PDB64 Cost-effectiveness of insulin Detemir versus insulin Neutral Protamine Hagedorn (NPH) in patients with type 1 diabetes mellitus in Spain

1. **Antonio Ramirez Arellano, PhD**
EU-HEOR, Novo Nordisk, Madrid, Spain
2. **Luis Lizán, MD PhD**
Outcomes'10, Castellón, Spain
3. **Cristobal Morales, MD**
Virgen de la Macarena Hospital, Seville, Spain
4. **Miriam Prades, MSc**
Outcomes'10, Castellón, Spain
5. **Daniel de Luis, MD**
Rio Hortega Hospital, Valladolid, Spain

INTRODUCTION

Type 1 diabetes mellitus (T1DM), which affects about 10% of all diabetes patients, is characterized by deficient insulin production and requires daily administration of insulin.[1] However, hypoglycemia and weight gain remain major limiting factors in the management of T2DM patients on insulin.[2] In recent years, long-acting insulin analogues such as insulin detemir and insulin glargine have provided a safer alternative to traditional long-acting human insulins such as Neutral Protamine Hagedorn (NPH) insulin.[3]

AIM

To estimate the short-term cost-effectiveness of insulin Detemir compared with NPH insulin when initiating insulin treatment in patients with T1DM in Spain.

METHODS

▪**Model.** A short-term cost-effectiveness model[4] was adapted to the Spanish public healthcare system. The main outcome variable was euros per quality-adjusted life year (€/QALY) gained.

▪**Perspective.** Spanish National Health System (NHS).

▪**Population.** Two hypothetical T1DM cohorts of 1,000 patients each.

▪**Time horizon.** 1 year.

▪**Clinical data input.** Insulin treatment effectiveness measures taken into account were incidence rate of non-severe hypoglycemia (NSH). NSH was defined as an event that patients manage by themselves.[4] The rate ratio of experiencing a NSH with insulin Detemir treatment vs. NPH was 0.84 [CI95% 0.74-0.97].[3] Three base cases were defined based on three incidence values of NSH in T1DM patients 35.5 [CI95% 22.8-48.2] (insulin treatment<5 years)[5], 29.0 [CI95% 16.4-41.8] (insulin treatment >15 years)[5] and 88.0 events/person-year (basal only therapy).[6]

▪**Utility data input.** The disutility associated to daytime and nocturnal NSH was -0.0041 and -0.0067 per event, respectively (mean=-0.0054).[7]

▪**Costs** (in Euros 2014). Insulin Detemir and NPH pharmacy costs[8] of €1.24 and €0.65/day, respectively, (assuming a daily defined dose of 40IU for both insulins[9]) and a NSH event cost of €5.02 (5.6 extra glycemia test strips[8] and one GP visit[10] following the event for ¼ of the cohort[11]) were considered for this analysis.

▪**One-way Sensitivity Analysis (OWSA).** OWSA was performed varying variables relative to:

1) Detemir/NPH hypoglycemia rate ratio (RR) (CI 95% low and high)[3];

2) Hypoglycemia disutility (100% daytime; 100% nighttime)[7];

3) Cost of NSH (±20%);

4) Cost of Detemir (±20%);

5) Cost of NPH (±20%);

▪**Probabilistic Sensitivity Analysis (PSA).** PSA was performed in order to estimate the impact of varying at once the values of all model variables, according to specific probability distributions.

RESULTS

▪**Deterministic analysis.** The lower frequency of NSH associated to Detemir vs. NPH treatment resulted in a quality-adjusted life year (QALY) gain in the Detemir arm relative to the NPH arm (Table 1). The ICER of Detemir vs. NPH in insulin-naïve patients with T1DM was estimated to be €7,681.96 in Spain (Table 1), which is below the acceptability threshold commonly referred for Spain[12] (€30,000/QALY).

Figure 1. *OWSA tornado plot showing the impact of varying the values of the variables related to effectiveness between treatments (NSH rate), utility decrease associated to NSH events, and costs (treatment and NSH management).*
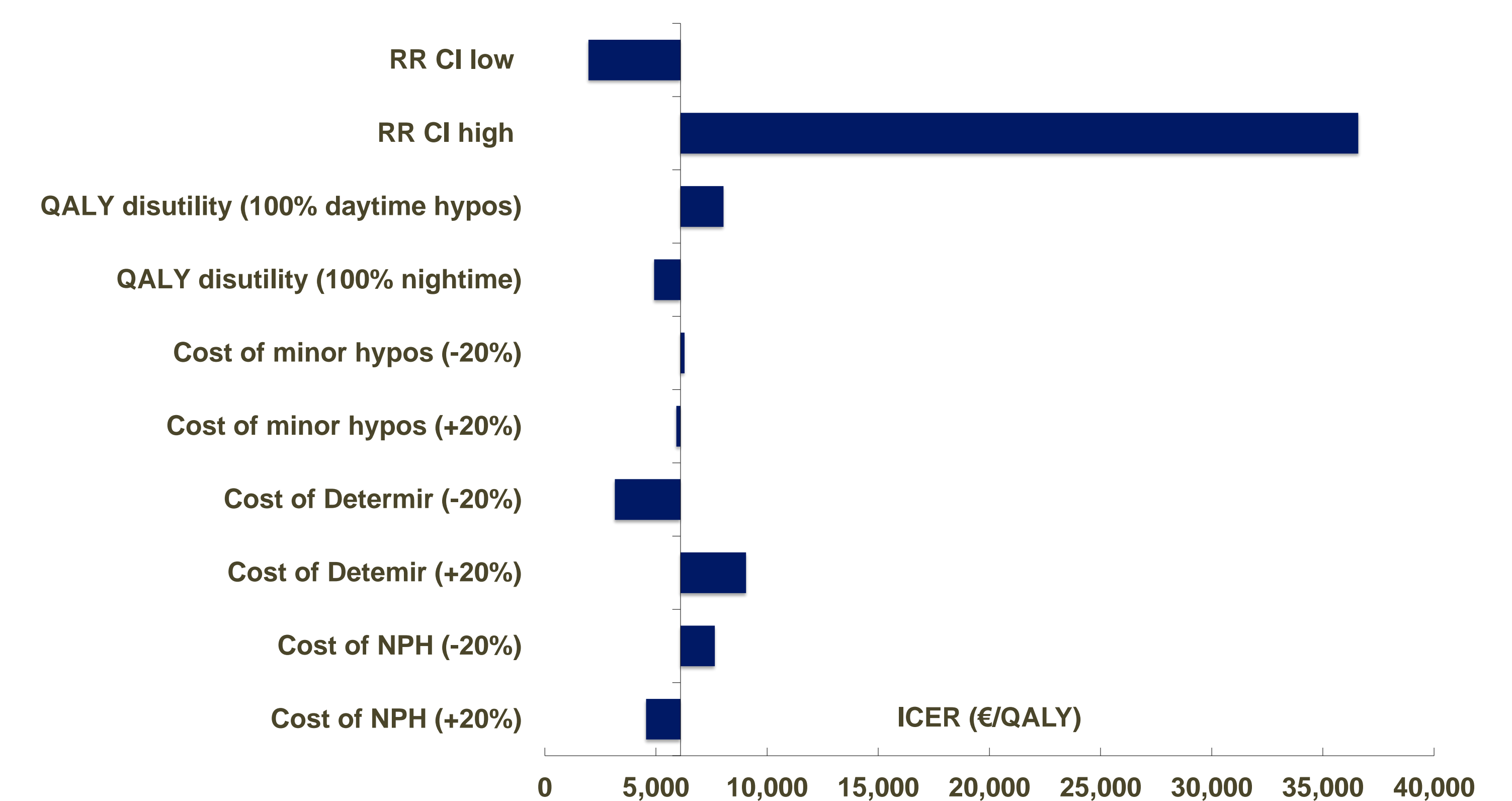
PSA. PSA shows that all cost estimations fall either in the more effective/less expensive (dominant) or in the more effective/more expensive (cost-effective depending on threshold) quadrant of the cost-effectiveness plane (Figure 2). The acceptability curve indicates that, with a threshold of €30,000/QALY, Detemir would be cost-effective with about 90% probability (Figure 3).

Figure 2. *Scatter plot of Detemir vs. NPH in the cost-effectiveness plane resulting from PSA with cost-effectiveness threshold marked at €30,000/QALY.*
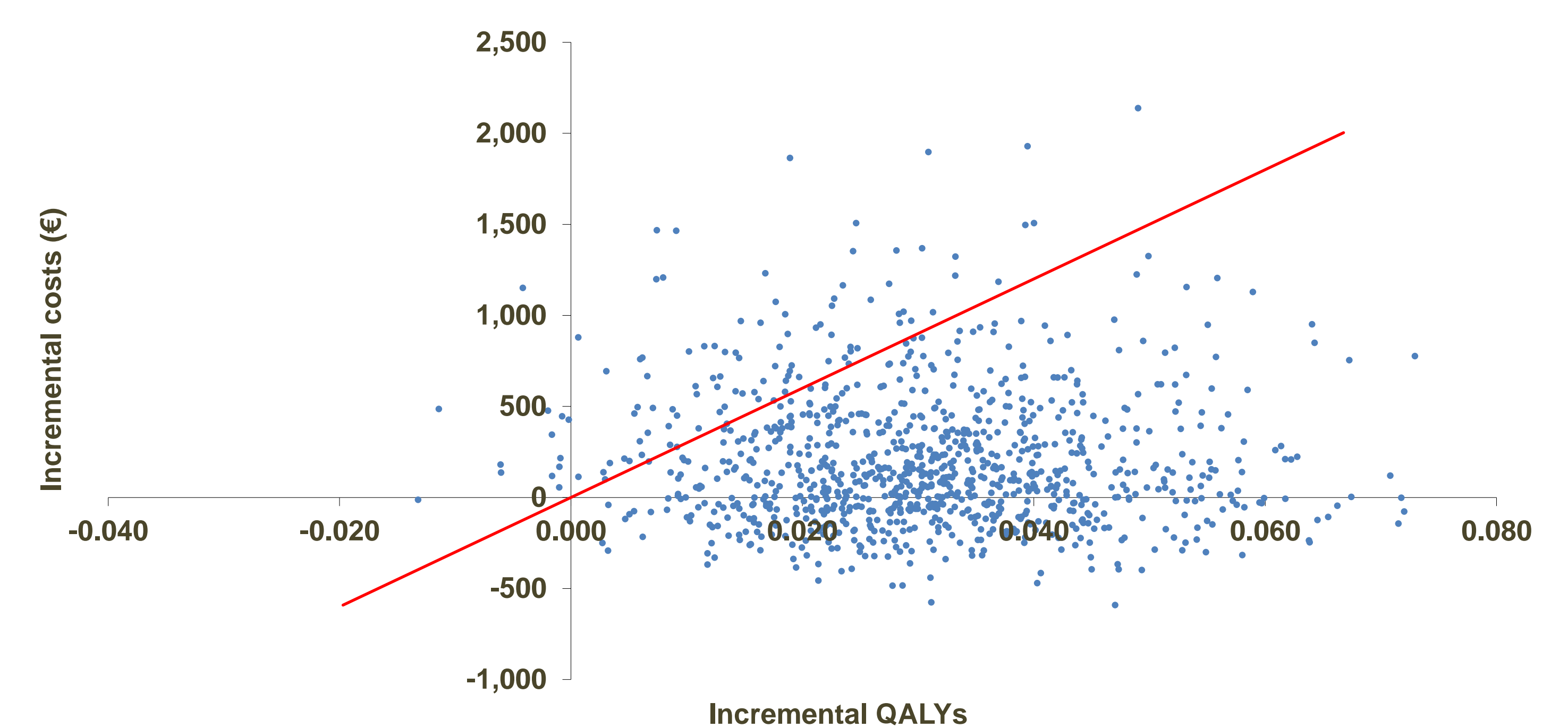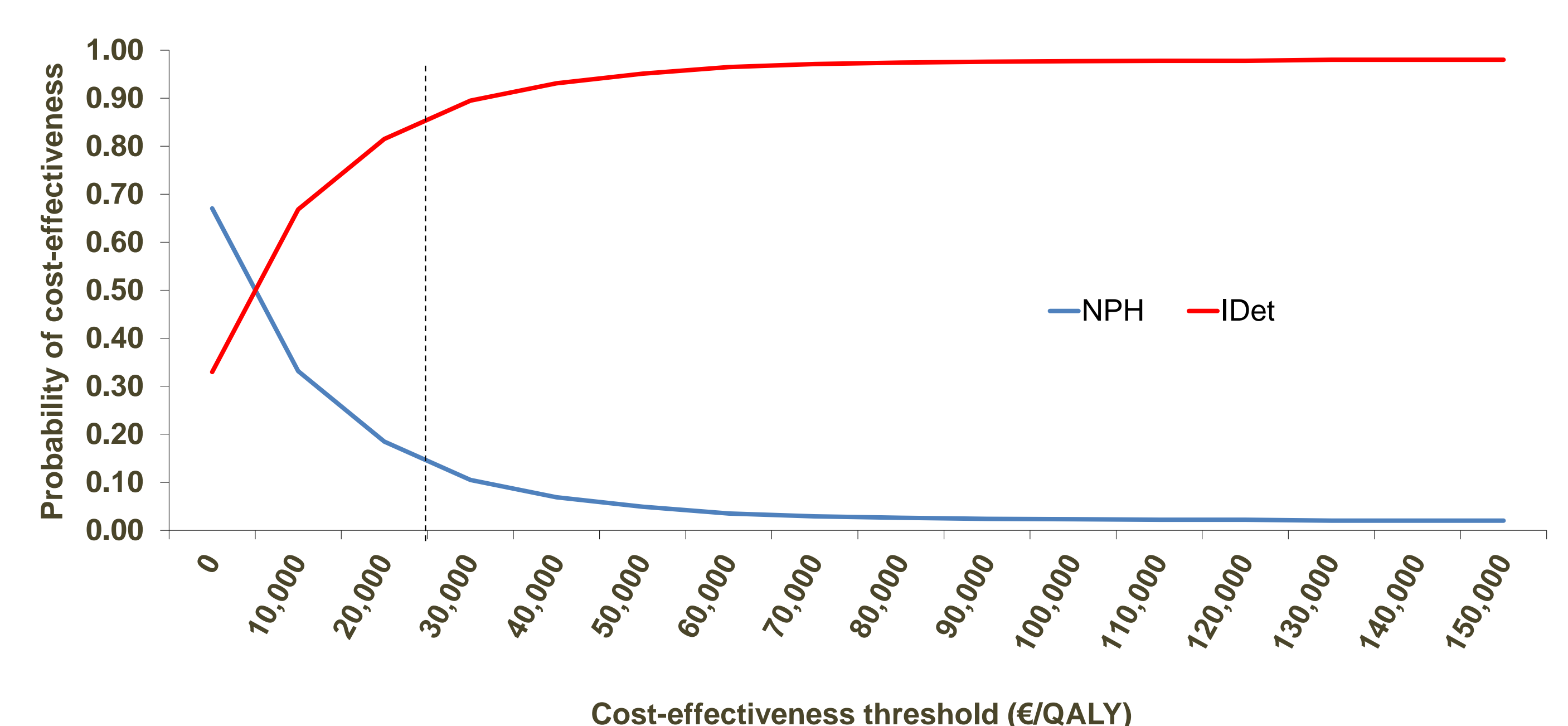

Figure 3. *Acceptability curve of Detemir vs. NPH in function of the cost-effectiveness threshold*

Table 1. *QALY gain, costs and ICER of 1-year treatment with insulin Detemir vs. NPH in three base cases defined according to NSH rate*

Treatment	NSH rate	QALYs	Incremental QALYs	Annual cost (€) Pharmacy	Annual cost (€) NSH	Annual cost (€) Total	Incremental Costs (€)	ICER (€/QALY)
Detemir	29.0	0.868	0.025	452.89	122.37	575.26	192.48	7,681.96
NPH		0.843		237.10	145.68	382.78		
Detemir	35.5	0.839	0.031	452.89	149.80	602.691	187.25	6,105.08
NPH		0.808		237.10	178.33	415.436		
Detemir	88.0	0.601	0.076	452.89	370.60	823.49	145.20	1,909.70
NPH		0.525		237.10	441.19	678.29		

OWSA. The different OWSAs performed (Figure 1) for NPH rate=35.5 show that the factor with the greatest impact on the ICER of Detemir vs. NPH is the Detemir/NPH hypoglycemia RR. In particular, assigning a Detemir/NPH RR close to 1 (upper 95%CI limit of the reference) would reduce clinical benefit to a non-relevant value, consequently increasing ICER.

CONCLUSIONS

The lower frequency of hypoglycemia associated to Detemir versus NPH treatment result in a significant QALY gain in the Detemir arm relative to the NPH arm. Despite its slightly higher pharmacy cost, Detemir is associated to decreased NSH costs with respect to NPH. Therefore, insulin Detemir is a cost-effective alternative to NPH insulin in the treatment of insulin-naive T1DM patients in Spain.

REFERENCES

1. WHO. Fact Sheets. Diabetes http://www.who.int/mediacentre/factsheets/fs312/en/ **2.** IDF Diabetes Atlas Executive Summary. http://www.idf.org/diabetesatlas/ **3.** CADTH Technol Overv. 2010;1(1):e0113 **4.** Valentine et al. Diabet Med. 2012;29:303-312. **5.** UK Hypoglycaemia Study Group. Diabetologia 2007;50:1140-7. **6.** Orozco-Beltrán et al. Diabetes Ther. 2014 ;5(1):155-68. **7.** Evans et al. Diabetes Obes Metab. 2014;16(4):366-75. **8.** Consejo General de Colegios Oficiales de Farmacéuticos. Available at: https://botplusweb.portalfarma.com/ ; Last acceded: February, 2014. **9.** WHO. ATC/DDD Index 2014. Available at: http://www.whocc.no/atc_ddd_index/ **10.** eSalud - Información económica del sector sanitario. Available at: http://www.oblikue.com/bddcostes/; Last acceded: February, 2014. **11.** Brod et al. Diabetes Obes Metab. 2013;15:546-57. **12.** Sacristán JA, et al. Gaceta Sanitaria. 2002;16(4):334-43.