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Be Careful What You Ask for: Effects of Benefit Descriptions on Diabetes Patients' Benefit-Risk Tradeoff Preferences

Lill-Brith von Arx, MSc[1,2,*], *F. Reed Johnson, PhD*[3], *Morten Raun Mørkbak, PhD*[1], *Trine Kjær*[1]

[1]*University of Southern Denmark, Odense, Denmark;* [2]*Novo Nordisk A/S, Soeborg, Denmark;* [3]*Duke Clinical Research Institute, Durham, North Carolina, USA*

ABSTRACT

Background: As more studies report on patient preferences for diabetes treatment, identifying diabetes outcomes other than glycated hemoglobin (HbA_{1c}) to describe effectiveness is warranted to understand patient-relevant, benefit-risk tradeoffs. **Objective:** The aim of the study was to evaluate how preferences differ when effectiveness (glycemic control) is presented as long-term sequela (LTS) risk mitigation rather than an asymptomatic technical marker (HbA_{1c}). **Methods:** People with type 2 diabetes and using insulin (n = 3160) were randomly assigned to four self-administered, discrete-choice experiments that differed by their presentation of effectiveness. Epidemiologic reviews were conducted to ensure a close approximation of LTS risk relative to HbA_{1c} levels. The relative importance of treatment benefit-risk characteristics and maximum acceptable risk tradeoffs was estimated using an error-component logit model. Log-likelihood ratio tests were used to compare parameter vectors. **Results:** In total, 1031 people responded to the survey. Significantly more severe hypoglycemic events were accepted for a health improvement in terms of LTS mitigation versus HbA_{1c} improvement (0.7 events per year; 95% confidence interval [CI]: 0.4–1.0 vs. 0.2 events per year 95% CI: –0.02 to 0.5) and avoidance of treatment-related heart attack risk (1.4 severe hypoglycemic events per year; 95% CI: 0.8–1.9 vs. 1 event per year; 95% CI: 0.6–1.3). This finding is supported by a log-likelihood test that rejected at the 0.05 level that respondent preference structures are similar across the different experimental arms of the discrete-choice experiment. **Conclusion:** We found evidence that benefit descriptions influence elicited preferences for the benefit-risk characteristics of injectable diabetes treatment. These findings argue for using carefully defined effectiveness measures to accurately take account of the patient perspective in benefit-risk assessments.

Keywords: A_{1c}, asymptomatic marker, discrete-choice experiment, health communication, long-term sequelae, severe outcome, stated preference research, technical terms, type 2 diabetes.

Introduction

Diabetes is a disease characterized by high levels of blood glucose, with a slow progression from insulin insensitivity to a state in which the individual may become dependent on pharmacologic insulin delivery [1]. Diabetes regimens impose a significant demand on the individual and involve a high degree of personal decision-making in the daily management of the disease [2]. Patients' ability to understand and use health information [3], and the association between such understanding and health outcomes [4,5], are widely discussed in the literature and receive increasing attention from health care decision makers.

For diabetes, this includes the ability to understand technical terms in relation to glycemic control, such as glycated hemoglobin (HbA_{1c}; termed A_{1c} in the following) [5]. This asymptomatic marker of glycemic control is the primary end point in most diabetes clinical investigations [6,7] and is applied in clinical practice to evaluate risk for more severe, long-term sequelae (LTS), such as visual or renal impairment, damage to hands or feet, and cardiovascular events [8]. Although a valuable prognostic tool in the clinic, the value of A_{1c} for patients is questioned in diabetes health communication [9–12]. This is a dilemma shared with other asymptomatic conditions, such as hypertension, cardiovascular disease, and osteoporosis. Suitability of the current practice in patient interactions of characterizing treatment effectiveness by A_{1c} improvement [13] has not been investigated. This article seeks to fill this gap in the literature.

A number of stated-preference (SP) studies have been conducted to elicit the relative importance of different diabetes treatment aspects for patients [14–33]. This study contributes to this literature by evaluating the results of a randomized, discrete-choice experiment (DCE) that examined the effect of presenting respondents with technical terms versus pragmatic descriptions of similar treatment benefits on a patient's stated benefit-risk preferences for injectable diabetes treatment. Based on the expectation that respondents perceive severe health outcomes differently than an asymptomatic technical marker [34–36], we tested the hypothesis

Conflicts of interest: Lill-Brith von Arx is a PhD scholar at the University of Southern Denmark and is employed at Novo Nordisk A/S, in which she has shares. Trine Kjær, Morten Raun Moerkbak, and F. Reed Johnson have no conflicts of interest to declare.

* *Address correspondence to:* Lill-Brith von Arx, University of Southern Denmark, Campusvej 55, 5530 Odense M, Denmark.
E-mail: lillvonarx@gmail.com.

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that elicited benefit-risk tradeoffs for diabetes treatment are sensitive to such differences in benefit description.

To test this hypothesis, respondents were randomized to DCEs that described effectiveness either as A_{1c} changes or LTS mitigation. Formats involving A_{1c} level changes were further subdivided by either adding an ordinal scale to the A_{1c} values or by providing patients with information on the risk of LTS associated with the A_{1c} test prior to choice-task completion. An important requirement of the study design was evaluating the epidemiologic evidence to ensure the approximation of the LTS risk associated with A_{1c} levels was as accurate as possible.

Our results should be of interest to researchers and health care providers who are seeking to understand patient preferences for outcomes, patient understanding of health information and regulators who are considering preference evidence in benefit-risk assessments of diabetes treatments. As regulatory frameworks evolve around benefit-risk evaluations based on patient-preference evidence, the need to identify patient-relevant benefit measures in diabetes treatment will be increasingly important.

Methods

A DCE was included in a 27-item survey distributed to insulin users with type 2 diabetes (n = 3160) in the county of Funen, Denmark, in September 2014. The DCE formed part of a large-scale, registry-enabled study combining self-reported information on health status and socioeconomic position with objective health measures transferred from routine clinical practice to the registry.

Selection of Attributes

The attributes and levels were developed on the basis of information gathered from qualitative research according to good-practice guidelines [37] and a systematic review of current practice in diabetes SP research [13]. In a number of these studies, treatment effectiveness is characterized by A_{1c}. We used the A_{1c} as the baseline effectiveness measure. Additional effectiveness measures salient to people with diabetes were identified through one-on-one patient and specialist interviews (n = 7) and focus groups with insulin users. Participants in focus groups (n = 12) were recruited through a diabetes clinic at Hilleroed Hospital, Denmark (see Appendix I in Supplemental Materials found at http://dx.doi.org/%2010.1016/j.jval.2016.11.023).

The DCEs differ in their description of treatment effectiveness but are designed to ensure consistency with the differences patients would experience clinically. Thus, the levels of LTS risk reduction are defined for each of the A_{1c} levels on the basis of epidemiological data [38,39]. The experiment had four arms. In arm 1 and 2, effectiveness is described as A_{1c}, with or without an ordinal description of levels. The elicitation format of arm 3 was the same as that for arm 1 but included information on the association between A_{1c} levels and long-term complication risk prior to completion of the choice task. The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) percent (%) unit for A_{1c} was applied, rather than the recently introduced National Glycohemoglobin Standardization Program (NGSP) unit (mmol/mol) [40]. This decision was based on focus-group participants' lack of familiarity with the ranges of the NGSP. In arm 4, effectiveness was characterized by the number of treated people who did not have LTS as a result of their glycemic control, with no mention of A_{1c}.

Also, based on focus-group results, possible weight loss was included as an attribute to represent benefit. Risk attributes included side effects in terms of severe and nonsevere hypoglycemic events described by the support required to manage the event. Finally, incremental heart attack risk was included as a possible treatment-inherent risk [41,42]. The definition of attribute levels was based on clinical and epidemiological data [43,44]. Table 1 provides an overview of the final attributes and levels, including a priori expectations regarding the signs of each of the coefficients. Examples of a choice question from each of the four elicitation formats are shown in Figure 1.

Comprehensive software (Ngene, ChoiceMetrics Pty Ltd, Sydney, Australia) was used to construct an unlabeled, Bayesian

Table 1 – Attributes and levels in the discrete choice experiments.

HbA_{1c}*	HbA_{1c} + ordinal scale	LTS	
Arm 1	Arm 2	Arm 4	Parameter Expected sign
6.0 %	6.0 % (very good)	9 of 10 without LTS	+
7.5 %	7.5 % (good)	7 of 10 without LTS	+
8.5 %	8.5 % (moderate)	5 of 10 without LTS	Ref
Attributes identical for all versions of the discrete choice experiments			
1-year weight change		None	Ref
		–4 kg	+
		–10 kg	+
Risk increase of HA due to treatment, per year		Yes (3 additional people of 1000)	÷
		No (no risk increase)	
Low BS requiring assistance others, per year†		None	Ref
		1 per year	÷
		2 per year	÷
Self-managed low BS, per month‡		1 event per month	Ref
		4 events per month	÷
		8 events per month	÷

BS, blood sugar; HA, heart attack; LTS, long-term sequela; Pts, patients; Ref, reference level.

* An additional discrete choice experiment, arm 3, informed respondents of the LTS risk associated with each level of HbA_{1c} before the choice task but was otherwise identical to arm 1.

† Severe hypoglycemic events.

‡ Nonsevere hypoglycemic events.