

Cost-effectiveness of insulin Detemir versus insulin Neutral Protamine Hagedorn (NPH) in patients with type 2 diabetes mellitus in Spain.

1. Antonio Ramirez Arellano
EU-HEOR, Novo Nordisk, Madrid, Spain;
2. Manuel Galán
Medical Department, Novo Nordisk, Madrid, Spain
3. Maria Giovanna Ferrario
Outcomes'10, Castellón, Spain
4. Silvia Paz
Outcomes'10, Castellón, Spain
5. Luis Lizán
Outcomes'10, Castellón, Spain

Introduction and purpose:

Due to the progressive beta-cell dysfunction that characterizes type 2 diabetes mellitus (T2DM), basal insulin replacement therapy is frequently required in addition to oral antidiabetic drugs (OADs)¹. Though, hypoglycemia and weight gain remain major limiting factors in the management of T2DM patients on insulin.

Non-severe hypoglycemia (NSH) events occur more frequently than severe events, and patients with increased numbers of NSH are at higher risk for long-term complications and mortality, reductions in quality of life, increased fear and anxiety, reduced work productivity, and increased healthcare costs.² Weight gain is also commonly associated with intensive insulin therapy, leading to increased risk of cardiovascular morbidity and mortality.³ In fact, the World Health Organization has estimated that 44% of the burden of diabetes comes from weight problems.⁴

Aim:

To assess the cost-effectiveness, with respect to hypoglycemia rate and weight gain, of insulin detemir versus Neutral Protamine Hagedorn (NPH) in insulin-naïve patients with T2DM in Spain.

Methods:

- Model.** A short-term (1 year) cost-effectiveness model³ was adapted to the Spanish public healthcare system.
- Effectiveness variables.** Insulin treatment effectiveness measures taken into account were incidence rate of non-severe hypoglycemia (NSH) and weight gain³, as glycemic control for both drugs was shown to be similar (NCT00104182).⁵ NSH was defined as an event with a plasma glucose level of <3.0mmol/l or any episode where patients experienced hypoglycemia symptoms dealing with them by themselves.⁵ Between arm difference in weight was -0.9Kg (p=0.005) for detemir vs. NPH insulin.⁵ The incidence of NSH in T2DM patients initiating insulin treatment was 4.08 events/person-year.⁶ The rate ratio of experiencing a NSH with insulin detemir treatment vs. NPH was 0.52 (CI95% 0.44-0.61).⁵
- Time horizon.** 1 year.
- Perspective.** Spanish National Health System (NHS).
- Costs** (expressed in Euros 2014). Insulin Detemir and NPH pharmacy costs⁷ (assuming a daily defined dose of 40IU for both insulins⁸) and the NSH event cost (1 extra glycemia test strip⁹ and one GP visit¹⁰ following the event for ¼ of the cohort) were considered for this analysis.³

- Utilities.** The utility decrement associated to weight gain and NSH was -0.0100 per BMI unit increase¹¹ and -0.0035 per event¹², respectively.
- One-way Sensitivity Analysis (OWSA).** OWSA was performed varying variables relative to:
 - 1) insulin treatment duration;
 - 2) hypoglycemia disutility;
 - 3) hypoglycemia incidence;
 - 4) Detemir/NPH hypoglycemia rate ratio;
 - 5) NPH cost;
 - 6) Detemir vs. NPH weight gain difference;
 - 7) weight disutility.

- 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 hypoglycemia and the smaller weight gain 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 T2DM was estimated to be €23,834/QALY in Spain (Table 1), which is below the acceptability threshold commonly referred for Spain¹³ (€30,000/QALY).

Table 1. QALY gain, costs and ICER of 1-year treatment with insulin detemir vs. NPH

Treatment	QALYs	ΔQALY	Costs	ΔCosts
Detemir	0,990	0,010	499,28	238,47
NPH	0,980		260,81	

- OWSA.** The different OWSAs performed (Figure 1) show that the factor with the greatest impact on the ICER of Detemir vs. NPH is the increased incidence of hypoglycemia due to longer previous insulin exposure (>5 years). This indicates that the higher is the associated rate of NSH, the higher is the benefit given by Detemir vs. NPH. Another factor having a high impact on ICER is decreasing the disutility associated to NSH, which implies assuming a less impairing impact of NSHs on the patient's health-related quality of life.

Figure 1. OWSA tornado plot showing the impact of varying the values of the variables related to effectiveness (NSH rate and weight gain) between treatments, utility decrease associated to NSH and weight gain, and costs (NPH and detemir).

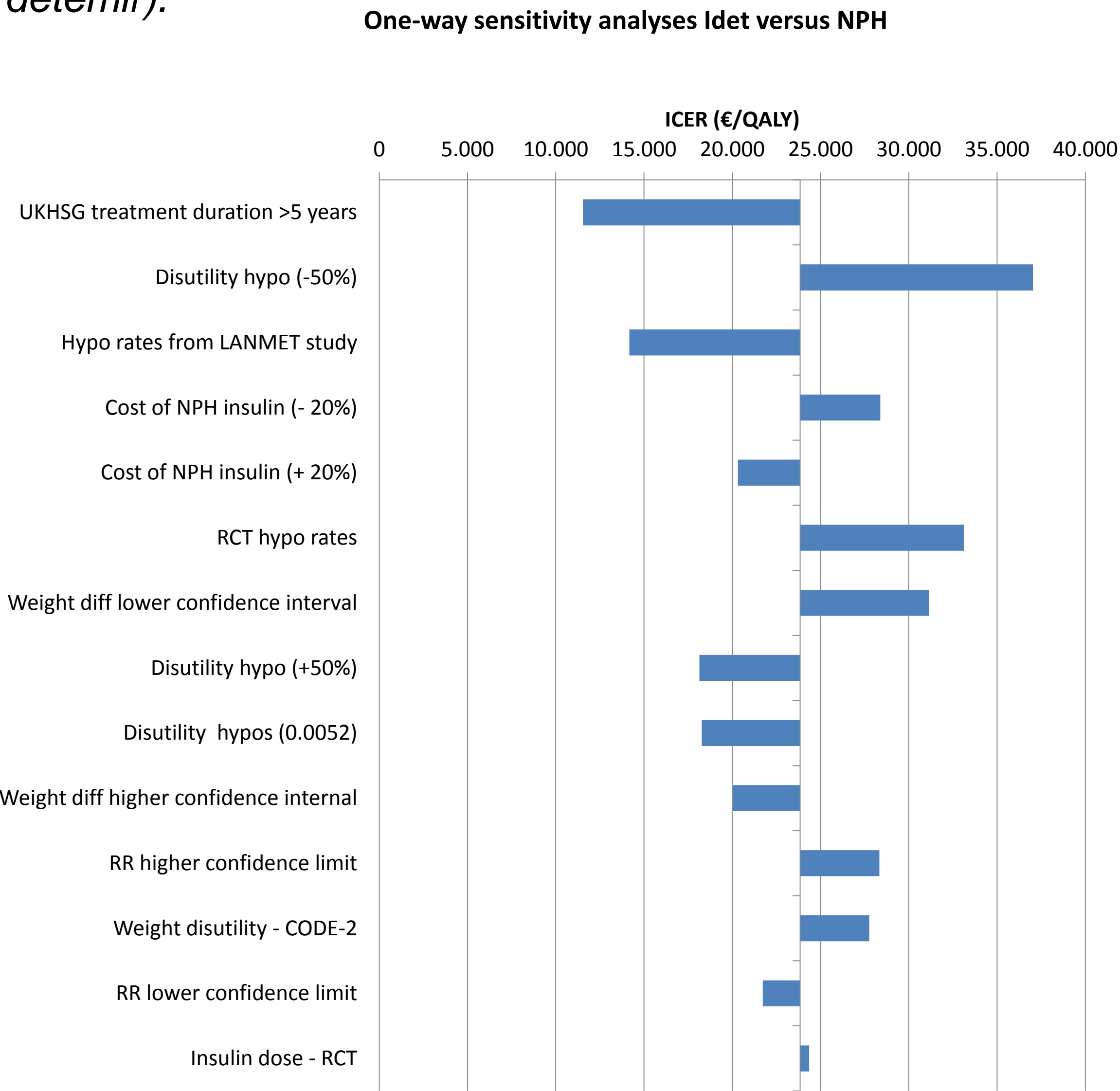


Figure 2 Scatter plot of Detemir vs. NPH in the cost-effectiveness plane resulting from PSA.

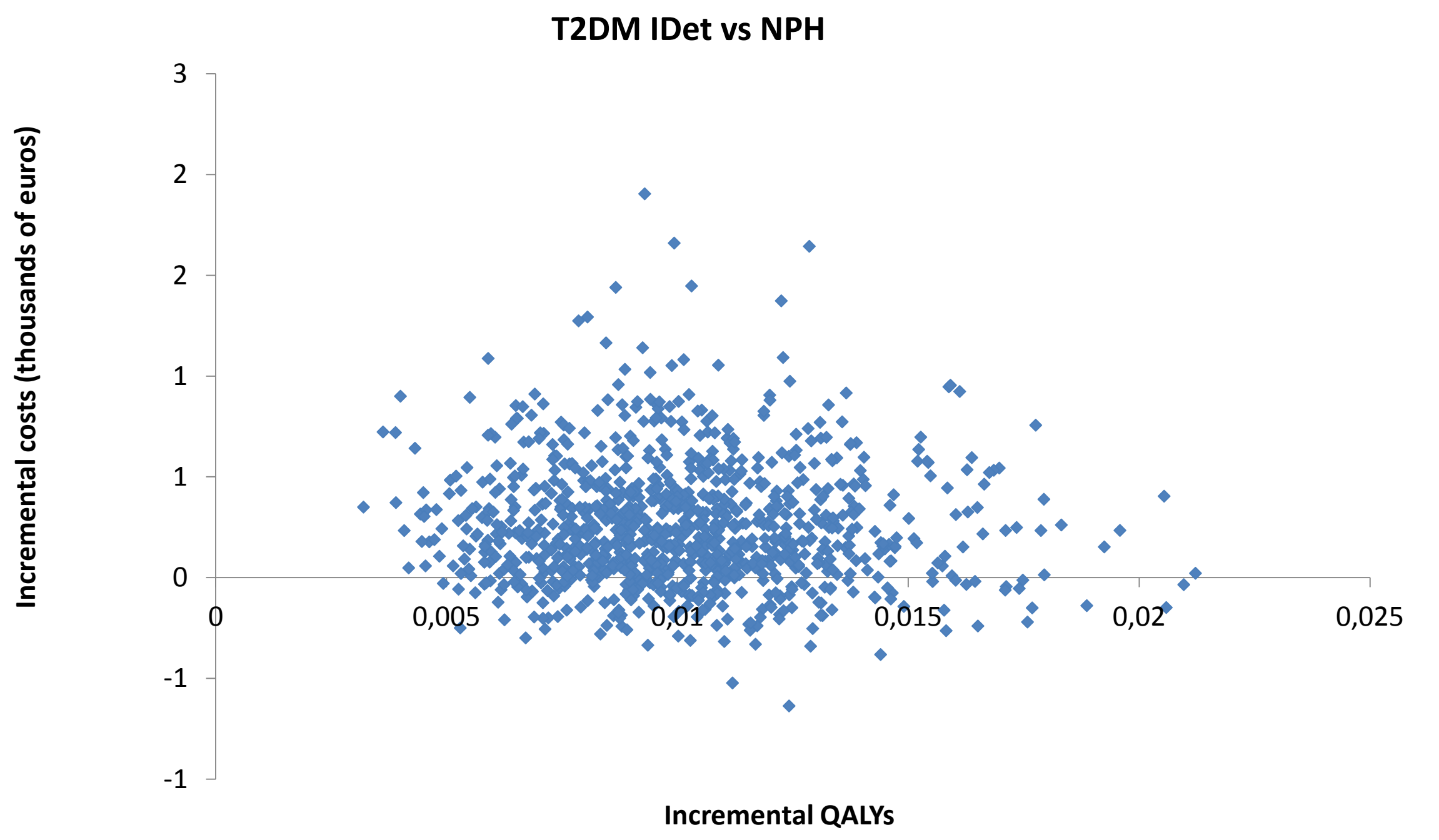
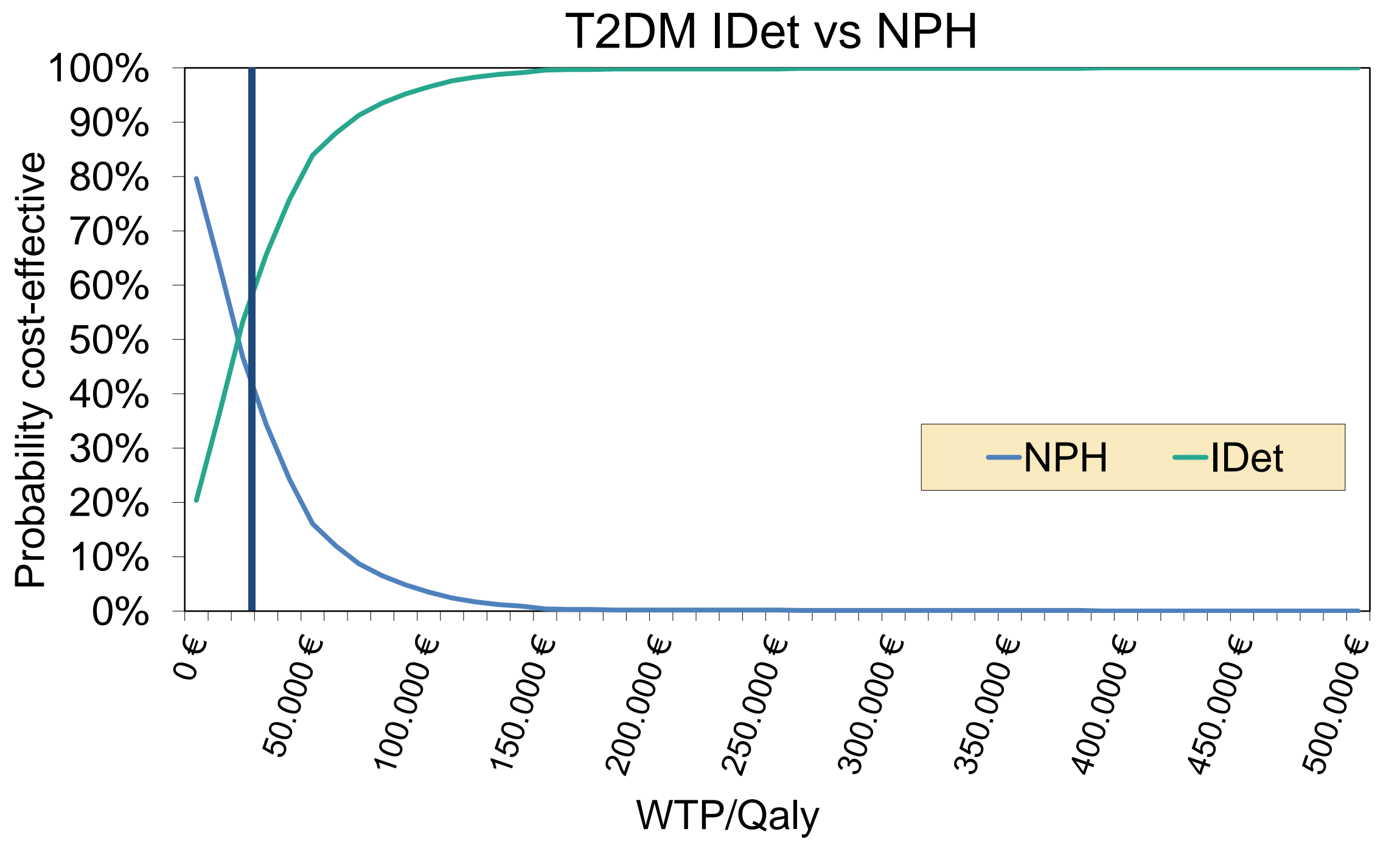


Figure 3 Acceptability curve of detemir vs. NPH in function of the cost-effectiveness threshold.



Conclusions

The lower frequency of hypoglycemia and the smaller weight gain associated to Determinir 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 T2DM patients in Spain.

References:

1. Inzucchi SE et al. Diabetologia. 2012;55(6):1577-96.
2. Williams SA et al. J Diabetes Complications. 2012;26(5):399-406.
3. Ridderstråle M et al. J Med Econ. 2013;16(4):468-78.
4. WHO. Obesity and overweight. 2011 Available at: www.who.int/mediacentre/factsheets/fs311/en
5. Philis-Tsimikas A et al. Clin Ther. 2006;28(10):1569-81.
6. UK Hypoglycaemia Study Group. Diabetologia 2007;50:1140-7.
7. Nomenclátor de facturación del Ministerio de Sanidad, Servicios Sociales e Igualdad. Available at: <http://www.msssi.gob.es/profesionales/nomenclator.do> Last acceded: February, 2014.
8. WHO. ATC/DDD Index 2014. Available at: http://www.whooc.no/atc_ddd_index/
9. Consejo General de Colegios Oficiales de Farmacéuticos. Available at: <https://botplusweb.portalfarma.com/> ; Last acceded: February, 2014.
10. eSalud - Información económica del sector sanitario. Available at: <http://www.oblikue.com/bddcostes/>; Last acceded: February, 2014.
11. Lee AJ et al. Diabet Med 2005;22:1482-6.
12. Currie CJ et al. Diabetologia 2006;49:2272-80.
13. Sacristán J A et al. Gaceta Sanitaria 2002;16(4):334-43.