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To cite this article: J. Jendle, M. Ridderstråle, O. Torfvitt, Å Ericsson & S. Larsen (2012) Willingness-to-pay for benefits associated with basal insulin treatment of type 2 diabetes, Journal of Medical Economics, 15:2, 261-263, DOI: [10.3111/13696998.2011.644408](https://doi.org/10.3111/13696998.2011.644408)

To link to this article: <https://doi.org/10.3111/13696998.2011.644408>



Published online: 06 Dec 2011.



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Research letter

Willingness-to-pay for benefits associated with basal insulin treatment of type 2 diabetes

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Keywords:

Health economics – willingness-to-pay – type 2 diabetes – basal insulin – insulin detemir – NPH insulin – discrete choice experiments – hypoglycemia

Accepted: 22 November 2011; published online: 6 December 2011
Citation: J Med Econ 2012; 15:261–63

Abstract

Data from a 20-week trial comparing insulin detemir and neutral protamine Hagedorn (NPH) insulin in insulin-naïve people with type 2 diabetes were analyzed using willingness-to-pay (WTP) data, a proxy for patient preference. The advantages of insulin detemir relative to NPH insulin with respect to a lower hypoglycemia rate and less weight gain were associated with a value of €27.87 per month.

Introduction

Absorption of human insulins such as basal neutral protamine Hagedorn (NPH) insulin is variable, and their use is associated with interprandial plasma concentration peaks that increase the risk of hypoglycemia¹. Meta-analyses have shown that glycemic control with long-acting insulin analogs is superior to that achieved with NPH insulin in people with type 1 diabetes, but not in people with type 2 diabetes^{2,3}. However, people with type 2 diabetes who switch from NPH insulin to the insulin analog insulin detemir could potentially improve their disease management by gaining less weight^{4,5}, and by having a lower risk of hypoglycemia^{4,5}. Current Swedish guidelines recommend that basal insulin analogs be considered as an alternative to NPH insulin in people with type 2 diabetes who have recurrent hypoglycemia or erratic glucose control⁶.

Discrete choice experiments (DCEs) can be used to measure the value people with diabetes place on each attribute of diabetes treatment and to calculate a person's preferences. This can be measured as willingness-to-pay (WTP) for attributes such as preventing weight gain or avoiding hypoglycemia. In a previous Swedish WTP study by Jendle *et al.*⁷, people with type 2 diabetes were willing to pay considerable amounts of money per month to prevent weight gain, reduce or avoid hypoglycemia, and reduce HbA_{1C} levels.

In this analysis, we used data from a multi-national clinical trial by Philis-Tsimikas *et al.*⁵, that compared insulin detemir with NPH insulin in insulin-naïve people with type 2 diabetes, and applied data from the Swedish WTP study⁷ to obtain a valuation of the potential improvements offered by insulin detemir. The trial by Philis-Tsimikas *et al.* was chosen because it is the only published study in insulin-naïve people with type 2 diabetes that directly compares a once-daily dose of insulin detemir with NPH insulin.

Methods

Estimates from a previous WTP study were applied to generate a valuation of those two treatment benefits from the source trial that showed significant differences between the insulin detemir and NPH insulin groups, namely the difference in weight gain and frequency of hypoglycemic events⁵. The valuations were calculated separately for the insulin detemir single evening dose. In the source trial, NPH insulin was administered in the evening only. The two relevant estimates from the WTP study were Swedish Kronor (SEK)107 per month to have one fewer hypoglycemic event per month and SEK265 per month to avoid a weight gain of 1 kg when compared with the current state⁷.

The number of hypoglycemic events per person with diabetes per month in the source study was calculated by dividing the number of hypoglycemic events per person with diabetes over the study period by 4.615 (the number of months in the 20-week study period). The DCE method used in the original WTP study estimated the marginal values of an isolated measured effect, which allows the values of two or more different variables to be aggregated. Hence, the WTP values associated with a reduction in the number of hypoglycemic events and a reduction in weight gain were added together.

The WTP study was carried out in Swedish people with diabetes, and WTP values were calculated in SEK. For this analysis, values are shown in Euros, derived by using an exchange rate of SEK1 = €0.112 (March 15, 2011).

Results and discussion

The calculated WTP valuations are shown in Table 1. Compared with patients on NPH insulin, there were 0.097 fewer hypoglycemic events per month in each patient who received insulin detemir as an evening dose. Weight gain was 0.9 kg less with insulin detemir than seen with NPH insulin. By applying the WTP values to the

hypoglycemia and weight gain differences, the combined WTP valuation of the treatment advantage (the sum of the two target outcomes) was €27.87 per month based on an evening dose of insulin detemir. The dominant driver of this was the lower weight gain seen with insulin detemir.

The national recommendation by the Swedish Board of Health and Welfare is that insulin treatment, when indicated in people with type 2 diabetes, should be given primarily as NPH insulin, premixed insulin, or rapid-acting insulin given at meal time. Long-acting insulin analogs, such as insulin glargine and insulin detemir, could be given if the person with diabetes experiences episodes of hypoglycemia on treatment with human insulin⁶. This differs from guidelines from some other countries which recommend initiation with insulin analogs in patients who may be at risk of hypoglycemia⁸. However, the results of this analysis suggest that the value of avoiding weight gain and, to a lesser extent, hypoglycemic events, by initiating therapy with an insulin analog, has a defined value for patients; this is relevant in the context of the Swedish reimbursement system, which relies on value-based pricing. WTP for a reduction in hypoglycemia was lower in our study than previously reported for Sweden¹, which may be due to the smaller difference in the incidence of hypoglycemia between the once-daily insulins in our study.

Indeed, while physicians place a higher importance on HbA_{1c} reduction than small differences in weight loss, patients in this study valued weight loss above reduction in HbA_{1c}. One reason why patients give a higher priority to weight control may be because they value the immediate impact of weight loss and link this to general well-being, more than they value the longer-term benefits of glycemic control of diabetes provided by HbA_{1c} reduction.

The timing of when to take either NPH insulin or long-acting insulin analogs during the day is not specified in the Swedish recommendations⁶. In clinical practice, basal insulin therapy is often given at bedtime in people with type 2 diabetes. No advantage in glycemic control has

Table 1. Derived willingness-to-pay values (in Euro, €) associated with differences between insulin detemir and neutral protamine Hagedorn insulin in source clinical trial. Both insulin treatments are dosed once daily.

	NPH insulin	Insulin detemir	Treatment difference (insulin detemir-NPH insulin)	Derived WTP valuation for treatment difference (€)	<i>p</i>
Patients (<i>n</i>)	164	169	—	—	
Hypoglycemic events (<i>n</i>)	153	82	—	—	
Hypoglycaemic events per person, <i>M</i>					
Study total (20 weeks)	0.933	0.485	0.448	—	
Per month	0.202	0.105	0.097	1.16 ^a	0.019
Weight gain during study, <i>M</i> (kg)	1.6	0.7	0.9	26.71 ^b	0.005
Total derived WTP valuation (€)	—	—	—	27.87	

^aApplying WTP value of SEK107 (€11.98) per hypoglycaemic event avoided per month.

^bApplying WTP value of SEK265 (€29.68) per kg weight gain.

NPH, neutral protamine Hagedorn; WTP, willingness-to-pay.

been shown when dosing insulin detemir twice daily to people with type 2 diabetes; on the contrary, the insulin dose needed is larger and the weight gain is higher when this administration is chosen⁹. As NPH was only given in the evening, this study made a direct comparison between the detemir evening dose and the NPH evening dose; data relating to the detemir morning dose were not included in the analysis.

The current analysis is based on a treatment comparison from one clinical trial only, as this is the only comparison of the treatments under study that used once-daily dosing in insulin-naïve people with diabetes. Application of WTP values to a wider range of clinical data, including observational studies, would enable us to produce a more robust valuation estimate of what might be the scenario in routine clinical practice. As people with type 2 diabetes in the WTP study were matched with people with diabetes from the Swedish National Diabetes Registry during selection, the WTP valuations should be generally representative of all people with type 2 diabetes in Sweden. Cultural and social differences might limit generalization of these findings to other countries, although a previous multi-national study that determined WTP values in the people with diabetes population found the same priorities as in the Swedish WTP study, ie avoidance of weight gain and hypoglycemia¹⁰. However, the WTP for better weight control, a reduction in hypoglycemia and better glycemic control as measured by HbA_{1c} may differ in other clinical settings where insulin analogs are more routinely used as first-line insulin treatment⁸.

Similar WTP analyses could be applied to data from other clinical trials to demonstrate the value of benefits that could be attained from other diabetes treatment changes, or in other patient populations.

Conclusions

The advantages of insulin detemir relative to NPH insulin with respect to a lower hypoglycemia rate and less weight gain in insulin-naïve people with type 2 diabetes are associated with a value to the person of €27.87 per month based on WTP values determined in Swedish people with diabetes.

Transparency

Declaration of funding

Funding for this work was provided by the sponsor Novo Nordisk, Scandinavia. All authors were actively involved at all stages of the preparation of the manuscript.

Declaration of financial/other relationships

JJ, MR, and OT have been involved in Novo Nordisk advisory boards and as consultants to Novo Nordisk, Scandinavia. ÅE and SL are employees of Novo Nordisk, Scandinavia.

Acknowledgments

Editorial assistance was provided by John Clarke and Martin Gilmour (ESP Bioscience, Crowthorne, UK) funded by Novo Nordisk, Scandinavia.

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