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ORIGINAL RESEARCH

Physician Perceptions of Dose Escalation for Type 2 Diabetes Medications in the United States

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ABSTRACT

Introduction: Medications used to treat type 2 diabetes (T2D) often require dose escalation to optimize effectiveness. Physician and patient perceptions of treatment characteristics of T2D medications have previously been examined, but little is known about perceptions of escalation to the optimal dose for each patient. This study examined physicians' perceptions of dose escalation for medications used to treat T2D.

Methods: Data on dose escalation and other factors influencing decision-making for treatment of T2D were collected via an online survey of endocrinologists and primary care physicians in the USA.

Results: The sample included 501 physicians (348 primary care physicians and 153 endocrinologists). Dose escalation was not frequently considered by physicians as a primary factor keeping patients' from reaching treatment goals (mentioned as a factor by only 7.6% of the sample) or a barrier to prescribing T2D medication (16.2%). Factors more likely to keep patients from reaching treatment goals included an unhealthy diet (86.6%) and medication adherence (77.4%). The most common reasons that physicians reported for escalating dose levels were the need for better glycemic control (reported by 89.8% of the sample), ability to decrease the total number of medications by increasing the dose of one medication (39.9%), and the need for the patient to lose weight (39.3%). Data reported by primary care physicians and endocrinologists followed similar patterns.

Conclusions: Although common with T2D treatments, escalating the dose of T2D medication was not perceived by physicians to be a significant barrier to attaining treatment goals or prescribing medication. Multiple factors contribute to the decision to escalate the dose of T2D medication.

PLAIN LANGUAGE SUMMARY

In early phases of initiating medication treatment for a patient with type 2 diabetes (T2D), it is common for physicians to increase from a

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lower initial dose to a higher end dose to maximize treatment benefit. This process is known as dose escalation. The purpose of this study was to examine physicians' perceptions of dose escalation for medications used to treat T2D. An online survey was designed to identify reasons why physicians in the US may choose to escalate or not escalate a dose of medication for T2D. In addition, physicians were asked about factors that keep patients from reaching treatment goals to identify whether the requirement for dose escalation is perceived to be a common barrier to successful treatment. The sample included 501 physicians (348 primary care, 153 endocrinologists). Dose escalation was not frequently considered to be a primary factor keeping patients' from reaching treatment goals or a barrier to prescribing medication for T2D. Dose escalation decisions are complex, driven by a range of factors such as glycemic control medication tolerability, the patient's body mass index, treatment guidelines, comorbidities, characteristics of the patient's entire treatment regimen, and potential cardiovascular benefits.

Keywords: Type 2 diabetes; Dose escalation; Online survey; Primary care physician; Endocrinologist; Treatment goal; Prescribing barrier

Key Summary Points

Why carry out this study?
Because dose escalation is a common attribute of medications used to treat type 2 diabetes (T2D), it is important to understand its impact.
Little is known about physicians' perceptions of escalation to the optimal dose for each patient.
The purpose of this study was to conduct an online survey of endocrinologists and primary care physicians in the US to examine their perceptions of dose escalation for medications used to treat T2D.
What was learned from the study?
Results suggest that most physicians, including endocrinologists and primary care physicians, do not perceive dose escalation to be a significant challenge.
Dose escalation was not perceived to be a significant barrier to attaining treatment goals or prescribing medication.
Decisions to escalate a dose are complex, driven by a range of factors such as glycemic control, medication tolerability, the patient's body mass index, treatment guidelines, comorbidities, characteristics of the patient's entire treatment regimen, and potential cardiovascular benefits.

INTRODUCTION

A growing body of literature has focused on attributes of medications used to treat type 2 diabetes (T2D). Attributes examined in previous research include dose frequency, dose flexibility, glucose monitoring, adverse event profile, requirements for reconstituting the medication, and ease of preparing and using injection devices [1–14]. Attributes of the treatment process have been shown to affect medication adherence, which can have an impact on treatment outcomes [15–21]. In addition to the impact on patients, these medication attributes can also affect physicians' perceptions of treatments for T2D [22], which directly influence their choice of medications to prescribe for their patients.

Relatively limited research has examined the impact of dose escalation. Dose escalation is the process of increasing a fixed dose of medication from a lower initial dose to a higher end dose to optimize the medication's acceptability and efficacy [23]. Dose escalation is commonly required during the early phases of treatment with oral and injectable T2D therapies, such as metformin, liraglutide, tirzepatide, dulaglutide, and semaglutide [24–26]. Dose escalation is different from the individualized dose

adjustments in response to changes in a physiological parameter, often called "dose titration." For example, patients treated with multiple daily insulin injections regularly adjust their dose based on blood glucose levels [27].

Because dose escalation is a common attribute of medications used to treat T2D, it is important to understand its impact. In a previous study examining the patient perspective, dose escalation was perceived to be one of the least important characteristics of treatment for T2D [27]. However, physicians' perceptions of dose escalation remain largely unknown. Therefore, the purpose of this study was to examine physicians' perceptions of dose escalation for medications used to treat T2D. An online survey was designed to identify reasons why physicians may choose to escalate or not escalate a dose of medication for T2D. In addition, physicians were asked about factors that keep patients from reaching treatment goals to identify whether the requirement for dose escalation is perceived to be a common barrier to successful treatment.

METHODS

Study Design

In this cross-sectional study, physicians completed an online survey designed to assess their perceptions of dose escalation. Before completing the survey, physicians provided electronic consent and completed online screening questions to determine whether they were eligible to participate. The online survey was designed to take approximately 20–30 min to complete, and physicians who completed the survey were reimbursed. Participants provided informed consent before completing the survey. All procedures and materials were approved by a central institutional review board (22131-01A, Ethical and Independent Review Services), which was conducted in accordance with the Declaration of Helsinki. All surveys were completed from July to September 2022.

Participants

Participants were primary care physicians and endocrinologists licensed to practice medicine in the USA. To be eligible for this study, physicians were required to have been in medical practice for $\geq$ 1 year, treated an average of $\geq$ 10 patients with T2D per month, and prescribed injectable T2D medication (i.e., insulin or glucagon-like peptide-1 receptor agonists) for $\geq$ 3 patients in the 6 months prior to survey completion. Physicians were excluded if they were practicing medicine in a state where the Sunshine Act prohibits participation (i.e., Vermont and Massachusetts). An estimated sample size of approximately 400 to 500 physicians (approximately 70% primary care physicians, 30% endocrinologists) was targeted, roughly equally distributed across four US regions (Northeast, Midwest, South, and West). As the planned analyses were descriptive without a key statistical comparison, no power analysis was conducted when determining the sample size target. The sample size target was determined on the basis of similar surveys published in the past as well as practical implications.

Participants were recruited through a healthcare provider (HCP) panel built over a period of approximately 12 years by sourcing HCP contact data through direct physician outreach, conferences, LinkedIn outreach, ZoomInfo, institution websites, and PubMed. HCP status is confirmed at the time of opting into the panel by verifying their National Provider Identifier and implementing other quality control metrics. Panelist data are periodically cross-checked against online databases to ensure profiling remains accurate as time passes. The recruitment strategy for most of the study was to conduct a spam-resistant continual email campaign, sending study invitations to verified primary care physicians and endocrinologists in the HCP panel. However, for the initial soft launch of 15 physicians, a controlled email campaign was used to avoid over-recruitment and pause data collection as needed to identify any potential issues with the survey prior to full launch. For the full launch, the continual email campaign was initiated, usually sending emails every 2 days during the study period. The email

invitation briefly described the study and how much time it would take. A link was provided in the email invitation for the participant to click and be screened. If the screening questions determined that the participant was eligible, the participant would continue by completing the online physician survey. For this study, a total of > 30,000 email invitations were sent, and recruitment was discontinued when the sample size target was reached.

Online Physician Survey

To inform development of the survey, four clinical experts (three physicians with experience treating T2D and one clinical researcher who designs trials of medication for T2D) were interviewed about dose escalation. They were asked about factors they consider when deciding whether to escalate the dose of T2D medication, advantages and disadvantages of dose escalation, and the importance of dose escalation relative to other attributes of medication used to treat T2D. The content of the online survey was based on input provided during these qualitative interviews with physicians and a clinical researcher.

The survey began with instructions for completion. Respondents were instructed to answer the questions while thinking about "the broad range of antihyperglycemic medications for type 2 diabetes, including oral treatment like metformin, empagliflozin, and oral semaglutide; basal and meal-time insulin; and non-insulin injectable medications like liraglutide, injectable semaglutide, and dulaglutide." Then, a series of questions were administered to determine whether the physicians met study inclusion criteria. Physicians who met criteria continued by completing three additional background questions (see physician characteristics in Table 1). The next set of questions assessed the importance of dose escalation relative to other medication attributes. These items asked physicians to select from a list of medication attributes (presented in Tables 2 and 3) to indicate which attributes most commonly prevent patients from reaching treatment goals and which attributes were most commonly perceived as a barrier to prescribing medication.

The final series of questions was designed to provide insight into physicians' decisions regarding dose escalation. For example, one question asked physicians to select from among a list of factors (presented in Table 4) they consider when deciding whether to escalate a dose of medication for T2D. Another item asked physicians to report the most common reasons for escalating a dose over the past 6 months, again by selecting from a list of potential reasons (presented in Table 5).

After each of the questions where physicians selected multiple responses from a list of options (i.e., Tables 2, 3, 4, 5), physicians were asked to rank their selections in order of importance. The exact wording of the key questions is presented in footnotes below the relevant tables.

After completing the draft survey, it was formatted for online completion and administered to the first 15 participants (i.e., 10 primary care physicians and 5 endocrinologists). Data collection was paused after these initial 15 participants so that results could be examined to ensure that the survey was functioning as intended. Results of the interim analysis led to two edits prior to continuing with data collection. First, the item assessing gender was moved to the screening section earlier in the survey so that gender could be considered as part of the screening criteria. Second, one question was deleted because it appeared to be potentially confusing. After making these two edits, the full data collection was allowed to proceed until the sample size target was met. Because no survey content was changed or added following the initial 15 completions, results from the pilot participants were included in the final dataset.

Statistical Methods

Descriptive statistics were used to summarize participants' responses and to characterize the sample in terms of sociodemographic characteristics and clinical background. For continuous variables, the mean, median, standard deviation, and range were calculated.

Table 1 Physician background information

Physician characteristics	Total sample (*N* = 501)	Primary care physicians (*N* = 348)	Endocrinologists (*N* = 153)	*P* value[a]
Years in medical practice (mean, SD)	18.7 (9.3)	18.8 (9.4)	18.4 (9.1)	0.606
Years managing or treating patients with T2D (mean, SD)	18.9 (9.3)	19.2 (9.4)	18.4 (9.2)	0.369
Practice setting description (*n*, %)				
Individual or small group practice	208 (41.5%)	161 (46.3%)	47 (30.7%)	0.004
Multi-specialty group practice	217 (43.3%)	135 (38.8%)	82 (53.6%)	
Hospital setting	57 (11.4%)	36 (10.3%)	21 (13.7%)	
Long-term care facility	6 (1.2%)	6 (1.7%)	0 (0.0%)	
Other	13 (2.6%)	10 (2.9%)	3 (2.0%)	
Gender (*n*, %)				
Male	320 (63.9%)	226 (64.9%)	94 (61.4%)	0.303
Female	176 (35.1%)	120 (34.5%)	56 (36.6%)	
Decline to respond	5 (1.0%)	2 (0.6%)	3 (2.0%)	
Region of practice in US (*n*, %)				
Northeast	130 (25.9%)	89 (25.6%)	41 (26.8%)	0.680
Midwest	117 (23.4%)	85 (24.4%)	32 (20.9%)	
South	139 (27.7%)	92 (26.4%)	47 (30.7%)	
West	115 (23.0%)	82 (23.6%)	33 (21.6%)	

SD standard deviation, *T2D* type 2 diabetes

[a]*P* values are for analyses comparing the two subgroups of participants in this table. The statistical tests were *t* tests for continuous variables and chi-square analyses for categorical variables

Categorical variables are reported as frequencies and percentages. Analyses were conducted with SAS software version 9.4 (SAS Institute, Cary, NC).

RESULTS

Sample Characteristics

Of the 602 physicians who were screened, 501 (83.2%) met criteria for study inclusion, including 348 (57.8%) primary care physicians and 153 (25.4%) endocrinologists (Fig. 1). The most common reasons for ineligibility were not being a primary care physician or endocrinologist (*n* = 47, 46.5%) and not seeing a sufficient number of patients with T2D per month (*n* = 13, 12.9%). The majority of physicians were male (*n* = 320, 63.9% of those who completed the survey), and most worked in either an individual or small group practice (*n* = 208, 41.5%) or a multi-specialty group practice (*n* = 217, 43.3%). Participants were roughly evenly distributed across the Northeast (*n* = 130, 25.9%), Midwest (*n* = 117, 23.4%), South (*n* = 139, 27.7%), and West (*n* = 115, 23.0%) regions of the US (Table 1).

Table 2 Factors preventing patients from reaching T2D treatment goals[a]

Factors that keep patients from reaching treatment goals (*n*, %)[b]	Total sample (*N* = 501)	Primary care physicians (*N* = 348)	Endocrinologists (*N* = 153)
Unhealthy diet	434 (86.6%)	306 (87.9%)	128 (83.7%)
Medication adherence problems (i.e., not taking medication as directed or skipping doses)	388 (77.4%)	272 (78.2%)	116 (75.8%)
Lack of exercise	360 (71.9%)	264 (75.9%)	96 (62.7%)
Difficulty obtaining medication	222 (44.3%)	147 (42.2%)	75 (49.0%)
Medication adverse events	140 (27.9%)	97 (27.9%)	43 (28.1%)
Missing healthcare visits	132 (26.3%)	94 (27.0%)	38 (24.8%)
Difficulty titrating doses based on blood glucose levels (e.g., with insulin)	106 (21.2%)	67 (19.3%)	39 (25.5%)
Challenges with using an injection device	97 (19.4%)	70 (20.1%)	27 (17.6%)
Frequency of medication doses	88 (17.6%)	57 (16.4%)	31 (20.3%)
Difficulty accessing healthcare	87 (17.4%)	60 (17.2%)	27 (17.6%)
Dose timing requirements (like having to take medication at a specific time)	60 (12.0%)	35 (10.1%)	25 (16.3%)
Onset of new comorbidities	54 (10.8%)	33 (9.5%)	21 (13.7%)
Physical limitations	41 (8.2%)	30 (8.6%)	11 (7.2%)
Difficulty escalating to an effective dose	38 (7.6%)	28 (8.0%)	10 (6.5%)
Cognitive issues	37 (7.4%)	28 (8.0%)	9 (5.9%)
Other reason not listed here	20 (4.0%)	13 (3.7%)	7 (4.6%)

T2D type 2 diabetes

[a]Physicians responded to the following question: "What are the primary factors that keep your patients from reaching their type 2 diabetes treatment goals, such as maintaining good glycemic control, losing weight, and reducing cardiovascular risk? (Check up to five of the most important factors)"

[b]Factors are sorted by total *N*, with the most commonly cited factors appearing first

Factors Preventing Attainment of T2D Treatment Goals

Unhealthy diet (86.6%), medication adherence problems (77.4%), and lack of exercise (71.9%) were the factors most commonly cited by physicians as preventing patients from reaching T2D treatment goals (Table 2). In contrast, few physicians (7.6%) selected "difficulty escalating to an effective dose" as a factor that prevented patients from reaching treatment goals. Of the 38 physicians (7.6%) who ranked "difficulty escalating to an effective dose" as one of the five most important factors preventing patients from reaching T2D treatment goals, only one (2.6%) ranked it as the most important factor. Reports of the primary care physicians and endocrinologists followed similar patterns.

Barriers to Prescribing T2D Medication

Over two-thirds of physicians (68.7%) reported that health plan formulary restrictions were a barrier to prescribing T2D medications

Table 3 Barriers to prescribing a medication for treatment of T2D[a]

Barriers that most frequently keep physicians from prescribing any specific medication for T2D (*n*, %)[b]	Total sample (*N* = 501)	Primary care physicians (*N* = 348)	Endocrinologists (*N* = 153)
Patient health plan formulary restrictions	344 (68.7%)	240 (69.0%)	104 (68.0%)
Injectable route of administration	230 (45.9%)	177 (50.9%)	53 (34.6%)
Risk of medication-related adverse events	200 (39.9%)	141 (40.5%)	59 (38.6%)
Patient preference	186 (37.1%)	131 (37.6%)	55 (35.9%)
Tendency to cause weight gain	161 (32.1%)	102 (29.3%)	59 (38.6%)
Insufficient efficacy for glycemic control	140 (27.9%)	82 (23.6%)	58 (37.9%)
Frequency of medication doses	118 (23.6%)	83 (23.9%)	35 (22.9%)
Insufficient effect on weight loss	110 (22.0%)	72 (20.7%)	38 (24.8%)
Durability of glycemic effectiveness	83 (16.6%)	47 (13.5%)	36 (23.5%)
Warnings and precautions in the drug label	82 (16.4%)	61 (17.5%)	21 (13.7%)
Challenges associated with escalating to an effective dose	81 (16.2%)	53 (15.2%)	28 (18.3%)
Difficulty titrating doses based on blood glucose levels (e.g., insulin)	80 (16.0%)	54 (15.5%)	26 (17.0%)
My lack of familiarity or experience with a particular medication	78 (15.6%)	69 (19.8%)	9 (5.9%)
Lack of evidence on cardiovascular outcomes	53 (10.6%)	35 (10.1%)	18 (11.8%)
Inconveniences associated with oral medication (e.g., size of pill, dose timing, food restrictions)	50 (10.0%)	32 (9.2%)	18 (11.8%)
Time required to train patients on how to properly use medication	46 (9.2%)	35 (10.1%)	11 (7.2%)
Need for refrigeration of the medication	38 (7.6%)	26 (7.5%)	12 (7.8%)
Other reason not listed here	32 (6.4%)	24 (6.9%)	8 (5.2%)

T2D type 2 diabetes

[a]Physicians responded to the following question: "When choosing among treatment options for your patients with type 2 diabetes, what are the barriers that most frequently keep you from prescribing any specific medication? (Check up to five of the most important barriers)"

[b]Barriers are sorted by total *N*, with the most commonly cited barriers appearing first

(Table 3). Other commonly reported barriers included an injectable route of administration (45.9%), concerns about the risk of medication-related adverse events (39.9%), patient preference (37.1%), and the tendency of some T2D medications to cause weight gain (32.1%). In comparison, "challenges associated with escalating to an effective dose" was reported to be a barrier to prescription less frequently (16.2%). When physicians were asked to rank the factors they consider to be barriers to prescription, health plan formulary restrictions were most commonly cited (by 67.4% of the sample) as the most important factor. Dose escalation was reported to be the primary barrier by 9.9% of the sample.

Table 4 Factors considered by physicians when deciding whether to escalate a dose of medication for T2D[a]

Factors considered by physicians when deciding whether to escalate a dose of medication to treat T2D (*n*, %)[b]	Total sample (*N* = 501)	Primary care physicians (*N* = 348)	Endocrinologists (*N* = 153)
Glycemic control and HbA1c	446 (89.0%)	312 (89.7%)	134 (87.6%)
Medication tolerability and adverse events	303 (60.5%)	207 (59.5%)	96 (62.7%)
Severity of the patient's diabetes	212 (42.3%)	155 (44.5%)	57 (37.3%)
Patient's current weight or BMI	192 (38.3%)	126 (36.2%)	66 (43.1%)
Treatment guidelines	187 (37.3%)	146 (42.0%)	41 (26.8%)
Comorbidities (e.g., hypertension, dyslipidemia, fatty liver)	173 (34.5%)	128 (36.8%)	45 (29.4%)
Escalating one antihyperglycemic medication dose may allow a patient to discontinue or decrease the dose of another medication	112 (22.4%)	65 (18.7%)	47 (30.7%)
Cardiovascular benefits of treatment	105 (21.0%)	71 (20.4%)	34 (22.2%)
Patient's reaction to a dose increase (e.g., escalation may feel discouraging to some patients)	81 (16.2%)	52 (14.9%)	29 (19.0%)
Recommendations in the drug label	74 (14.8%)	44 (12.6%)	30 (19.6%)
Patient's ability to make changes	74 (14.8%)	60 (17.2%)	14 (9.2%)
Patient's cardiovascular history	70 (14.0%)	49 (14.1%)	21 (13.7%)
Escalating the dose of one antihyperglycemic medication may complicate polypharmacy because you may need to adjust the dose of another medication	58 (11.6%)	40 (11.5%)	18 (11.8%)
Patient's age	39 (7.8%)	29 (8.3%)	10 (6.5%)
Difficulties for you and your office associated with changing from one dose to another (e.g., writing a new prescription, more follow-up appointments, patient training)	35 (7.0%)	23 (6.6%)	12 (7.8%)
Escalating a dose may be lower priority than other aspects of the patient's care (e.g., managing blood pressure, adjusting cholesterol medications)	28 (5.6%)	22 (6.3%)	6 (3.9%)
Reluctance to waste medication (e.g., if patient just picked up a 90-day supply of a dose, they may not want to change to a new dose)	26 (5.2%)	17 (4.9%)	9 (5.9%)
Duration of the patient's diabetes	22 (4.4%)	11 (3.2%)	11 (7.2%)

BMI body mass index, *HbA1c* glycated hemoglobin, *T2D* type 2 diabetes

[a]Physicians responded to the following question: "What are the factors you consider when deciding whether to escalate the dose of medication used to treat type 2 diabetes? (Check up to five of the most important factors)"

[b]Factors are sorted by total *N*, with the most commonly cited factors appearing first

Table 5 Reasons for escalating a dose of medication for their patients with T2D[a]

Most common reasons physicians have escalated a dose for patients with T2D in the past 6 months (*n*, %)[b]	Total sample (*N* = 501)	Primary care physicians (*N* = 348)	Endocrinologists (*N* = 153)
Patient needed more HbA1c benefit or glycemic control	450 (89.8%)	317 (91.1%)	133 (86.9%)
By increasing the dose of one medication, you were able to decrease the patient's total number of pills or injections	200 (39.9%)	126 (36.2%)	74 (48.4%)
Patient needed more weight loss	197 (39.3%)	123 (35.3%)	74 (48.4%)
There were no tolerability concerns at a lower dose, which made it possible to increase the dose	194 (38.7%)	130 (37.4%)	64 (41.8%)
You were trying to maximize cardiovascular benefits of treatment	167 (33.3%)	126 (36.2%)	41 (26.8%)
A higher dose was recommended in treatment guidelines	110 (22.0%)	88 (25.3%)	22 (14.4%)
A higher dose was recommended in the drug label	40 (8.0%)	22 (6.3%)	18 (11.8%)
Patient requested a higher dose	15 (3.0%)	11 (3.2%)	4 (2.6%)

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HbA1c glycated hemoglobin, *T2D* type 2 diabetes

[a]Physicians responded to the following question: "In the past 6 months, what are the most common reasons you have escalated a dose for your type 2 diabetes patients? (Check up to five reasons)"

[b]Reasons are sorted by total *N*, with the most commonly cited reasons appearing first

Factors Contributing to Decisions About Dose Escalation

To identify factors that physicians consider when deciding whether to escalate a dose of medication for T2D, they were asked to select the five most important factors from the list of 18 factors presented in Table 4. "Glycemic control and HbA1c" were selected as one of the five most important factors by 446 physicians (89.0% of the sample). Of these 446, 74.9% reported that this was the most important factor contributing to dose escalation decisions. "Medication tolerability and adverse events" appears to be a second primary factor, selected by 60.5% of the sample. While no other factors were selected by a majority of the sample, the other common factors included severity of the patient's diabetes (42.3%), the patient's current weight or body mass index (BMI) (38.3%), treatment guidelines (37.3%), and comorbidities (34.5%). Responses to this question followed similar patterns for the primary care physicians and endocrinologists (Table 4).

Respondents were also asked about the most common reasons they have escalated a dose for patients during the past 6 months (Table 5). Consistent with results in Table 4, they reported most commonly escalating a dose because their patients required more glycemic control (89.8%). Other reasons that were somewhat commonly cited included the ability to decrease total medication burden by increasing the dose of one medication (39.9%), the need for more weight loss (39.3%), and the fact that there were no tolerability concerns at a lower dose, which made it possible to increase the dose (38.7%). Physicians were also asked about the factors that cause them not to escalate a dose for one of their patients. The most commonly cited reasons were the potential for adverse events at a higher dose (68.5%), additional glycemic control was not needed (66.3%), dosing limitations associated with comorbidities such as chronic kidney disease (49.7%), and the patient's age (25.0%). Reasons for escalating and not escalating a dose followed similar patterns for the primary care physicians and endocrinologists.

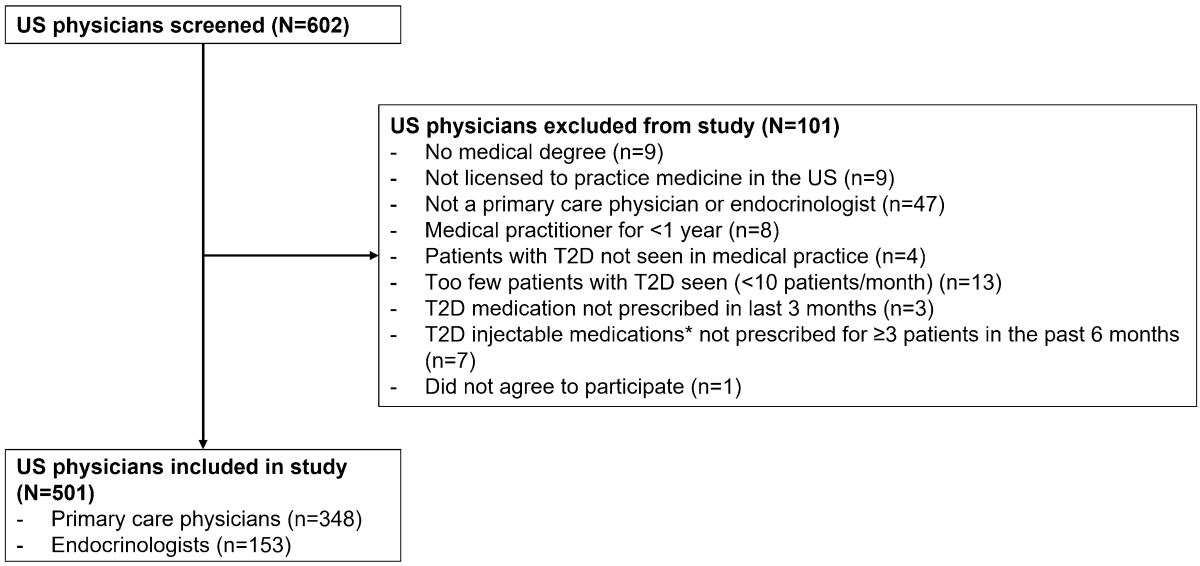

Fig. 1 Participant disposition. T2D, type 2 diabetes. *Excluding rescue medications

DISCUSSION

Previous research has examined patient and physician perceptions of a wide range of attributes of medications for treatment of T2D [9, 14]. For example, medication attributes shown to have an impact on patient preference include glycemic control, adverse event profile, dose frequency, injection device, dose flexibility, and medication preparation requirements [14]. However, the current study is the first to focus on dose escalation for the treatment of T2D. Results of the current survey suggest that endocrinologists and primary care physicians may not perceive dose escalation to be a significant challenge. These findings add to a previous study indicating that patients perceived dose escalation to be one of the least important characteristics of treatments for T2D [27].

Only 16.2% of physicians in this sample reported that dose escalation was a potential barrier to prescribing medication for their patients with T2D. Furthermore, only 7.6% considered dose escalation requirements to be one of the top five factors preventing patients from reaching treatment goals. The factors that were most commonly believed to interfere with treatment goals tended to be related to patient behavior, such as unhealthy diet, medication adherence, lack of exercise, and missing healthcare visits. In addition, a range of treatment process attributes were perceived to interfere with treatment goals more commonly than dose escalation (e.g., the need to titrate doses based on glucose levels, dose frequency, dose timing requirements). In general, these results were similar across the subgroups of endocrinologists and primary care physicians. Overall, these findings help place dose escalation in context of other T2D medication attributes. From the physician perspective, requirements for dose escalation appear to be a less important concern than the effects of the medication as well as other treatment process attributes.

Results also provide insight into physicians' decision-making regarding dose escalation. Responses to several questions in this survey indicate that decisions to escalate a dose are complex, driven by a range of factors. The need for increased glycemic control was the most commonly reported reason that physicians escalate a dose, but they reported considering multiple factors when making these decisions, including medication tolerability, the patient's current weight or BMI, treatment guidelines,

comorbidities, characteristics of the patient's entire treatment regimen, and potential cardiovascular benefits.

Findings should be interpreted in the context of several limitations. First, the survey was conducted with a sample of physicians who treat T2D; therefore, results cannot provide insight into the patient perspective. It is possible that patients could have different views of dose escalation requirements, and future research is needed to examine the patient perspective.

Second, because this survey was designed to be administered efficiently to a large number of physicians, structured responses were provided for each question. This structured quantitative approach does not allow for the rich detailed responses that can be gathered in qualitative interviews or questions with free-text response fields. It is possible that a less structured approach could identify additional factors contributing to dose escalation decisions. For example, frequency of interaction with their HCPs as well as quality of shared decision-making with these HCPs [28, 29] could be additional factors that have an impact on ultimate treatment goals. In addition, the survey was designed to be brief, which means that some potentially relevant questions were not addressed. For example, the number of participants who recently performed a dose escalation is not known.

Finally, there may be limitations associated with the representativeness and generalizability of this sample of physicians in the US. Although recruitment targets ensured a geographically diverse sample from across the US, the HCP panel recruitment approach does not necessarily ensure that the sample is nationally representative. Furthermore, physicians working in other countries with different healthcare systems could have different priorities related to dose escalation. Therefore, generalizability of the current results to other countries is unknown, and future research should examine issues associated with dose escalation outside the US.

CONCLUSIONS

This study adds to previous research on physicians' perceptions of attributes of treatments for T2D. Results suggest that physicians consider multiple factors when deciding whether to escalate a dose for their patients, including effectiveness, tolerability, and a range of patient characteristics. Overall, responses to this survey suggest that physicians who treat T2D do not perceive the requirement for dose escalation to be a significant barrier to achieving treatment goals or prescribing a specific medication.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. Louis S. Matza and Jessica B. Jordan are employees of Evidera, a company that received funding from Eli Lilly and Company for time spent conducting this research. Kristina S. Boye and Raleigh Malik are employees of and own stock in Eli Lilly and Company.

Ethical Approval. Participants provided informed consent before completing the survey. All procedures and materials were approved by a central institutional review board (22131-01A, Ethical and Independent Review Services), which was conducted in accordance with the Declaration of Helsinki. All surveys were completed from July to September 2022.

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