 (13.6%)	57 (22.3%)	4 (19%)	
7: I completely follow		26 (12.6%)	2 (9.1%)	51 (19.9%)	3 (14.3%)	
Don't Know		2 (1%)	0 (0%)	2 (0.8%)	0 (0%)	
Factors that may or may not be important when considering a prescription medication for T2DM		Reduces blood sugar levels effectively	146 (63.2%)	12 (52.2%)	12 (52.2%)	192 (63.4%)
		Does not have high risks of long-term safety	100 (43.3%)	10 (43.5%)	10 (43.5%)	127 (41.9%)
	Does not have high risks of short-term safety	61 (26.4%)	6 (26.1%)	6 (26.1%)	62 (20.5%)	
	Protects from the complications	126 (54.5%)	10 (43.5%)	10 (43.5%)	158 (52.1%)	
	Improves quality of life	101 (43.7%)	7 (30.4%)	7 (30.4%)	170 (56.1%)	
	Will prevent from having to take insulin	117 (50.6%)	13 (56.5%)	13 (56.5%)	118 (38.9%)	
	Affordable	115 (49.8%)	12 (52.2%)	12 (52.2%)	112 (37%)	
	Easy to take or administer	72 (31.2%)	7 (30.4%)	7 (30.4%)	120 (39.6%)	
	Has a weekly dosing schedule	12 (5.2%)	0 (0%)	0 (0%)	13 (4.3%)	
	Don't have to take it every day	24 (10.4%)	2 (8.7%)	2 (8.7%)	12 (4%)	
	Has daily dosing schedule	28 (12.1%)	1 (4.3%)	1 (4.3%)	113 (37.3%)	
	Less frequent dosing schedule	76 (32.9%)	5 (21.7%)	5 (21.7%)	86 (28.4%)	
	Conditions aware of that could be a result of non-treatment	Macular edema or diabetic retinopathy	162 (70.1%)	17 (73.9%)	—	19 (73.1%)
		Kidney disease	142 (61.5%)	14 (60.9%)	—	12 (46.2%)
		Foot or leg ulcer	147 (63.6%)	15 (65.2%)	—	12 (46.2%)
Neuropathic pain		78 (33.8%)	6 (26.1%)	—	9 (34.6%)	
End organ damage due to diabetes		86 (37.2%)	7 (30.4%)	—	8 (30.8%)	
None		38 (16.5%)	2 (8.7%)	—	5 (19.2%)	
Likelihood to start treatment after being aware of the potential complications	Very unlikely	1 (4.3%)	1 (4.3%)	—	2 (9.5%)	
	Somewhat unlikely	0 (0%)	0 (0%)	—	1 (4.8%)	
	Neither likely nor unlikely	9 (39.1%)	9 (39.1%)	—	8 (38.1%)	
	Somewhat likely	4 (17.4%)	4 (17.4%)	—	5 (23.8%)	
	Very likely	4 (17.4%)	4 (17.4%)	—	5 (23.8%)	
	Don't know	5 (21.7%)	5 (21.7%)	—	0 (0%)	

also identified that T2DM respondents who were on treatment with an OAHA or discontinued treatment had better improvement in glucose levels compared with drug-naïve respondents who have ever been recommended prescription medicines. This elevates the importance of drug treatment for better glucose and T2DM control.

Additionally, we observed that most of the drug naïve respondents who have ever been recommended prescription medicines had relatively high employment rates. Previous studies have only shown an association of diabetes with unemployment, where greater percentage of people with diabetes were either retired or unable to work [17]. On the other hand, our findings showed that drug naïve respondents who ever recommended prescription medicines had relatively high employment rate, possibly due to their younger age. We postulate that these patients might be busier with time-constraints for engagement into treatment compared to

patients who were on treatment or discontinued treatment – posing it as one of the potential treatment barriers for these respondents.

Besides the socio-economic factors, other barriers for treatment initiation include poor patient-physician communication. Our study showed that more than 50% of respondents on OAHA treatment or discontinued treatment felt that their physicians explained the prescription medicines to them clearly while only 30% of drug naïve respondents who have ever been recommended prescription medicine felt the same. Thus, poor patient-physician communication could be one of the barriers of T2DM treatment initiation among drug naïve respondents. Also, while more than half of the respondents currently on treatment reported that physicians focussed on the importance of taking the medication along with D&E, only 20% of drug naïve respondents who have ever been

recommended prescription medicines reported the same. This also correlates with our adherence data, where we observed that drug naïve respondents who have ever been recommended prescription medicines had relatively lower adherence to D&E. Previous studies have shown that effective patient-physician communication supported by continuous care leads to improvement in patient satisfaction, adherence to treatment plans and health outcomes [18,19]. Thus, there is a need to establish a trusting relationship with physicians to address patients' fears or concerns which currently impede them to initiate treatment.

Some of the factors responsible for patients' reluctance to treatment initiation in a US study included patients' feeling of failure of suboptimal glycemic control, anxiety about hypoglycaemia, complexity of disease management, inconvenience and poor education about T2DM and available therapies which eventually prevents them from treatment initiation [20]. Our findings on respondents' feelings on treatment is similar, wherein, we found that majority of drug naïve respondents who have ever been recommended prescription medicines and who discontinued treatment felt worried, embarrassed, fearful and frustrated with T2DM diagnosis and taking medicines. On the other hand, respondents on OAHA treatment felt hopeful and optimistic about their treatment as well as their physicians' recommendation of prescription medicines.

Interestingly, we also observed that most of the respondents who discontinued treatment felt that their physician clearly explained to them about prescription medicines. One of the possible reasons of discontinuing treatment despite clarity about prescription medications could be that most of these respondents had a decrease in their HbA1c levels versus their levels during their initial diagnosis. It is possible that patients discontinued their treatment since they saw improvement in their HbA1c. Importantly, we observed that less than 15% of the respondents who discontinued treatment reported that the physicians discussed the importance of staying on medication long-term. Since previous research has shown non-adherence to treatment as one of the major factors that could lead to morbidity and mortality [21], reinforcing the importance of staying on medication long-term is crucial. Another important factor which influenced respondents' decision to discontinue treatment was the dosing schedule: 23.1% of them were extremely dissatisfied with the dosing frequency (3 times daily). Our findings are in line with previous studies which have showed association of higher dosing frequency with medication non-adherence [22–24].

We also looked into the awareness of all respondents about the implications of not undergoing T2DM treatment. Interestingly, it was seen that more than 50% of respondents were not aware of neuropathic pain and end organ damage as potential complications of untreated T2DM. Also, 35%–48% of respondents might consider to start/restart treatment upon knowing the potential complications. Thus, reinforcing the complications associated with untreated T2DM is needed across all T2DM respondents.

Besides the objective of understanding the barriers towards treatment initiation/discontinuation we also assessed the patient's motivations to start/restart prescription medications for T2DM. Among drug naïve T2DM respondents as well as those on treatment, some of the motivations towards a new treatment were its affordability, safety and ability to lower blood sugar levels. Besides that, advice or recommendation of physicians and other health care professional also plays an influential role in final decision of all T2DM patients. Thus, overall factors such as treatment efficacy, safety, convenience for administration, affordability, physician's recommendations, and less dosing frequency were identified as some of the important factors that might motivate patients to start/restart taking prescription medications.

Our study has some limitations. This study was conducted by using patient panels such as NHWS [10–12], so the data may not represent general Japanese suspected/diagnosed T2DM population. Also, this study was a self-reported, online cross-sectional survey, hence some biases such as reporting bias, recall bias and channeling bias might exist.

Our study highlights the factors associated with reluctance to initiate or continue OAHA treatment for T2DM in Japan. It is important that the potential barriers identified in this study should be addressed when planning intervention strategies targeted at T2DM patients.

Conflicts of interest

Takekazu Kubo, Kotoba Okuyama and Shigeru Tokita are employees of MSD K.K. Xiahong Zhao and Shikha Singh are employees of Kantar Health and received a consulting fee from MSD K.K. during the conduct of the study.

Authors contributions

Xiahong Zhao, Takekazu Kubo, Kotoba Okuyama and Shigeru Tokita contributed to protocol development, data analysis, review of the data and creation of manuscript. Takekazu Kubo, Kotoba Okuyama and Shigeru Tokita provided substantive comments on the methodology and edits of the manuscript. Shikha Singh was involved in writing of the manuscript. All authors contributed to the data analysis, drafting and revising the paper and gave final approval of the version to be published and agreed to be accountable for all aspects of work.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.dsx.2019.01.034>.

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