

Sennhauser, Michèle; Zweifel, Peter

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Socioeconomic Institute
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Author's address:

Michèle Sennhauser

E-mail: michele.sennhauser@soi.uzh.ch

Peter Zweifel

E-mail: pzweifel@soi.uzh.ch

Publisher

Sozialökonomisches Institut
Bibliothek (Working Paper)
Rämistrasse 71
CH-8006 Zürich
Phone: +41-44-634 21 37
Fax: +41-44-634 49 82
URL: www.soi.uzh.ch
E-mail: soilib@soi.uzh.ch

A Pharmaceutical Innovation: Is it Worth the Money? Whose Money?

Michèle Sennhauser* and Peter Zweifel*

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* Socioeconomic Institute, University of Zurich, Hottingerstrasse 10, 8032 Zurich.
Corresponding author: Michèle Sennhauser (michele.sennhauser@soi.uzh.ch)

Abstract

This study seeks to provide evidence for deciding whether or not a pharmaceutical innovation should be included in the benefit list of social health insurance. A discrete choice experiment (DCE) was conducted in Germany to measure preferences for modern insulin therapy. Of the 1,100 individuals interviewed in 2007, 200 suffered from type 1 diabetes, 150 from insulin-treated type 2 diabetes, and 150 from insulin-naive type 2 diabetes. The long-acting insulin analogue "Insulin Detemir" is compared to human insulin as the status quo. The DCE contains two price attributes, copayment and increased contributions to health insurance. As one would expect, non-affected non-diabetics and insulin-naive diabetics exhibit higher willingness-to-pay (WTP) values through copayment (adjusted for probability of contracting diabetes), while affected type 1 and insulin-treated type 2 diabetics have higher WTP through increased contributions. However, WTP values exceed the extra treatment cost in both financing alternatives, justifying inclusion of the innovation in the benefit list from a cost-benefit point of view.

JEL-Classification: I11, H51, I18

Keywords: Health insurance, Discrete choice experiment, preferences, diabetes

1 Introduction

Health care expenditure (HCE) and especially pharmaceutical expenditure is rising in almost all developed countries. For example, in the United States the share of pharmaceutical expenditures in total HCE increased from 9 percent in 1996 to 13 percent in 2006 (OECD [2009]). In order to curb this surge, several countries have introduced a cost-effectiveness standard for new pharmaceuticals. This led to the creation of the MEOPAC scheme in Australia, NICE in the United Kingdom, and IQWIG¹ in Germany. In Germany, the pharmaceutical bill paid for by statutory health insurance (GKV) increased from 22 billion Euro in 2004 to 26 billion in 2007, or from 1.00 percent of GDP to 1.07 percent (VGRdL [2009]). Before 2007, pharmaceutical innovations had to meet safety and efficacy benchmarks to be included in the GKV list of benefits. Now, they also have to be cost-efficient. However, from the point of view of the insured individuals, inclusion is justified if both potential and actual patients exhibit a willingness to pay (WTP) that exceeds the cost of treatment with the new product.

This study seeks to provide evidence for deciding whether or not a pharmaceutical innovation for modern insulin therapy, with the long-acting insulin analogue Insulin Detemir² should be included in the benefit list of social health insurance. There are two reasons why this preparation is of special interest. First, diabetes prevalence is higher than ever in industrialized countries and continues to increase rapidly. The World Health Organization (WHO) projects the number of diabetics worldwide to rise from 170 million in 2000 to 360 million by 2030 (World Health Organization [2007], Wild et al. [2004]). In Germany the prevalence of diabetes is 4 to 10 percent between 40 and 59 years of age and 18 to 28 percent for people over age 60 (Hauner [2008]). Second, Insulin Detemir may well constitute a test case. IQWIG recommended to drop short-acting insulin analogues from the benefit list, judging it not to be cost-efficient. However, this recommendation entirely neglected preferences of (potential) patients, dismissing the drug's innovative aspects as therapeutically unimportant. It is expected that it will come to a decision over long-acting insulin analogues soon.

Preferences for a long-acting insulin analogue in comparison to conventional therapy (using human insulin) are derived from a discrete choice experiment (DCE) conducted in Germany in the Fall of 2007. Participants are 1,100 members of GKV, of whom 200 suffer from type 1 diabetes³, 150 from insulin-treated type 2 diabetes, and 150 from insulin-naive type 2 diabetes⁴. Distinguishing

¹ Institute for Quality and Efficiency in Health Care

² Modern insulin therapy uses long- and short-acting insulin in combination. Whereas rapid-acting insulin covers insulin need during mealtimes, long-acting insulin assures base-level supply. Whereas human insulin is genetically identical to insulin from the human pancreas, insulin analogue differs slightly to improve the insulin's properties.

³ Type 1 diabetics are treated with insulin from the beginning of their disease.

⁴ Diabetics of type 2 are called "insulin-naive" if they are not treated with insulin (yet) but with oral anti-diabetics.

these groups allows to estimate ex-ante WTP for non-diabetics and insulin-naive diabetics on the one hand and ex-post WTP for insulin-treated patients on the other. Four attributes describing insulin therapy were included, viz. risk of hypoglycemia, weight gain during the first six months of insulin treatment, need to prepare the insulin before injections, and flexibility in time of injection. Finally, there are two attributes for the mode of payment, financing through patients themselves (copayment) and through increased health insurance contributions, respectively. This permits to test whether the innovation has a favorable benefit-cost ratio regardless of the boosting of WTP caused by health insurance.

There are four main questions to be answered. (1.) Is there positive WTP for the pharmaceutical innovation of long-acting insulin analogue Insulin Detemir? (2.) If so, which product attributes contribute to WTP? (3.) Is there preference heterogeneity between non-affected non-diabetics and insulin-naive type 2 diabetics on the one hand and type 1 diabetics and insulin-treated type 2 diabetics on the other? (4.) Is the benefit-cost ratio of the innovation favorable regardless of whether it is financed jointly through increased GKV contributions or by patients through copayment?

The paper is organized as follows. Section 2 presents the questionnaire design with the attributes and their levels. Then theory behind DCEs is briefly presented in Section 3, with emphasis on the difference between ex-ante and ex-post WTP measurement. Hypotheses are formulated in Section 4 before presenting descriptive statistics in Section 5. Section 6 contains the empirical evidence and hypothesis tests. The four questions raised are answered in the concluding Section 7.

2 The Discrete Choice Experiment

2.1 Data Collection

The DCE was conducted in Germany in the Fall of 2007. Because one of the main research questions is whether Insulin Detemir should be financed through contributions to GKV or copayment, only GKV members (some 90 percent of the population) were asked to participate. To investigate heterogeneity in preferences, the sample was made to comprise 200 individuals who suffer from type 1 diabetes, 150 who are insulin-treated type 2 diabetics, and 150 who are insulin-naive type 2 diabetics and 600 non-diabetics, bringing up the total to 1,100 respondents. While the sample design allocated the non-diabetics randomly across the 12 Länder (states), ages, and gender, it distributed the type 2 diabetics equally over three age groups, viz. 46-55, 56-65, and over 65 because type 2 diabetes occurs almost exclusively past age 45. The minimum duration of diabetes treatment (insulin injections or oral therapy) was six months. Because it is difficult to find patients suffering from type 1 diabetes, randomization was limited to the 12 Länder.

2.2 Questionnaire, Attributes, and Questionnaire Design

Although both rapid- and long-acting insulin are required for successful therapy, this study only takes into consideration long-acting insulin, viz. the long-acting insulin analogue "Insulin Detemir". The status quo is therapy with long-acting human insulin. For the DCE, six attributes reflecting the differences in the properties of long-acting human insulin and insulin analogue Insulin Detemir are retained. They are described in the following.

The first attribute is risk of hypoglycemia (*Hypo*, see Table 1), one of the main side effects of insulin therapy. Its incidence depends on the individual, the dose of insulin needed, individual habits, and the insulin preparation. Studies suggest that incidence is lower with Insulin Detemir than with human insulin (see Hermansen et al. [2004], Home et al. [2004], Russell-Jones et al. [2004], Vague et al. [2002], Robertson et al. [2004] or Kolendorf et al. [2004]). However, the magnitude of the decrease varies across studies. Whereas Kolendorf et al. [2004] find reductions of 18 percent overall and of 50 percent for nocturnal hypoglycemia, Vague et al. [2002] estimate them to be 22 and 34 percent, respectively. On average, the overall decrease can be estimated at 30 percent. Therefore, with the risk being specified as 100 percent in the status quo, the alternative incidence levels are 75 and 50 percent. Note that the levels specified need not be realistic; what matters is that they are sufficiently different from the status quo to cause a preference for the alternative at least in a few cases (otherwise nothing can be learned about respondents preferences, see below).

Table 1: Product attributes and levels

Attribute	Status quo	Alternative
Risk of hypoglycemia <i>Hypo</i>	100 %	100% / 75% / 50%
Weight change <i>Weight</i>	+ 2,5 kg	+ 2.5 kg / \pm 0 kg / - 1.0 kg
Preparation <i>Preparation</i>	Yes	Yes / No
Time of injection <i>Time</i>	Predetermined	Predetermined / More flexible
Copayment <i>Copayment</i>	None	None / 50 / 150 / 300 Euro*
Increase in contribution <i>Contribution</i>	None	None / +0.5% / +1.0% / +2.0%

*1 Euro = 1.25 US\$ at 2008 exchange rates.

Obesity (*Weight*) is a major problem of type 2 diabetes patients. 80 percent of them suffer from obesity according to Russell-Jones and Khan [2007]. Correspondingly, Häussler et al. [2005] found a significantly higher BMI (Body Mass Index) in diabetes 2 patients than in the overall German population. Insulin therapy makes this problem even more acute. As a side effect of treatment with human insulin, patients gain weight, especially during the first months of insulin therapy. The UK Prospective Diabetes Study (UKPDS) Group [1998] found a 2.5 kg increase over 6 months on average. However, Insulin Detemir can mitigate the weight gain or even cause a weight loss (see Hermansen and Davies [2007], Haak et al. [2003] and Russell-Jones and Khan [2007]). Therefore, weight gain constitutes the second attribute of the DCE, with 2.5 kg defining the status quo value. No weight change and a weight loss of 1 kg are levels in the alternative.

Before every injection, human insulin has to be swung to achieve uniform dilution (*Preparation*). This procedure guarantees an optimal amount of insulin to be injected. Failing it, a suboptimal amount of insulin is injected and blood sugar levels cannot be adequately controlled (Schleser-Mohr [2007]). Insulin Detemir can be injected immediately, without swinging. Therefore, the status quo preparation needs to be prepared, whereas the alternative preparation can be injected immediately without risk.

Another difference between long-acting human insulin and Insulin Detemir is the flexibility in the time of injection (*Time*, see Table 1 again). Human insulin reaches its maximum effect often after a few hours (Sorani and Younis [2006]). The time of the bedtime injection therefore is set at 10 pm to avoid insufficient insulin levels in the early morning. Insulin analogue has a different action profile. Its maximum effect occurs later (see Kurtzhals [2007]), allowing patients to inject insulin already before 10 pm, usually between dinner and bedtime. However, time of injection should not vary from day to day.

To analyze preferences for the mode of financing (individually by diabetics themselves through copayment or collectively through increased GKV contributions), two financial attributes are included, viz. copayment (*Copayment*) and an increase in health insurance contributions (*Contribution*). The additional costs of Insulin Detemir compared to human insulin amounts to 226 Euro on average per year and diabetic. At present, patients face no copayment for Insulin Detemir. The levels of the alternatives are a copayment of 50 Euro, 150 Euro, and 300 Euro, respectively. As to the contributions to health insurance, respondents were asked to look up the actual amount paid to establish an individual-specific status quo. Contributions are estimated to increase by 8.54 Euro per year⁵ and GKV member if Insulin Detemir is added to the benefit list. On average this corresponds to an increase of 0.5 percent of annual health insurance contributions. The alternative levels included are increases of 0.5, 1, and 2 percent, respectively.

The pretest was conducted by a professional market research institute. The pretest consisted of 30 face-to-face interviews. All attributes proved to be significant predictors of choice, with the exception of contributions. Initially, the increases in contributions were 0.25, 0.5, and 1 percent. Apparently, this range was not sufficient to affect decisions; therefore, it was scaled up to 0.5, 1, and 2 percent.

For the main survey, a D-optimal design was constructed, using GOSSET (see Kuhfeld et al. [1994] and Sloane and Hardin [2007]). Out of the 576 possible combinations, 30 were retained and divided into three card sets. Consistency was tested by including weakly dominated alternatives.

⁵ On average, extra cost of treatment with Insulin Detemir rather than human insulin is 226 Euro per year and diabetic. Multiplied by the number of insulin-treated diabetics in Germany (=1.9 billion, see Giani et al. [2004]) and divided by the number of GKV members paying contributions (=50.471 billion, see BMG [2007]) one obtains 8.54 Euro per year and diabetic.

3 Theoretical Background

3.1 Discrete-Choice Theory

Based on random utility theory (see Luce [1959], Manski and Lerman [1977], McFadden [1974], McFadden [1981] and McFadden [2001]), DCE are designed to investigate individuals' preferences for (non-)marketed goods or goods that do not exist yet.

In a DCE participants are asked repeatedly to choose several times between a fixed status quo and an alternative whose attributes take on different values each time.⁸ When choosing between alternatives, a rational individual will always select the alternative with the higher level of expected utility. Neglecting the expectation operator for simplicity, the decision-making process can thus be seen as a comparison of utility values (see Section 3.2 below) determined by

$$U_{ij} \equiv v(a_j, p_j, y_i, s_i, \varepsilon_{ij}) \quad (1)$$

where U_{ij} represents the indirect utility value attained by individual i in alternative j . It depends on the vector of attributes a_j , price p_j , the income of individual i , y_i , and socioeconomic characteristics denoted by s_i . Finally, ε_{ij} is an error term that varies over alternatives and individuals. Provided the error term is additive, the individual will choose alternative k over alternative l if

$$u(a_k, p_k, y_k, s_i) + \varepsilon_{ik} \geq u(a_l, p_l, y_l, s_i) + \varepsilon_{il}, \quad (2)$$

where $u(\cdot)$ is the deterministic component of the utility function $v(\cdot)$. Unlike ε_{ij} , this component can be estimated from observed choice behavior. For this purpose it is assumed that the probability of choosing the alternative k over l , P_{ik} , equals the probability of the difference in equation (2) occurring. Solving for the difference in error terms, one obtains

$$P_{ik} = Prob[\varepsilon_{il} - \varepsilon_{ik} \leq u(a_k, p_k, y_k, s_i) - u(a_l, p_l, y_l, s_i)]. \quad (3)$$

For any inference about the left-hand side of inequality (3), a probability law for $\omega = (\varepsilon_{il} - \varepsilon_{ik})$ must be assumed. Since the logistic distribution assumes independence of irrelevant alternatives (IIA), the normal distribution is used here, resulting in probit estimation. It is assumed that errors are correlated between the choices of a given respondent but not across respondents, calling for random effects specification. With the utility function linear in parameters (Louviere et al. [2000]), one has

$$\Delta U_{ik} = \beta_0 + \beta_1 a_{1k} + \beta_2 a_{2k} + \dots + \beta_L a_{Lk} + \omega_{ij}, \quad (4)$$

with $\omega_{ik} = \mu_i + \nu_{ik}$. Here, a_{1l}, \dots, a_{Lk} are the attributes of the alternative in consideration. According to equation (3) only differences in utility matter. Thus, fixed characteristics of respondents drop out. The β s are the parameters to be estimated.

Based on Hanemann [1983], the marginal rate of substitution between two attributes m and n is equal to the ratio of the derivatives of the indirect utility function with respect to the two attributes,

$$MRS = \frac{\partial v / \partial a_m}{\partial v / \partial a_n} = \frac{\beta_m}{\beta_n}. \quad (5)$$

Defining n as a financial attribute allows to interpret the negative of the marginal rate of substitution as a marginal WTP for attribute m .

3.2 Ex-ante vs. Ex-post Willingness To Pay

A special feature of this study is that it seeks to measure WTP of both individuals who do not suffer from the disease or do not need insulin yet (ex-ante) and insulin-treated diabetes patients (ex-post). Whereas the utility gained (or lost) from a change in treatment is a real and immediate utility change for insulin-treated diabetics, it is an expected utility for non- and insulin-naive diabetics, which can be written as

$$EU_{ij} = \pi_i \cdot U_{ij}(\text{Therapy}|\text{Diabetic}) + (1 - \pi_i) \cdot U_{ij}(\text{Therapy}|\text{Non-Diabetic}), \quad (6)$$

where π_i is the individual-specific probability to come down with insulin-treated diabetes. For patients treated with insulin, π_i is equal to 1. The second term of eq. (6) becomes zero, and eq. (6) boils down to U_{ij} , the individual's utility experienced from alternative j . When substituting the attributes described in Section 2.2 into eq. (1), utility for insulin-treated diabetics becomes

$$U_{ij} = \beta_0 + \beta_1 \text{Hypo}_{ij} + \beta_2 \text{Weight}_{ij} + \beta_3 \text{Preparation}_{ij} + \beta_4 \text{Time}_{ij} \\ + \beta_5 \text{Copayment}_{ij} + \beta_6 \text{Contribution}_{ij} + \varepsilon_{ij}. \quad (7)$$

For people not suffering from the disease and insulin-naive diabetics, π_i is between zero and one. Their expected utility function therefore reads,

$$EU_{ij} = \pi_i \cdot (\beta_0 + \beta_1 \text{Hypo}_{ij} + \beta_2 \text{Weight}_{ij} + \beta_3 \text{Preparation}_{ij} \\ + \beta_4 \text{Time}_{ij} + \beta_5 \text{Copayment}_{ij} + \beta_6 \text{Contribution}_{ij}) \\ + (1 - \pi_i) \cdot (\beta_0 + \beta_6 \text{Contribution}_{ij}) + \omega_{ij} \quad (8)$$

Recall that the variables in eq. (7) represent the differences between the alternative using Insulin Detemir and the conventional therapy using human insulin. For example Hypo_{ij} is the probability of suffering from hypoglycemia when treated with Insulin Detemir minus this probability when treated with human insulin. Consequently, the values for Hypo , Weight , Preparation , Time , and Copayment are set equal to zero in case of no disease because they do not vary across alternatives. However, health insurance contributions do vary since in some alternatives the preparation is paid for by the GKV where every member pays for the medications covered.

There are two main reasons for a non-diabetic person to have a positive WTP for diabetes treatment, viz. altruism and/or buying a call option for better treatment in case of coming down with the disease. Focusing on the second, one sees that the first term of eq. (8) shows the change in expected utility in case the person comes down with diabetes and therefore has positive WTP for a call option on innovative treatment. The higher the probability π_i , the higher the probability to exercise this option, and the higher WTP. With regard to altruism, the second term of eq. (8) represents the change in utility of a person who stays healthy. In this case, β_0 can be interpreted as WTP due to altruism. Eq. (8) can be rewritten as

$$EU_{ij} = \beta_0 + \pi_i\beta_1Hypo_{ij} + \pi_i\beta_2Weight_{ij} + \pi_i\beta_3Preparation_{ij} + \pi_i\beta_4Time_{ij} + \pi_i\beta_5Copayment_{ij} + \beta_6Contribution_{ij} + \omega_{ij}. \quad (9)$$

This equation holds for non-diabetics as well as for diabetics. For the latter, π_i equals 1 if treated with insulin, causing eq. (9) and (7) to be identical. Finally, the calculation of WTP has to be modified as well. If the financial attribute (n) is specified to be copayment, eq. (5) holds. However, if it is GKV contributions, the probability of becoming a diabetic has to be taken into account,

$$WTP = -\pi_i \cdot \frac{\beta_k}{\beta_6}. \quad (10)$$

4 Hypotheses

This section is devoted to the foundation of hypotheses concerning WTP values.

Hypothesis H1:

FROM THE GKV MEMBERS' POINT OF VIEW, INSULIN DETEMIR GENERATES AN ADDITIONAL UTILITY COMPARED TO HUMAN INSULIN.

Increases in contributions and copayment will always have a negative effect on utility. However, this hypothesis states that the other attributes generate enough additional utility compared to human insulin, to make its total effect positive.

Hypothesis H2:

WTP VALUES FOR THE ATTRIBUTES ARE IN THE FOLLOWING RANK ORDER.

H2.1 DECREASING THE RISK OF HYPOGLYCEMIA HAS THE HIGHEST WTP, FOLLOWED BY AVOIDING WEIGHT GAIN.

H2.2 WTP FOR MORE FLEXIBILITY IN TIME OF INJECTION IS CONSIDERABLY LOWER THAN FOR AVOIDING WEIGHT GAIN.

H2.3 WTP FOR NO NEED TO SHAKE THE PREPARATION BEFORE INJECTION IS VERY LOW, NOT SIGNIFICANTLY DIFFERENT FROM ZERO.

Hypoglycemia is a traumatic experience. Symptoms of hypoglycemia include shakiness, dizziness, confusion, and difficulty to speak, just to mention a few. Severe hypoglycemia can cause loss of consciousness and even death. Therefore the highest WTP is expected for a decrease in this risk. The hypothesis that avoiding weight gain generates the next-highest WTP is supported by Hermansen and Davies [2007]. They found that patients often take a precautionary snack to avoid hypoglycemia, accepting weight gain as the consequence. However, avoiding weight gain generates a higher WTP than more flexibility in time of injection. Whereas at the beginning of the disease patients might swing the preparation intensively to avoid mistakes, they gain experience permitting them to save time and effort. Therefore WTP for this attribute is predicted to be significantly lower than for the other ones.

Hypothesis H3:

THERE IS SIGNIFICANT HETEROGENEITY OF WTP VALUES BETWEEN DIABETICS AND NON-DIABETICS AND BETWEEN DIABETES SUBGROUPS.

The difference in experience with using insulin might be the key reason for heterogeneity in preferences. Whereas type 1 and insulin-treated type 2 diabetics have used insulin before, non-diabetics and insulin-naive type 2 diabetics have not. For instance, they do not know what a hypoglycemic situation feels like and how it can be handled.

Hypothesis H4:

NON-AFFECTED RESPONDENTS AND DIABETICS NOT TREATED WITH INSULIN PREFER FINANCING THROUGH PATIENTS THEMSELVES IN THE GUISE OF COPAYMENT, WHEREAS INSULIN-TREATED PATIENTS PREFER FINANCING THROUGH CONTRIBUTIONS.

Both diabetics and non-diabetics are predicted to have positive WTP for Insulin Detemir; however, WTP values of non-diabetics and insulin-naive diabetics are higher when the financing occurs through copayment than through health insurance contributions. Conversely, WTP values of type 1 and insulin-treated type 2 diabetics are higher when financing occurs through health insurance contributions.

5 Descriptive Statistics

Table 2 gives an overview of the data base. Approximately 50 percent of the respondents are female. Average age is higher for type 2 diabetics than the rest of the sample because this disease occurs primarily among the elderly (although the number of children suffering from type 2 diabetes has been increasing substantially). Respondents were asked to mark their subjective health status on a visual analog scale ranging from 0 (very bad health) to 100 (very good health). Non-diabetics reported the highest average value of 73, insulin-treated type 2 patients, the lowest of 53. Type 2 diabetics also have the highest BMI with 28 (insulin-treated) and 27 (insulin-naive), respectively. This matches the findings of the UK Prospective Diabetes Study (UKPDS) Group [1998] stating that obesity is highly prevalent among type 2 diabetics.

Average net household income is 1,904 Euro per month. Insulin-naive diabetics of type 2 have a lower income (1,783 Euro) than non-diabetics (1,975 Euro). This difference is in accordance with Häussler et al. [2005] who found a negative correlation between prevalence of type 2 diabetes and income. Because contributions to GKV are defined as a percentage of (labor) income, higher income leads to higher contributions. While the function is nonlinear because the percentage varies between sick funds and regions, non-diabetics do pay a higher contributions on average than the others. Some 41 percent of them also have at least one supplementary insurance contract, compared to 30 percent for type 1 diabetics and 31 percent for insulin-treated diabetics. This reflects the fact diabetics treated with insulin present high risks to private health insurers offering supplementary coverage, causing high premiums or exclusion clauses to be applied.

The lower part of Table 2 contains information about duration of illness and incidence of diabetic complications. Type 1 diabetics on average have been suffering for 17 years from the disease at the time of the DCE. For type 2 diabetics this value drops to 8 to 9 years. Only 18 percent of type 2 diabetes patients with insulin treatment do not suffer from any complication. For insulin-naive type 2 diabetics, this number is 23 percent and for type 1 diabetics, 27 percent. High blood pressure is the most common complication, followed by diabetic neuropathy, diabetic feet, and diabetic retinopathy. Strokes, hearth attacks, as well as amputations, are most common among type 2 diabetics with insulin therapy.

Table 2: Descriptive statistics

Variable	All respondents	Non-diabetics	Type 1 diabetics	Type 2 diabetics with insulin	Type 2 diabetics insulin-naive
n	1,100	600	200	150	150
Socioeconomic variables and health status					
Age	51.10 (16.18)	47.70 (16.54)	44.67 (15.17)	61.99 (9.74)	62.11 (9.44)
Female*	51.49	52.25	50.49	50.65	50.65
Subj. health status ¹	66.46 (23.27)	72.56 (22.46)	62.06 (22.63)	53.70 (21.95)	61.33 (20.74)
BMI ²	26.17 (4.54)	25.26 (4.16)	26.45 (5.32)	28.18 (4.50)	27.35 (3.98)
Health insurance					
Income ³	1903.75 (1,014.85)	1,974.55 (1,055.40)	1,814.07 (1,022.41)	1,866.67 (918.88)	1,783.22 (918.07)
GKV contribution ⁴	1,879.60 (703.91)	1914.77 (727.90)	1,832.82 (719.00)	1,894.09 (630.44)	1,787.76 (650.30)
Supplementary insurance*	37.03	40.51	30.20	31.17	38.16
Duration of illness and incidence of diabetes complications					
Years of illness					
Diabetes complication*			17.32	8.60	8.03
High blood pressure*			72.87	81.82	76.97
Diabetic foot*			43.07	63.64	59.21
Diabetic neuropathy*			20.30	30.52	16.45
Diabetic retinopathy*			32.67	35.06	27.63
Stroke / heart attack*			10.89	14.94	7.24
Amputation*			8.91	12.39	5.26
			1.49	3.90	1.32

* In percent of the respective population

1: Subjective health status, 0 = "very bad", 100 = "very good"

2: Body Mass Index

3: Net income per household per year in Euro

4: Health insurance contribution per year in Euro

Standard errors in parentheses.

6 Empirical Results

6.1 Overall Willingness To Pay

As a first step, it is important to know whether the attributes retained are relevant and have the expected impacts on utility. Table 3 presents the estimation results of eq. (9), relating to both diabetic and non-diabetic participants in the DCE. Since the healthy were asked to envisage having diabetes, their subjective probability π_i was set to one. Therefore, the parameter estimates shown in the first column coincide with the β 's of eq. (9). However, they must be probability-weighted for deriving estimates that apply to GKV members in general who would pay increased contributions. Coefficients and marginal effects weighted by the average subjective probability of coming down with diabetes are displayed in the last two columns of Table 6.1. Subjective probabilities (π_i) were measured in the questionnaire using a visual analogue scale from 0 percent (will never become insulin-treated diabetic) to 100 percent (will become insulin-treated diabetic with certainty). For diabetics already treated with insulin, π_i is equal to one resulting in an average value ($\bar{\pi}$) of 53 percent.

All coefficients are highly significant and have the expected signs. The positive value of the constant can be interpreted as follows. If the specification of the utility function had been perfect, then the difference between the alternative and the status quo would be entirely due to the differences in attributes. There would be no reason to expect a constant different from zero. However, there may be individual characteristics not accounted for that give rise to a bias in favor or against the status quo. In the present case, the positive constant points to a preference in favor of the alternative and hence a bias against the status quo.

Table 3: Results of a random-effects probit estimation without subgroups

Attribute	Exp. sign	$\hat{\beta}$	z-value	Marg. effect	$\hat{\beta} * \bar{\pi}$	Marg. effect* $\bar{\pi}$
Constant		0.7632	15.77			
Hypoglycemia ¹	+	0.0065	14.07	0.002	0.004	0.001
Weight ²	+	0.1380	13.27	0.051	0.073	0.027
Preparation ³	±	0.2947	8.41	0.108	0.157	0.059
Flexibility ³	+	0.1704	4.94	0.063	0.091	0.034
Copayment	-	-0.0055	-39.97	-0.002		
Contribution	-	-0.0047	-5.23	-0.002	-0.003	-0.001
σ_u		0.51				
ρ		0.20				

¹: Decrease of the risk of hypoglycemia

²: Avoiding weight gain

³: Dummy-variable, 0 = status quo, 1 = alternative

Using eqs. (5) and (10), marginal WTP values depending on the mode of financing (copayment and increase in contributions, respectively) can be estimated. The upper part of Table 4 shows the results for copayment, the lower, for contributions. For both modes, preference for the alternative is very high, viz. 262 and 162 Euro per year. In most DCE, status quo bias is negative, indicating resistance against change (see e.g. Zweifel et al. [2007], Telser and Zweifel [2002]). In the case of diabetes treatment, the respondents seem to be willing to pay for a shift away from the status quo. Since in addition all marginal WTP (MWTP) values for the attributes are significantly positive, Insulin Detemir is valued positively, as predicted by Hypothesis H1.

As to the risk of hypoglycemia, respondents are willing to pay an estimated 1.19 Euro per year for a 1 percentage point reduction through copayment and 1.39 Euro through contributions. The second amount decreases to 0.74 Euro per year when weighted by average probability $\bar{\pi}$ (see lower part of Table 4). To avoid 1 kg of weight gain, respondents are willing to pay 25 Euro through copayment or 16 Euro through higher yearly contributions, respectively. To compare the importance of the two attributes, consider a 100 percent change. For the risk of hypoglycemia, a 100 percent decrease has an approximate WTP of 119 (copayment) and 139 Euro (contribution), respectively. For fully avoid-

Table 4: Marginal WTP for product attributes

Attribute	MWTP	Standard error		z-value	MWTP* $\bar{\pi}$
		Delta M. ⁴	Boots. ⁵		
Financing through copayment					
Constant	261.54	8.54	9.11	16.29	
Hypoglycemia ¹	1.19	0.09	0.10	13.48	
Weight ²	25.15	1.90	2.19	13.23	
Preparation ³	53.69	6.34	6.31	8.47	
Flexibility ³	31.04	6.29	6.37	4.94	
Financing through health insurance contribution					
Constant	161.75	29.20	41.11	5.54	161.75
Hypoglycemia ¹	1.39	0.28	0.40	4.87	0.74
Weight ²	29.25	5.79	8.80	5.05	15.55
Preparation ³	62.46	13.87	18.48	4.50	33.21
Flexibility ³	36.11	10.20	13.31	3.54	19.20

¹: Decrease of the risk of hypoglycemia by 1 percentage point

²: Avoiding weight gain

³: Dummy variable, 0 = status quo, 1 = alternative

⁴: Standard errors calculated using the Delta Method

⁵: Standard errors calculated using bootstrapping with 1,000 replications

All MWTP values are in Euro per year, 1 Euro = 1.4 US\$ at 2008 exchange rates.

Table 5: Non-marginal WTP for product attributes

Attribute	WTP through copayment	WTP through contribution
Constant	261.5	161.8
Hypoglycemia ¹	35.7	22.2
Weight ²	62.9	38.9
Preparation ³	53.7	33.2
Flexibility ³	31.0	19.2
Total	444.8	275.3
Total net of Constant	183.3	113.5

¹: Decrease of the risk of hypoglycemia by 30 percentage point

²: Avoiding a 2.5 kg weight gain

³: Dummy variable, 0 = status quo, 1 = alternative

All WTP are in Euro per year.

ing the weight gain of 2.5 kg on average (see Section 2.1), which also amounts to a 100 percent change, the WTP value is 63 (= 2.5*25.15, copayment) and 73 Euro (= 2.5*29.25, contribution). Hence, regardless of mode of financing, respondents value decreasing the risk of hypoglycemia almost two times higher than avoiding weight gain, corroborating H2.1. As to WTP for increased flexibility in the timing of the injection, the values amount to 31 (copayment) and 19 Euro (contribution), respectively. This is much less than the 63 and 73 Euro for avoiding weight gain, in accordance with H2.2.

The possibility to inject insulin without any preparation is worth 54 (copayment) or 33 Euro per year (contribution), respectively. Since these values clearly differ from zero, they constitute evidence against H2.3. A seemingly minor innovation (from the medical point of view) is clearly valued by consumers. However, it is valued less than avoidance of either hypoglycemia or weight gain. For instance, the difference between 1.19 Euro (hypoglycemia, copayment) and 54 (preparation, copayment) has statistical significance in view of the small standard errors displayed in Table 4.

Since H1 (positive value of the innovation) is confirmed, the question arises as to its total WTP value. As described in Section 2.2, Insulin Detemir corresponds to the following changes in attributes. Risk of hypoglycemia decreases by 30 percent in comparison to treatment with human insulin. Whereas patients gain 2,5 kg on average with human insulin, there is no weight change with Insulin Detemir. The preparation does not need to be swung, and the time of injection is more flexible. Following Hanemann [1983], non-marginal WTP associated with these changes is computed as the marginal WTP multiplied by the change of the attribute's value. These component values are then summed up to obtain total WTP for the product (see Johnson and Desvousges [1997]). The results of these calculations are shown in Table 5. Total WTP for the innovation amounts

to 445 Euro per year if financed through copayment and 275 Euro if financed through an increase in contributions. Approximately 60 percent of this WTP comes from bias in favor of the alternative. If it is subtracted, 183 and 114 Euro result, respectively. The highest component value comes from the difference in weight gain, viz. 63 Euro (copayment) and 39 Euro (contribution), the lowest from flexibility of injection timing.

6.2 Total Willingness To Pay across Subgroups

To obtain group-specific WTP values, eq. (9) was estimated separately for non-diabetics, type 1 diabetics, and type 2 insulin-naive as well as insulin-treated diabetics. Group-specific MWTP values (not shown) are multiplied by the changes in attributes levels due to Insulin Detemir and summed, in full analogy to Table 5. The resulting non-marginal WTP values across subgroups are presented in Table 6. Sum I comprises all component WTP values, sum II only the significant ones. Standard errors (not shown) are small enough to conclude that there is preference heterogeneity between these four groups, confirming H3. Non-diabetics and insulin-naive type 2 diabetics have similar preferences, as do type 1 and insulin-treated type 2 diabetics.

Moreover, comparison of the upper and the lower part of Table 6 shows that the mode of payment matters, but not entirely in the way predicted by H4. As stated by H4, WTP values among diabetics should be higher when the financing of the innovation occurs through increased GKV contributions rather than copayment, while among the non-affected, it should be the other way round. Now non-diabetics indeed exhibit a higher total WTP value when financing is through copayment. They are joined by the insulin-naive diabetics who apparently deem themselves not to be affected. On the other hand, type 1 diabetics do have higher WTP when financing occurs through increased contributions, but the difference is not statistically significant. For insulin-treated type 2 diabetics, the ordering is as expected at first sight (sum I). Their WTP is extremely high when they envisage financing through increased contributions rather than copayment. However, not a single component value is significantly different from zero, causing sum II to be zero as well. Apparently, opinions are very divided among these patients concerning Insulin Detemir as soon as it were to be paid for by increased contributions.

The high WTP values estimated for non-diabetics in the case of copayment also merit discussion. It is doubtful that they would be verified in a real purchase decision. Rather, being importantly due to a high constant, they point to a strong bias in favor of the alternative - provided those affected pay for the innovation themselves.

Finally, the entries of Table 6 can also be interpreted in the following way. The high copayment-related WTP values of non-diabetics and insulin-naive diabetics suggest that they prefer financing through patients themselves. Conversely,

insulin-treated patients prefer financing jointly through health insurance contributions. However, whatever the group considered and regardless of mode of payment, WTP for Insulin Detemir measured by sum I exceeds its cost of treatment (estimated at 226 Euro per year). If measured by sum II, this is also true, with the only exception of type 2 insulin-treated patients. Therefore, by a benefit-cost criterion, including this product in the GKV list of benefits appears to be justified.

Table 6: Non-marginal WTP across subgroups

Attribute	Non-Diabetics	Diabetics		
		Type 1	Type 2 Insulin-naive	Type 2 Insulin-treated
Financing through copayment				
Hypoglycemia ¹	38.53	27.95	43.98	29.25
Weight ²	71.80	37.49	50.16	71.53
Flexibility ³	25.22	(24.37)	46.45	50.71
Preparation ³	56.62	48.28	(25.85)	72.17
Constant	597.47	106.90	286.55	94.62
Sum I	789.63	244.99	452.99	318.29
Sum II*	789.63	220.62	427.14	318.29
Financing through increased contribution				
Hypoglycemia ¹	11.32	34.11	17.65	(100.11)
Weight ²	21.09	45.75	20.13	(244.76)
Flexibility ³	7.41	(29.74)	18.64	(173.53)
Preparation ³	16.63	58.92	(10.38)	(246.97)
Constant	175.51	130.46	115.00	(323.79)
Sum I	231.96	298.99	181.80	1,089.16
Sum II*	231.96	269.35	171.43	0.00

¹: Decrease of the risk of hypoglycemia by 30 percentage point

²: Avoiding a 2.5 kg weight gain

³: Dummy-variable, 0 = status quo, 1 = alternative

*: Only significant values

Values in parentheses are not statistically different from zero.

7 Conclusions

This study revolves around the issue of whether a particular pharmaceutical innovation should be included in the benefit list of a social health insurer. From a cost-benefit perspective and neglecting distributional concerns, inclusion is justified if the insured have a willingness to pay (WTP) that exceeds the cost of treatment with the new product. The case in question is modern insulin therapy, using the long-acting insulin analogue "Insulin Detemir". Preferences for this preparation in comparison to conventional therapy (using human insulin) are derived with the help of a discrete choice experiment. It involved 1,100 members of German statutory health insurance (GKV) in 2007, of whom 200 suffer from type 1 diabetes, 150 from type 2 diabetes treated with insulin, 150 are insulin-naive type 2 diabetics, and 600 are non-diabetics. The novelty of the experiment lies in two aspects. First, distinguishing these groups allows to estimate both ex-ante WTP for non-diabetics and ex-post WTP for diabetic patients. Second, including the mode of payment (copayment vs. increasing GKV contribution) permits to test whether the innovation has a favorable benefit-cost ratio regardless of the way it is financed. Based on the results reported in the text, four research questions can be answered.

- (1.) Is there positive WTP for the long-acting insulin analogue Insulin Detemir? Yes, there is compared to the conventional therapy using long-acting human insulin (Table 5). Components of this total value are WTP for reduction of the risk of hypoglycemia by 30 percentage points, no weight gain rather than 2.5 kg during the first six months of the therapy, relief from the need to prepare the preparation before each injection, and flexibility in the timing of the injection.
- (2.) Which product attributes contribute to total WTP? All product attributes have positive WTP values. For comparison purposes, a hypothetical 100 percent reduction of the risk of hypoglycemia and of the weight gain are considered because the other attributes are (0,1) variables. In accordance with expectations, the maximum contributions comes from risk reduction with respect to hypoglycemia, followed by avoiding weight gain. The other attributes are less valued, as predicted.
- (3.) Is there preference heterogeneity across morbidity groups, viz. non-diabetics, type 1 diabetics, insulin-treated type 2 diabetics, and insulin-naive type 2 diabetics? Yes, there is heterogeneity. Total WTP values differ significantly between subgroups. Insulin-naive type 2 and non-diabetics have similar preferences, as do type 1 and insulin-treated type 2 diabetics.
- (4.) Is the benefit-cost ratio of the innovation favorable regardless of whether it is financed jointly through increased GKV contributions or by patients themselves through copayment? Yes, this is the case, with the one exception of type 2 insulin-treated diabetics, whose WTP values are very high but lack statistical significance. Also, whereas non-diabetics and insulin-naive diabetics exhibit

higher WTP values if financing is through copayment, insulin-treated diabetics have higher values if financing is through insurance contributions. This can be interpreted as a preference for financing through copayment on the part of non-diabetics and insulin-naive diabetics and through insurance of the part of insulin-treated diabetics. However, since even non-diabetics' WTP is higher than the actual treatment cost of Insulin Detemir regardless of mode of payment, its inclusion in the GKV list of benefits can be justified.

These conclusions are subject to a number of reservations. First, the WTP estimates may be biased upward because participants in the experiment may not be representative of the GKV population. Indeed, the average net household income in the sample is below average, which may result in a general dissatisfaction with the status quo driving up WTP for alternative treatment of diabetes as well. Second, the attributes mentioned only describe differences in treatment using an insulin analogue compared to human insulin which might not describe treatment of diabetes using insulin in a sufficient way. Depending on the sign of the correlation between the left-out and the included attributes, WTP values reported are over- or underestimated. Finally, one may judge the cost-benefit standard adopted here as inappropriate. On the one hand, benefits in terms of Quality Adjusted Life Years rather than money should be measured according to some writers (see e.g. Williams and Cookson [2000], Culyer [1990], or Drummond et al. [2005]). On the other hand, average WTP values neglect distributional issues.

While these concerns may well be valid, they are unlikely to overthrow the major findings of this study. First, there is clear evidence suggesting that not only the avoidance of hypoglycemia and weight gain but also attributes that typically are judged medically irrelevant such as no need for preparation (swinging) and flexibility in the timing of the injection are valued attributes of insulin therapy. In addition, these attributes are valued by diabetes patients and potential patients alike. Second, these valuations add up to total amounts that exceed the marginal cost of the innovation, with the only exception of type 2 insulin-treated diabetics whose WTP values, while sizable, cannot be distinguished from zero due to excess heterogeneity. It is difficult to conceive of biases so strong and distributional weightings so skewed to conclude that WTP values of GKV members likely do not satisfy inclusion of this pharmaceutical innovation in the benefit list.

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