

Physician Preferences for Extra-Glycemic Effects of Type 2 Diabetes Treatments

Christine Poulos · Juan Marcos González ·
Lauren J. Lee · Kristin S. Boye ·
F. Reed Johnson · Jay P. Bae · Mark A. Deeg

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ABSTRACT

Introduction: The purpose of this study was to quantify United States (US) and United Kingdom (UK) physicians' preferences for attributes of type 2 diabetes treatments.

Methods: Samples of general practitioners (GPs) and endocrinologists in the US ($n = 204$) and the UK ($n = 200$) completed a discrete-choice experiment in which respondents chose

between pairs of hypothetical type 2 diabetes treatments in a series of trade-off questions. The questions described hypothetical injectable treatments with differing levels of attributes, such as glucose control and treatment side effects. Relative importance of attributes was estimated by a multivariate regression model for limited dependent variables. These results were used to calculate how the predicted probability of choosing hypothetical type 2 diabetes treatments varies with changes in given attributes.

Results: The most important attributes to physicians were glucose control, risk of a fatal myocardial infarction (MI), and weight change. For US physicians, glucose control was about twice as important as gastrointestinal side effects, 5 times more important than changes in depression symptoms, and 20 times more important than liver monitoring. For UK physicians, reduction in MI risk was about 1.5 times more important than glucose control, 2.5 times more important than gastrointestinal side effects, and 10 times more important than liver-monitoring requirements. Preferences were similar among physicians in the US and the UK and among GPs and endocrinologists.

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C. Poulos (✉) · J. M. González · F. R. Johnson
RTI Health Solutions, 200 Park Offices Drive,
Research Triangle Park, NC 27709, USA
e-mail: cpoulos@rti.org

L. J. Lee · K. S. Boye · J. P. Bae · M. A. Deeg
Eli Lilly and Company, Indianapolis, IN 46285, USA

Present Address:
L. J. Lee
Daiichi Sankyo, Inc., Parsippany, USA



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Conclusions: Physicians valued type 2 diabetes treatments that go beyond glycemic control, although mitigating different complications and comorbidities was not equally as important.

Keywords: Conjoint analysis; Diabetes treatments; Discrete-choice-experiment survey; Extra-glycemic effects; Glycemic control; Patient preferences; Type 2 diabetes mellitus

INTRODUCTION

Diabetes causes significant clinical and economic burden in the US and the UK [1–4]. Achieving effective glycemic control in patients with diabetes reduces microvascular complications, as well as long-term risks of macrovascular disease [5]. Even with glycemic control, complications and comorbidities, including cardiovascular disease, depression, and obesity, have significant effects on both the clinical and economic burden of type 2 diabetes. In particular, patients with type 2 diabetes have two to four times higher risk of cardiovascular disease than adults without diabetes, which constitutes the largest share of the cost of diabetes [1, 5, 6]. Depression is at least twice as prevalent among individuals with diabetes as it is among non-diabetics, increasing the risk of diabetic complications [7, 8]. Finally, obese adults are much more likely to have diabetes than adults who are not obese [3]. About 13% of the expenditures on metabolic conditions (including the estimated annual costs of \$92.6 billion on obesity in the US) are attributable to diabetes [3, 9, 10]. In addition, liver abnormalities are more prevalent among individuals with diabetes; thus, managing diabetes could be complicated by liver-related alterations in drug metabolism, drug interactions, and risk of hepatotoxicity [11].

An additional challenge is that almost one-third of diabetic patients do not adhere to their treatment regimen, leading to poorer glycemic control and increased risk of complications, hospitalizations, and death [12–14]. A recent review identified more frequent or complex dosing, treatment-related weight gain, persistent gastrointestinal (GI) side effects, and depression to be among the factors that impair adherence [15].

Diabetes outcomes are improved when management goes beyond glycemic control to managing comorbidities and complications [5], and such therapies have been a focus of research and clinical practice [16]. However, little is known about how prescribing physicians weigh the relative importance of glucose control, managing comorbidities and complications, and other treatment attributes that could affect adherence. The objective of this study was to quantify US and UK physicians' preferences for extra-glycemic benefits of type 2 diabetes relative to other attributes of type 2 diabetes treatments. There are no type 2 diabetes treatments with proven depression benefits, and most treatments (with the exception of thiazolidinediones) do not require liver monitoring. Thus, the latter two outcomes are novel with respect to existing treatments, and this study is exploratory in terms of understanding preferences for these outcomes.

A discrete-choice-experiment (DCE) survey provided data on physician respondents' evaluations of pairs of hypothetical diabetes treatments. Treatment profiles described hypothetical injectable treatments with differing levels of treatment attributes. DCE is a valid and reliable survey technique for eliciting trade-offs to quantify the relative importance respondents assign to attributes and outcomes of health interventions [17, 18].

These methods increasingly are used to quantify preferences for treating diabetes and other health conditions [19–22].

MATERIALS AND METHODS

A DCE is based on the principle that medical treatments are comprised of multiple characteristics. Physicians' disposition to prescribe a treatment depends on the characteristics of both the treatment and the patient being treated. In a DCE, respondents make hypothetical prescribing decisions about constructed treatment alternatives. The researcher controls the features of the treatment alternatives and the patient characteristics; physicians' patterns of choices are analyzed to estimate the implicit relative importance weights physicians use to identify preferred treatment alternatives [17, 23].

Survey Development, Pretests, and Administration

This study described hypothetical injectable type 2 diabetes treatments using seven treatment features (or attributes) based on published literature, consultation with clinical experts, and one-on-one interviews with physicians. The treatments of interest were non-insulin injectables used to treat patients who had failed to respond to two or three oral medications. The following criteria were used to identify attributes that: (a) were of potential therapeutic interest; (b) were clinically relevant; (c) reflected other, nonclinical features of concern to physicians; and/or (d) incorporated physicians' assessments of patient concerns. The resulting attributes included: glucose control [treated hemoglobin A1c (HbA1c) levels], weight change, frequency of injection,

Table 1 Attributes and levels in type 2 diabetes treatments surveys

Treatment attribute	Level
Glucose control within 3 months	Reduces HbA1c to 7.0%
	Reduces HbA1c to 8.0%
	Reduces HbA1c to 8.3%
Frequency of injections	2 injections/day
	1 injection/day
	1 injection every other day
	1 injection/week
Liver monitoring test	1 injection/month
	Not required
	Every month for the first 3 months, then quarterly as long as the patient takes the medicine
Change in body weight	5% weight gain
	No change
	5% weight loss
	10% weight loss
Mild to moderate nausea, diarrhea, and/or vomiting 3–4 times/week	20% weight loss
	None
	Resolves after taking medicine for 2 weeks
	Continues as long as patient takes medicine
Changes in the risk of a fatal MI over 5 years	No effect
	Reduces 5-year risk of fatal MI by 5/1,000 (from 25/1,000 to 20/1,000)
	Reduces 5-year risk of fatal MI by 15/1,000 (from 25/1,000 to 10/1,000)
Changes in depression symptoms	No reduction in symptoms
	From moderate to mild depression
	From moderate to no depression

HbA1c hemoglobin A1c, *MI* myocardial infarction

GI side effects, requirement for liver monitoring, reduction in the 5-year risk of a fatal myocardial infarction (MI), and reduction in depression symptoms (Table 1).

The first section of the survey instrument obtained information on physicians' characteristics and experience in treating patients with type 2 diabetes, as well as their target level of glucose control for a type 2 diabetes patient with the following characteristics: aged 45–65 years, obese class II

(body mass index 35–40 kg/m²), sedentary lifestyle, moderate depression (a score of 15–19 on the Patient Health Questionnaire or a score of 14–18 on the Hamilton Depression Rating Scale), failure to respond to two or three oral agents, and an HbA1c level of 9%. The second section provided physician respondents with definitions of the treatment attributes and levels. Levels are specific values for the treatment attributes. For example, weight change is an attribute, which may take on several possible levels such as 5% weight gain, 5% weight loss, or 10% weight loss. MI risks were presented as frequencies [24]. The third section included the trade-off questions that asked physicians to choose which of two hypothetical injectable treatment profiles they would recommend as the next line of treatment

for the patient described (Fig. 1). All hypothetical treatments were injectables, because injectables often are the next line of treatment for patients with the target profile.

The draft survey instrument was pretested and refined based on in-depth, semistructured interviews conducted with 15 physicians in the US and 5 physicians in the UK. The objectives of the pretests were to test the understandability of the survey instrument, the appropriateness of descriptive information, and the cognitive burden of the trade-off questions. The US pretests were completed first. The final survey instrument for the US study was adapted for the UK, and the UK pretests were used to evaluate whether any cultural adaptations were necessary to facilitate comprehension of the survey concepts. As with the final sample,

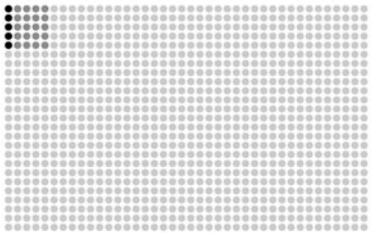
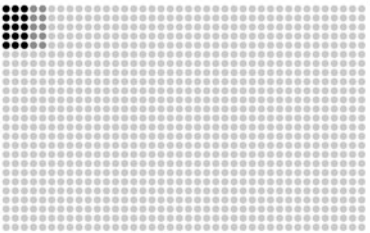
Medicine Features	Medicine A	Medicine B
Current glucose control within 3 months	Reduces HbA1C to 8.3%	Reduces HbA1C to 7.0%
Changes in body weight	5% weight <u>gain</u>	20% weight <u>loss</u>
Changes in depression symptoms	From moderate depression to no depression	No reduction in symptoms
Changes in the risk of a fatal MI over 5 years	 Prevents 5 of 25 cases	 Prevents 15 of 25 cases
Frequency of injections	1 injection per month	2 injections per day
Liver monitoring test	Not required	Every month for the first 3 months, then quarterly as long as the patient takes the medicine
Mild to moderate nausea, diarrhea, and/or vomiting 3-4 times per week	None	Continues as long as patient takes medicine
Which treatment would you choose if these were the only treatments available?	Medicine A <input type="radio"/>	Medicine B <input type="radio"/>

Fig. 1 Example of a choice question for the patient profiled with a baseline HbA1c level of 9%. *HbA1c* hemoglobin A1c, *MI* myocardial infarction

around half of the US pretest respondents were endocrinologists and the other half were primary care physicians, internists, or family practitioners. All UK pretest respondents were general practitioners (GPs). The sample in the UK had more experience, having been in practice at least 16 years, while the US sample had 1 to >25 years of experience. The UK sample treated fewer patients per week, on average, than the US sample. As described below, similar differences in experience and number of patients were observed in the full study sample.

As a result of the pretest findings, the survey instrument was adapted to improve the descriptive information, and to reduce the cognitive burden of the trade-off questions. Statements were added regarding what the hypothetical treatments would be in addition to oral treatments, and that the treatment outcomes already accounted for potential interactions between glucose control, weight loss, and MI risk. The question about target HbA1c was added as physicians in the pretests reported various HbA1c targets. In addition, the glucose control attribute was changed from describing changes in HbA1c (e.g., “0.7% reduction”) to describing the level to which HbA1c was reduced. The GI side effects attribute was refined to describe the severity of symptoms, and a number of revisions to the patient profile were made, including adding the baseline level of HbA1c, narrowing the BMI range from 35–45 kg/m² to 40–45 kg/m², and dropping a second patient profile in which the patient had no depression. A number of minor editorial changes were also made based on the pretests, and the final survey instrument was programed for online administration.

To create the stimuli used to construct the treatment profiles and pairs in the choice questions, we employed a D-efficient

experimental design that resulted in 96 hypothetical treatment pairs [25–27]. Because the quality of responses to choice questions declines as the number of choice tasks increases, leading to fatigue or cognitive burden [28, 29], we divided the 96 paired comparisons in the experimental design into eight survey versions, each containing 12 choice questions. Each physician was randomly assigned to one of the eight versions of the experimental design, and the order of the choice questions was also randomized for each respondent.

Sample Recruitment

Physicians from an online opt-in physician panel were invited to complete the survey by e-mail. Physicians were recruited to the panel by phone, online, or face-to-face interviews with eligibility verified by a third party at their place of work. As an opt-in panel, some potential selection bias might exist, such as panel members being more interested in and/or more available for participation in survey research. Invitations to participate in the survey were sent to a random sample of panel members who met the sample inclusion criteria: (1) board-eligible or board-certified primary care physicians in the US or GPs in the UK or endocrinologists from either country, and (2) treat patients with type 2 diabetes regularly. The panel recruitment and study recruitment procedures were the same in the US and the UK.

There are no power calculations for DCEs [30]. Most published conjoint analysis studies have a sample size between 100 and 300 respondents [18]. However, minimum sample size depends on a number of criteria, including the question format, the complexity of the choice task, the desired precision of the results, and the need to conduct subgroup analyses [30]. Given the results of a recent meta-regression

[30], the research team's previous experience, previously published studies [18], and an interest in estimating separate results for the UK and US samples, the study aimed to interview 200 respondents in each country.

The Office of Research Protection and Ethics at Research Triangle Institute granted a consent exemption for this study, indicating that this research did not meet the definition of human (or animal) subjects research. US physicians received a \$55 cash honorarium for participating in the survey. UK GPs received the equivalent of a \$66 cash honorarium, while UK endocrinologists were given the equivalent of \$75. The 25-minute online survey was administered in February 2012.

Statistical Analysis

The pattern of physicians' responses to the choice questions was analyzed using a random-parameters logit (RPL) model. Results from the RPL model are log-odds estimates relative to the mean effect normalized at zero and represent the weighted effect of each treatment attribute level on respondents choosing a profile containing that attribute level. These estimates also can be interpreted as preference weights indicating the relative strength of preference for each attribute, and differences between preference weights indicate the relative strength of preference for changes among attribute levels in the study.

The parameter estimates were combined with the treatment profiles in the experimental design to obtain a conjoint-utility index that indicated the average value score that physicians would assign to prescribing the treatment of interest to the target patient. The conjoint-utility index was used to examine how predicted choice probabilities (the likelihood that one

treatment would be chosen over another treatment) would change in response to changes in a single medication attribute, other factors held constant.

RESULTS

Physician Sample Characteristics

E-mail invitations to participate in the survey were sent to 691 physicians in the US and 1,915 physicians in the UK. Of these, 264 US physicians (38.2%) and 306 UK physicians (15.9%) responded. Of the physicians who responded, 204 (77.3%) in the US and 200 (65.4%) in the UK met the inclusion criteria and completed the survey.

One respondent in each of the US and UK samples had no variation in their treatment-profile choices (always picked treatment A or treatment B). They were deleted from the sample as this lack of variation in response likely indicated that they did not pay attention to the choice questions. The final sample sizes used for analysis were therefore 203 physicians in the US and 199 in the UK.

The characteristics of the respondents the US and UK samples are shown in Table 2. The average UK physician was younger and had not been in practice as long as the average US physician ($P < 0.05$). UK physicians treated fewer patients than US physicians ($P < 0.05$), and a larger percentage of the UK physicians selected higher target HbA1c levels for the patient profile ($P < 0.01$).

Preferences for Treatment Attributes

Figure 2 presents the estimated log-odds preference estimates for US and UK physicians and the 95% confidence intervals (CI) for the seven treatment attributes. The estimated

Table 2 Summary of physicians' characteristics

Characteristic	Statistic or category	US	UK
		<i>n</i> = 203 <i>n</i> (%)	<i>n</i> = 199 <i>n</i> (%)
Percent of respondents who were women		42 (20.7%)	47 (23.6%)
Mean respondent age in years (SD) ^{*a}		52.5 (9.5)	44.5 (8.2)
Number of years in practice ^{*b}	Less than 1 year	0 (0.0%)	0 (0.0%)
	1–3 years	3 (1.5%)	0 (0.0%)
	4–6 years	13 (6.4%)	11 (5.5%)
	7–9 years	11 (5.4%)	12 (6.0%)
	10–15 years	42 (20.7%)	73 (36.7%)
	16–20 years	40 (19.7%)	46 (23.1%)
	21–25 years	52 (25.6%)	37 (18.6%)
	More than 25 years	42 (20.7%)	20 (10.1%)
Type of practice ^c	Office-based private practice (general practice) ^d	177 (87.2%)	96 (48.2%)
	Hospital-based private practice (NHS hospital)	23 (11.3%)	108 (54.3%)
	Academic hospital-based practice (private practice)	23 (11.3%)	10 (5.0%)
	Other—not specified (other—not specified)	3 (1.5%)	0 (0.0%)
Respondent's area of specialization	Primary care (general practice) ^d	5 (2.5%)	93 (46.7%)
	Family medicine (general medicine)	43 (21.2%)	11 (5.5%)
	Internal medicine (N/A)	54 (26.6%)	N/A
	Endocrinology (endocrinology/diabetology)	100 (49.3%)	95 (47.7%)
	Other (specialty not specified)	1 (0.5%)	0 (0.0%)
Number of patients with type 2 diabetes treated each week ^{*b}	5 patients or less	3 (1.5%)	4 (2.0%)
	6–10 patients	7 (3.5%)	13 (6.5%)
	11–20 patients	20 (9.9%)	45 (22.6%)
	21–30 patients	44 (21.7%)	41 (20.6%)
	31–40 patients	21 (10.3%)	32 (16.1%)
	41–50 patients	38 (18.7%)	34 (17.1%)
	51–75 patients	38 (18.7%)	19 (9.6%)
	76–100 patients	22 (10.8%)	7 (3.5%)
More than 100 patients	10 (4.9%)	4 (2.0%)	

Table 2 continued

Characteristic	Statistic or category	US	UK
		<i>n</i> = 203 <i>n</i> (%)	<i>n</i> = 199 <i>n</i> (%)
Target level of HbA1c for patient profile ^{a,c}	4.0%	0 (0.0%)	1 (0.5%)
	4.5%	1 (0.5%)	0 (0.0%)
	5.0%	1 (0.5%)	4 (2.0%)
	5.5%	2 (1.0%)	5 (2.5%)
	6.0%	18 (8.9%)	9 (4.5%)
	6.5%	81 (39.9%)	32 (16.1%)
	7.0%	90 (44.3%)	79 (39.7%)
	7.5%	10 (4.9%)	69 (34.7%)

N/A not applicable, *NHS* National Health Service, *SD* standard deviation, *UK* United Kingdom, *US* United States

* The difference between the characteristics in the US and UK samples was statistically significant ($P < 0.01$)

^a A two-tailed *t* test was used to test for differences in mean age of the respondents between countries

^b A Pearson's Chi-squared test was used to test for differences in the patterns of responses in this categorical variable between countries

^c Results may sum to more than 100% because multiple responses were permitted

^d Categories in parentheses are used in the UK version of the instrument. US and UK response categories shown in the same cell are not necessarily parallel

^e The patient profiled in the survey had the following characteristics: aged 45–65 years, obese class II (BMI 35–40 kg/m²), sedentary lifestyle, moderate depression (score of 15–19 on the Patient Health Questionnaire or score of 14–18 on the Hamilton Depression Rating Scale), and failure to respond to two or three oral agents

preference weights were generally consistent with the natural order of attribute levels (e.g., lower HbA1c levels were preferred to higher HbA1c levels). In three instances, the order of measured preference weights were inconsistent with the expected order of preference for the attribute levels: one injection per day was preferred to one injection every other day in the US sample; one injection per week was preferred to one injection every month in the US sample; and GI side effects that resolved after taking the medication for 2 weeks were preferred to no GI side effects in the UK sample. However, the differences between disordered preference weights were not statistically significant ($P > 0.05$).

The difference between the most-preferred and least-preferred level of an attribute

indicates the overall relative importance of each attribute, conditional on the attributes and levels shown in the survey. The overall relative importance of all medication attributes except glucose control were similar across the US and UK samples ($P > 0.05$), indicating that physicians in the US and UK samples had similar preferences. However, glucose control was more important to US physicians than to UK physicians ($P < 0.01$).

Although glucose control was the most important attribute for US physicians, the relative importance of this attribute was not significantly different from the importance of reducing the 5-year risk of experiencing a fatal MI, and change in body weight, which were the second and third most important attributes. For UK physicians in the sample, a reduction in the

5-year risk of experiencing a fatal MI was the most important attribute, followed by change in body weight and glucose control. For physicians in both countries, liver monitoring and changes in depression symptoms were the least important attributes of the medication.

GPs and endocrinologists in both countries had similar preferences for treatment attributes. In the US, preference weights for treatment

attributes were not significantly different between GPs and endocrinologists ($P > 0.05$). However, in the UK, GPs had significantly lower preference weights for liver monitoring requirements ($P < 0.05$), whereas endocrinologists did not distinguish between medications requiring liver monitoring and those that did not ($P > 0.05$). The overall

Changes in Treatment Attributes

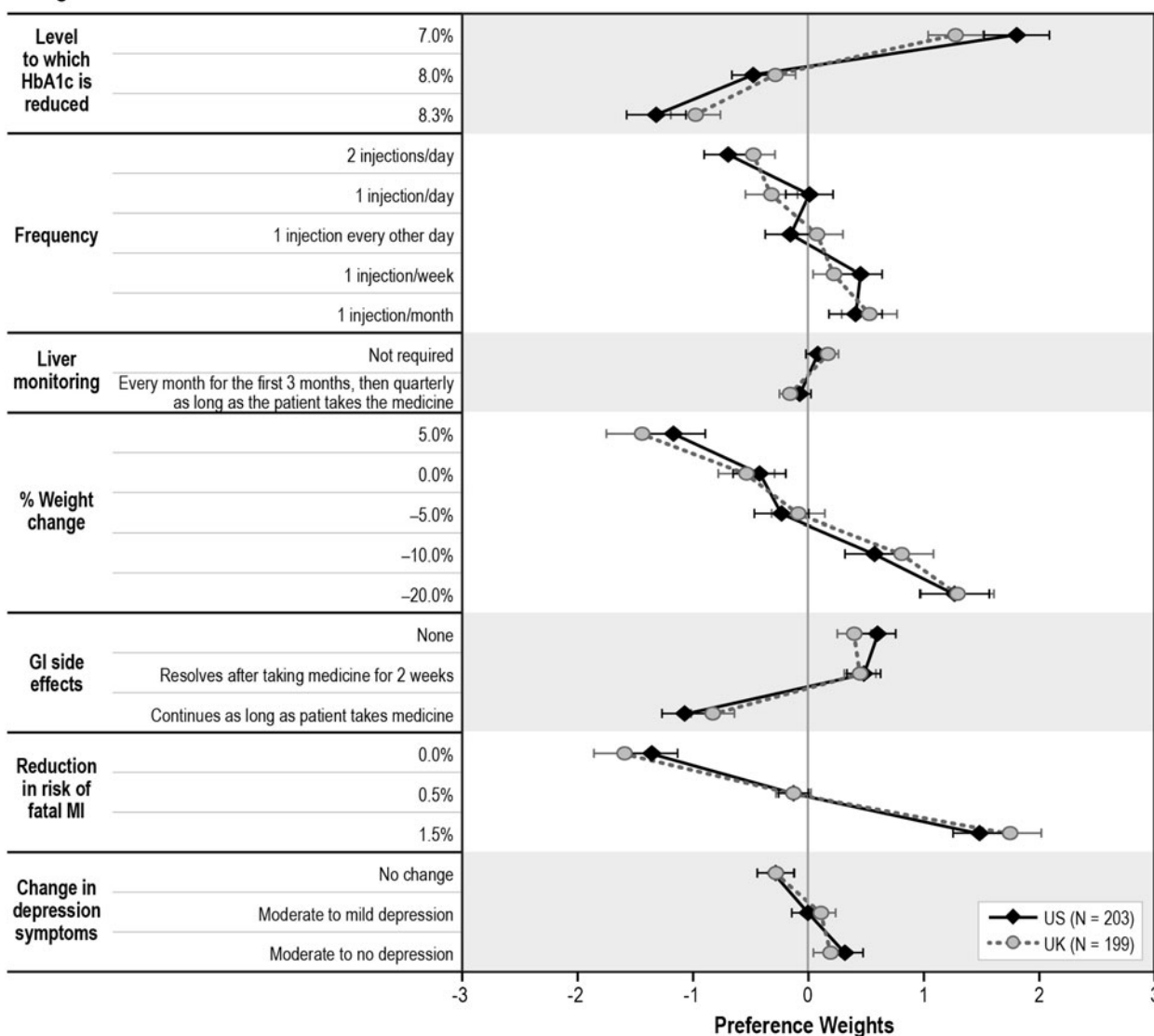


Fig. 2 Estimated physicians’ preference weights for attributes of type 2 diabetes treatments (95% CIs). *CI* confidence interval, *GI* gastrointestinal, *HbA1c* hemoglobin A1c, *MI* myocardial infarction

relative importance of the remaining attributes was not significantly different between UK endocrinologists and GPs ($P > 0.05$).

Figure 3 summarizes selected marginal choice probabilities. All marginal choice probabilities for the study are reported in an online Appendix. For example, if a treatment further improves HbA1c to 7.0% compared with 8.3% from a baseline level of 9%, the predicted choice probability for that treatment increases

by 46 and 41 percentage points in the US and UK samples, respectively. If depression benefits improve from having no effect on moderate depression symptoms to eliminating moderate depression symptoms, the predicted choice probability increases by 15 and 12 percentage points in the US and UK samples, respectively.

The largest marginal choice probabilities in both the US and UK samples were associated with the largest changes in glucose control

Changes in Treatment Attributes

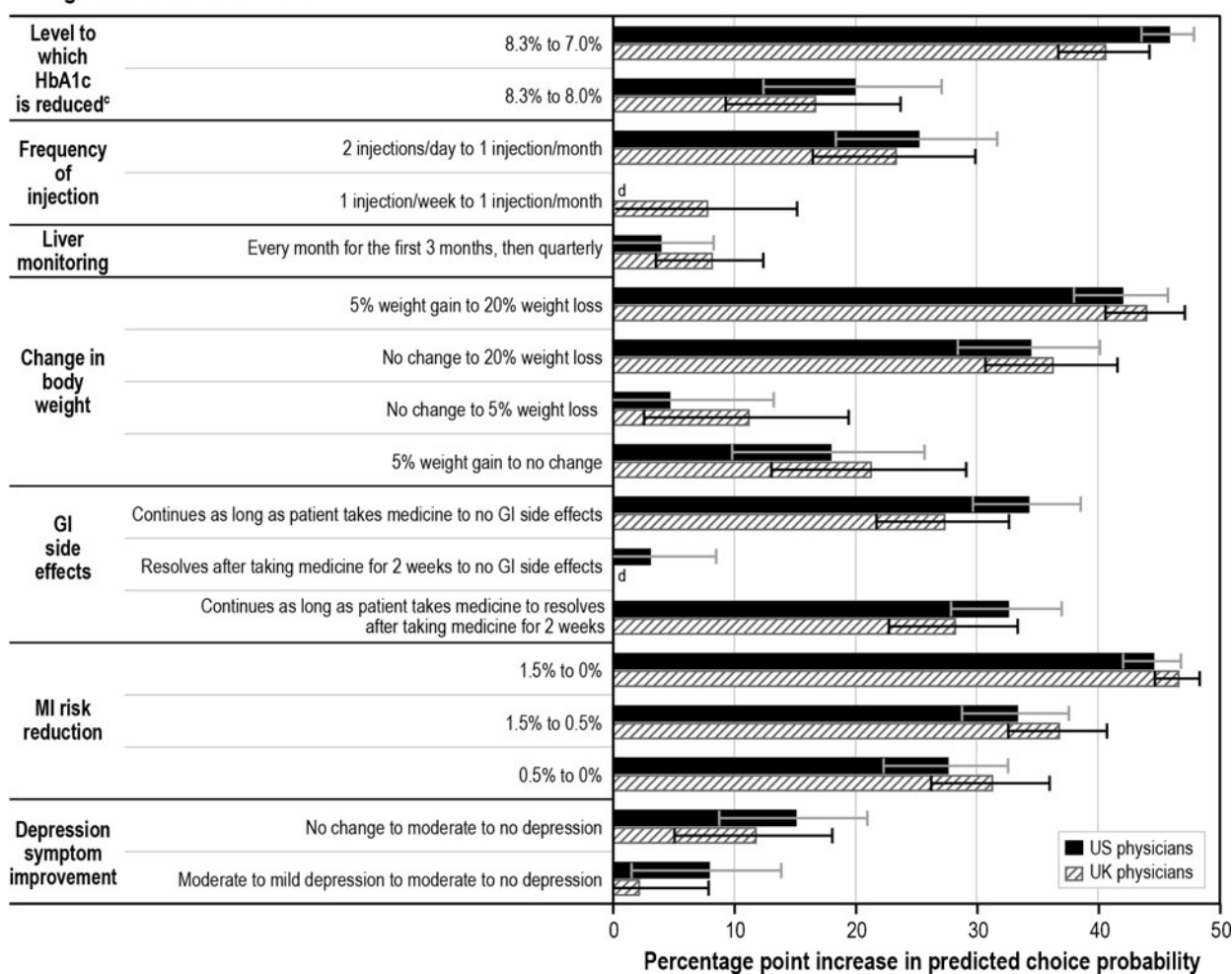


Fig. 3 Selected estimates of marginal choice probabilities for given improvements in medication attributes^{a,b}. *HbA1c* hemoglobin A1c, *GI* gastrointestinal, *MI* myocardial infarction. ^aThe estimates implicitly assume that all attributes other than that being valued remain unchanged. ^bBrackets indicate 95% CIs. ^cThe patient profile indicated

that the patient had a baseline HbA1c level of 9%. ^dThe marginal choice probability was not calculated for this change, because the estimated preferences for this sample were not consistent with the natural ordering of the medication feature

(from 8.3 to 7.0%), body weight (from 5% weight gain to 20% weight loss), and the 5-year risk of fatal MI (from 0 to 1.5%) (Fig. 3). In the US sample, the smallest positive marginal choice probability (4%) was associated with changes in liver monitoring requirements (from monitoring liver enzymes every month for the first 3 months, then quarterly as long as the patient takes the medicine, to no liver monitoring requirements). In the UK sample, the smallest positive marginal choice probability (2%) was associated with changes in depression symptoms.

Larger changes in GI side effects (from continuing as long as patient takes medicine, to either resolving after 2 weeks, or no GI side effects) were more important than relatively small changes in efficacy (from an HbA1c of 8.3 to 8.0%). Also, avoiding a 5% weight gain was two to three times as important to physicians as a 5% weight loss (Fig. 3). That is, avoiding a 5% weight gain was predicted to increase the choice probability by 18 or 21 percentage points, depending on the sample, while a 5% weight loss would increase the choice probability by only 5 or 11 percentage points, on average.

To assess whether preference differences were due to differences in age and experience between the US and UK physicians, interaction terms were added to the US and UK models. Respondents' reported age and years of experience were interacted with each treatment-attribute variable. The significance of the all age interactions and all experience interactions were tested separately; neither set of interactions was found to be statistically significant. Given that the estimates for the age interaction terms and experience interaction terms represent adjustments to preference weights based on respondents' age and years of experience, respectively, these results indicate that there was no statistically

significant effect of age or experience on preferences for treatment attributes.

DISCUSSION

US and UK physicians in our sample valued type 2 diabetes treatments that would go beyond glycemic control (i.e., HbA1c reduction) to help control diabetes complications and comorbidities. Physicians placed about as much overall importance on cardiovascular and weight benefits from diabetes treatments as they placed on glucose control. Physicians did not place much overall importance on depression benefits or on requirements for liver monitoring. We can only speculate about why physicians value some extra-glycemic benefits more than others. Physicians may place greater weight on familiar attributes than on attributes that are not present in currently marketed diabetes medications.

Our survey-development activities indicated that the links between diabetes and both weight and cardiovascular outcomes were well documented in the literature and well understood by the physicians who participated in the pretests. However, the links between type 2 diabetes and depression are not as well documented, and pretest physicians varied in the extent to which they considered diabetes and depression to be correlated. Some physicians in the pretest also noted that there are numerous effective and inexpensive depression medications currently available, and one physician was concerned that combining treatments would limit the extent to which depression medications could be titrated.

On average, physicians placed a low weight on liver monitoring requirements. Many of the pretest physicians noted that they test diabetes patients' glucose levels frequently and can

conduct a liver monitoring test using the blood drawn for that purpose without changing treatment practices.

To our knowledge, there has been only one previously published study of physicians' preferences for type 2 diabetes treatments. Porzolt and colleagues [31] examined German physicians' relative preferences for glucose control, side effects, convenience, and weight change. Our findings are consistent with their results, that weight change was as important to German physicians as glucose control.

Larger changes in GI side effects were more important than relatively small (and less clinically meaningful) changes in efficacy, and about as important as changes in fatal MI risk and larger changes in weight loss. Many pretest physicians stated that GI side effects were key factors in treatment adherence and persistence.

Physicians had a strong aversion to weight gain. This has been observed in other studies [32] and suggests that avoiding even a relatively small weight gain among patients like the one described in the survey is more important than a similarly small weight loss.

The study was conducted in the US and the UK to explore physicians' relative preferences for extra-glycemic control outcomes in two settings with different health care systems. Preferences for type 2 diabetes treatment outcomes generally were similar in the two samples. The three most important attributes in the US sample were glucose control, MI risk reduction, and weight change, though the importance differences were not statistically significant. The three most important attributes in the UK sample were the same, however, glucose control was less important than MI risk reduction ($P < 0.05$) while the importance differences for weight change and MI risk reduction were not statistically different. Glucose control was less important in the UK sample than in the US

sample ($P < 0.01$). The reason for this is not clear from the study, though differences in experience and the health care systems could play a part. Physicians in the UK were younger, on average; had been practicing fewer years; and reported higher target HbA1c levels for the patient profiled in the survey than the US sample. However, regression analyses suggested that age and experience did not influence estimated preferences. It is possible that the differences are due to other differences in the study populations, perhaps related to different response rates in the US and the UK. The same processes and criteria were used to recruit physicians to the panel and to invite physicians to participate in the study, but there are potentially many other factors (e.g., holidays, professional conferences, other studies in same topic) that may have influenced enrollment differently between the two countries. However, we are not aware of any information indicating that other factors may have affected the response rates in this study.

Finally, at the time of the survey, the American Diabetes Association standards of care [33] indicated that lowering HbA1c to $<7\%$ was a reasonable goal for many non-pregnant adults and the National Institute for Health and Care Excellence's (NICE) quality standard [34] defined clinical best practice as an HbA1c target between 6.5 and 7.5%. Further, the NICE quick reference guide for the management of type 2 diabetes suggests that target HbA1c levels be individualized, with less stringent targets ($<7.5\%$) for patients on multiple therapies. The fact that guidelines in the UK permitted higher HbA1c targets could partially account for the fact that more UK physicians than US physicians selected higher HbA1c targets for the profiled patient.

Based on the pretests, discussions with clinical experts, and reviews of publicly

available information about treatment and referral guidelines, we hypothesized that there would be differences in preferences between endocrinologists on the one hand and all other specialties that treat diabetes on the other. While all of these specialties treat patients with type 2 diabetes, it appears that endocrinologists tend to see more advanced or acute cases (though there may be exceptions). The results indicated that the preferences of GPs and endocrinologists were similar in both the US and the UK, with the exception of differences in preference for liver monitoring among GPs and endocrinologists in the UK.

Despite the increasing use of DCE in health applications to elicit preferences, this approach has several limitations. First, physician choices among hypothetical treatment profiles do not have the same clinical consequences as actual choices. We minimized the potential for hypothetical bias by offering treatments that mimic real-world trade-offs as closely as possible. Second, physicians' actual medication choices may differ from predicted choices because actual choices depend on a number of clinical, institutional, and financial factors that were beyond the scope of this study. This study limited the characterization of hypothetical diabetes treatments to seven treatment attributes and excluded, for example, the risk of pancreatitis. The US Food and Drug Administration (FDA) [35] and recent literature [36, 37] have highlighted controversies about the possible risks of pancreatitis and pancreatic cancer associated with some diabetes treatments. Third, we cannot fully judge how representative our physician samples were or whether our results are generalizable to all physicians in the US and the UK. Fourth, the results we present relate to the patient profile that physicians were asked to consider. The sample was insufficient to explore physician

preferences for different patient profiles. Finally, this study was not designed to support development of treatment guidelines or to provide clinical advice.

The study also has a number of strengths from using best practices [17]. In particular, the survey was carefully designed in collaboration with clinical experts, was pretested using in-depth interviews with physicians in the US and the UK, and employed a state-of-the-art experimental design. The choice data were analyzed using advanced RPL methods that avoid estimation bias from unobserved variation in preferences across the sample and within-sample correlation in the choice sequence for each respondent. We also tested for the effect of systematic preference differences by age, experience, and medical specialty.

CONCLUSION

This study provides evidence that physicians place about as much importance on a type 2 diabetes medication's cardiovascular and weight outcomes as they place on glucose control. We found broad consensus about treatment priorities among physicians with different personal and professional characteristics who treat diabetic patients. These findings are consistent with the challenges in diabetes care, in which cardiovascular disease and obesity continue to be problems. However, physicians place relatively low importance on the attributes describing depression benefits and liver monitoring requirements in this study. As the literature regarding the links between diabetes and depression and liver abnormalities matures, physicians and stakeholders should become better informed about these links and physicians' relative preferences for type 2 diabetes treatments may change.

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At the time of the study, Lauren J. Lee was a full time employee and stock owner of Eli Lilly and Company.

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Jay P. Bae is a full time employee and stock owner of Eli Lilly and Company.

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Compliance with ethical guidelines. The Office of Research Protection and Ethics at Research Triangle Institute granted a consent exemption for this study. This article does not contain any studies with human or animal subjects performed by any of the authors.

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APPENDIX

See Table 3.

Table 3 Estimates of marginal choice probabilities for given improvements in medication features (95% CI)

Medication feature	Improvement in medication feature	Marginal choice probability (in percentage points)	
		US physicians	UK physicians
Level to which HbA1c is reduced	8.3–7.0%	46 (44, 48)	41 (37, 44)
	8.0–7.0%	41 (37, 44)	33 (28, 38)
	8.3–8.0%	20 (13, 27)	17 (9, 24)
Frequency of injection	2 injections/day to 1 injection/month	25 (19, 32)	23 (17, 3)
	1 injection/day to 1 injection/month	10 (1, 19)	20 (12, 28)
	1 injection every other day to 1 injection/month	14 (5, 22)	11 (3, 20)
	1 injection/week to 1 injection/month	0 ^a	8 (0, 15)
	2 injections/day to 1 injection/week	26 (20, 32)	17 (10, 23)
	1 injection/day to 1 injection/week	11 (4, 18)	13 (6, 20)
	1 injection every other day to 1 injection/week	15 (7, 23)	4 (–5, 12)
	2 injections/day to 1 injection every other day	13 (6, 21)	14 (6, 21)
	1 injection/day to 1 injection every other day	0 ^a	10 (1, 18)
2 injections/day to 1 injection/day	17 (9, 24)	4 (–4, 12)	

Table 3 continued

Medication feature	Improvement in medication feature	Marginal choice probability (in percentage points)	
		US physicians	UK physicians
Liver monitoring	Every month for the first 3 months, then quarterly as long as the patient takes the medicine to not required	4 (−1, 8)	8 (4, 13)
Change in body weight	5% weight gain to 20% weight loss	42 (38, 46)	44 (41, 47)
	No change to 20% weight loss	34 (29, 40)	36 (31, 42)
	5% weight loss to 20% weight loss	32 (25, 38)	30 (23, 37)
	10% weight loss to 20% weight loss	17 (8, 26)	12 (2, 22)
	5% weight gain to 10% weight loss	35 (29, 41)	41 (36, 45)
	No change to 10% weight loss	23 (16, 30)	29 (23, 36)
	5% weight loss to 10% weight loss	19 (10, 28)	21 (13, 30)
	5% weight gain to 5% weight loss	22 (14, 29)	30 (23, 36)
	No change to 5% weight loss	5 (−4, 13)	11 (3, 20)
Mild to moderate nausea, diarrhea, and/or vomiting 3–4 times/week	5% weight gain to no change	18 (10, 26)	21 (13, 29)
	Continues as long as patient takes medicine to no GI side effects	34 (30, 39)	27 (22, 33)
	Resolves after taking medicine for 2 weeks to no GI side effects	0.3 (−3, 9)	0 ^a
Changes in the risk of a fatal MI over 5 years	Continues as long as patient takes medicine to resolves after taking medicine for 2 weeks	33 (28, 37)	28 (23, 33)
	0–1.5%	45 (42, 47)	47 (45, 48)
	0.5–1.5%	33 (29, 38)	37 (33, 41)
Changes in depression symptoms	0–0.5%	28 (22, 33)	31 (26, 36)
	No change to moderate to no depression	15 (9, 21)	12 (5, 18)
	Moderate to mild depression to moderate to no depression	8 (2, 14)	2 (−4, 8)
	No change to moderate to mild depression	8 (2, 13)	10 (4, 15)

The estimates implicitly assume that all attributes other than that being valued remain unchanged

CI confidence interval, *HbA1c* hemoglobin A1c, *MI* myocardial infarction

^a The marginal choice probability was not calculated for this change, because the estimated preferences for this sample were not consistent with the natural ordering of the medication feature

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