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Cost-effectiveness of insulin detemir compared with NPH insulin in people with type 2 diabetes in Denmark, Finland, Norway and Sweden

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Abstract

Objective: To assess the cost-effectiveness of insulin detemir compared with Neutral Protamine Hagedorn (NPH) insulin when initiating insulin treatment in people with type 2 diabetes mellitus (T2DM) in Denmark, Finland, Norway and Sweden.

Methods: Efficacy and safety data were derived from a 20-week multicentre randomised controlled head-to-head clinical trial comparing insulin detemir and NPH insulin in insulin naïve people with T2DM, and short-term (one-year) cost effectiveness analyses were performed. As no significant differences in HbA_{1c} were observed between the two treatment arms, the model was based on significant differences in favour of insulin detemir in frequency of hypoglycaemia (Rate-Ratio = 0.52; CI: 0.44 - 0.61) and weight gain (Δ 0.9 kg). Model outcomes were measured in Quality Adjusted Life Years (QALYs) using published utility estimates. Acquisition costs for insulin and direct healthcare costs associated with non-severe hypoglycaemic events were obtained from National Health Service public sources. One-way and probabilistic sensitivity analyses were performed.

Results: Based on lower incidence of non-severe hypoglycaemic events and less weight gain, the QALY gain from initiating treatment with insulin detemir compared with NPH insulin was 0.01 per patient per year. Incremental cost-effectiveness ratios for the individual countries were: Denmark, Danish Kroner 170,852 (€22,933); Finland, €28,349; Norway, Norwegian Kroner 169,789 (€21,768); and Sweden, Swedish Krona 226,622 (€25,097) per QALY gained. Possible limitations of the study are that data on hypoglycaemia and relative weight benefits from a clinical trial were combined with hypoglycaemia incidence data from observational studies. These populations may have slightly different patient characteristics.

Conclusions: The lower risk of non-severe hypoglycaemia and less weight gain associated with using insulin detemir compared with NPH insulin when initiating insulin treatment in insulin naïve patients with type 2 diabetes provide economic benefits in the short-term. Based on cost/QALY threshold values, this represents good value for money in the Nordic countries. Using a short-term modelling approach may be conservative as reduced frequency of hypoglycaemia and less weight gain may also have positive long term health-related implications.

Introduction

Both the United Kingdom Prospective Diabetes Study (UKPDS) and the Diabetes Control and Complications Trial demonstrated that intensive glycaemic control reduces long-term complications in type 1 (T1DM) and type 2 diabetes (T2DM)¹⁻⁴. In the UKPDS performed in people with T2DM, the risk of any diabetes-related complication was 12% lower in the intensive therapy group³. However, the improved glycaemic control with intensive therapy also conferred an increased risk of hypoglycaemia and was associated with a significantly higher weight gain compared with less intensive therapy³. The presence of non-severe hypoglycaemia is associated with lower quality of life and an increased prevalence of a number of diabetes-associated complications⁵⁻⁷. Fear of hypoglycaemia is a major concern for many patients, it may contribute to sub-optimal insulin treatment, particularly in intensively treated patients, and it is a critical limiting factor in glucose control management⁸. As a group, people with diabetes fear hypoglycaemia more than they fear the long-term complications of diabetes⁹. Furthermore, hypoglycaemia is associated with direct healthcare costs associated with the event and indirect costs due to work time lost^{10,11}.

Weight gain is also commonly associated with intensive insulin therapy, especially among patients with T2DM^{12,13}, and is linked to increased risk of cardiovascular morbidity and mortality¹⁴⁻¹⁶. Additionally, obesity has a negative impact on patients' health-related quality of life^{17,18}, and concerns about weight gain are associated with distress, poor physical and psychological well-being and non-adherence to glucose lowering medications¹⁹. In a Swedish study where patients' willingness to pay (WTP) for health improvements associated with antidiabetes treatments was assessed, it was found that patients were willing to pay on average €23.51 per month to avoid one kg weight increase and €15.61 per month for each kg of weight loss²⁰.

Consequently, the main targets in diabetes management are to achieve a near-normal blood glucose level to reduce the risk of long-term complications, maintain the smallest possible risk of hypoglycaemia, and minimise weight gain in order to maintain health-related quality of life and improve adherence to treatment.

Long-acting insulin analogues more accurately mimic the physiological human insulin profile and provide an alternative to human insulins, such as Neutral Protamine Hagedorn (NPH) insulin. The insulin analogue insulin detemir causes fewer hypoglycaemic events and less weight gain, leading to improvements in quality adjusted life-years (QALYs) compared with NPH insulin^{21,22}.

The aim of this study was to assess the cost-effectiveness of using once-daily insulin detemir versus once-daily NPH insulin in patients initiating insulin therapy in Denmark, Finland, Norway and Sweden. The study was based on treatment benefits related to reduction in hypoglycaemic events and less weight gain as observed in a head-to-head clinical trial²³.

Methods

Health economic analyses were performed reflecting the short-term treatment dilemma of balancing glycaemic control with cost of care and quality of life. The cost-effectiveness of initiating insulin treatment with insulin detemir compared to NPH insulin was estimated based on published differences in their hypoglycaemia and weight profiles assuming an equal effect on blood glucose control as measured by change in HbA_{1c}²³. Clinical input data for the analyses were derived from a 20-week multicentre randomised head-to-head clinical trial comparing initiation with insulin detemir (morning or evening) to NPH insulin (once daily in the evening) in 504 insulin naïve T2DM patients. Patients were randomised in a 1:1:1 ratio²³.

For the cost-effectiveness analyses, data from the insulin detemir evening arm and NPH insulin evening arm were utilised as these best reflect current standard treatment practice in the Nordic countries. Data from other studies comparing insulin detemir and NPH insulin were not included as these have mainly been based on twice daily treatment regimens, which are not considered to reflect current standard treatment practice^{24,25}.

A one year cost-effectiveness analysis (CEA) model was developed in Microsoft Excel (Microsoft Ltd, Redmond, Washington, USA). Cumulative costs and utility decrements associated with hypoglycaemic events and weight gain together with the medication acquisition costs were estimated for each treatment arm to calculate an incremental cost-effectiveness ratio (ICER). The relative rate of non-severe hypoglycaemia with insulin detemir compared with NPH insulin was applied to the rate of hypoglycaemia in the NPH insulin treatment group to estimate the number of events prevented by using insulin detemir instead of NPH insulin. The weight difference between the treatment groups was assumed to affect patient's quality of life throughout the year. Only direct healthcare costs were included in the analyses. This approach assumes that there would be no significant differences in long-term disease progression based on differences in HbA_{1c} as predicted from the treat-to-target trial design²³. In comparing the differences between treatment arms only parameters where statistically significant differences were observed between the two treatment

arms were included. Parameters that were not statistically significantly different between the treatment arms were assumed to reflect random variation and were not included as relevant model parameters in the analyses.

Input data

Hypoglycaemia

In the clinical trial²³, occurrence of hypoglycaemia was based on all registered events in the intention-to-treat cohort (all randomised and treated patients regardless of compliance) and analysed as recurrent events in a Cox regression analysis. People with recurrent severe hypoglycaemia (i.e., requiring assistance) or hypoglycaemia unawareness were excluded from the trial programme (in total 166 patients failed the screening criteria for the study). Since this may have led to an underestimation of the incidence of hypoglycaemia compared with real-world event rates, observational data from the UK Hypoglycaemia Study Group (UKHSG) were used in the analyses to better reflect the true incidence of hypoglycaemia²⁶. As the UKHSG data were collected up until 2004, the rates of hypoglycaemia from this study were assumed to reflect the incidence rates in the NPH treatment arm. Non-severe hypoglycaemia was defined as an event with a plasma glucose level of <3.0 mmol/l or any episode where patients experienced symptoms associated with hypoglycaemia and the individual dealt with the episode alone²³. Severe hypoglycaemia was defined as any hypoglycaemic episode where assistance from another person was required. The incidence of non-severe hypoglycaemia among people with T2DM on insulin for less than two years was 4.08 episodes per person-year and the event rate for those on insulin for more than five years was 10.20 per person-year²⁶. In the base-case analysis, the lower rate of events was used to reflect the event rate in the NPH treatment arm. This may be an overly conservative estimate since the frequency of hypoglycaemia tends to increase with longer treatment duration²⁶. Sensitivity analyses were performed using the higher rate of non-severe hypoglycaemia.

A crude rate ratio was calculated from the rate of overall confirmed hypoglycaemic events in the two treatment arms in the head-to-head randomised clinical trial. The rate ratio was used to estimate the

number of non-severe hypoglycaemic events prevented by using insulin detemir compared with NPH insulin (RR = 0.52, CI: 0.44 - 0.61)²³. There were too few severe hypoglycaemic events reported in the clinical trial to estimate any rate ratios between insulin detemir and NPH for severe events²³. This may have been due to the selection criteria for the trial (see above).

Weight

There was an increase in body weight following insulin initiation in both treatment groups²³. Weight gain in the insulin detemir arm was significantly lower than in the NPH insulin group (0.7 kg versus 1.6 kg, mean difference -0.91 kg, $p = 0.005$, $\Delta\text{BMI} = -0.32 \text{ kg/m}^2$).

Health-related quality of life

Non-severe hypoglycaemic events are associated with a relatively short-term disutility from the event itself and a longer-term disutility from the fear of repeated hypoglycaemic events²⁷. A disutility estimate for non-severe hypoglycaemic events was derived using a postal survey including 1305 respondents²⁸. Based on the correlation between changes in the fear of hypoglycaemia score and changes in the EQ-5D score, a disutility for hypoglycaemic events was estimated for a three month period following the event (-0.01418); providing a yearly utility decrement of -0.0035 per non-severe hypoglycaemic event. This estimate was used in the analyses. Severe hypoglycaemic events were not included in the analyses as there were too few observations in the clinical trial to estimate any risk reductions for severe hypoglycaemic events.

Studies have shown that at a BMI above 25 kg/m^2 , weight gain is associated with lower overall quality of life in people with diabetes^{17,18}. A study performed by Lee et al (2006)²⁹, assessed the association between increasing BMI and the impact on health-related quality of life among diabetes patients using the EQ-5D score. The disutility associated with increasing BMI was adjusted for age. A 1-unit increase in BMI for T2DM patients was associated with a disutility of -0.0100²⁹. This utility decrement estimate was used in the health economic analyses in the present investigation.

Healthcare costs

Acquisition costs for insulins in the four countries (Denmark, Finland, Norway and Sweden) were based on a pack price for 5 x 3 ml FlexPen (NPH insulin [Insulatard FlexPen, Novo Nordisk A/S, Bagsværd, Denmark] and insulin detemir [Levemir FlexPen, Bagsværd, Denmark]) at pharmacy selling price (PSP) excluding VAT, obtained from public sources³⁰⁻³³. For comparability, all cost estimates are reported in Euros. Average yearly exchange rates from the European Central Bank have been used to convert the costs into Euros. An exchange rate of DKK 7.45³⁴, NOK 7.80³⁵ and SEK 9.03³⁶ was used.

The daily dose was assumed to be 40 international units (IU) for both treatment regimens, based on the World Health Organization's (WHO's) defined daily dose (DDD)³⁷. As no significant differences in drug doses were observed in the clinical trial it was considered most appropriate to use DDD for the analyses. No discounting was applied due to the short time horizon of the analysis.

A recent survey conducted in the UK, USA, Germany and France indicated an increase in visits to healthcare professionals (HCP) following non-severe hypoglycaemic events¹⁰. In the survey, 25% of patients reported having additional HCP contact following a non-severe hypoglycaemic event. As no country-specific data are available for Denmark, Finland, Norway and Sweden it was assumed that the same proportion of patients would visit an HCP in the Nordic countries. Country-specific input data are shown in Table 1.

Threshold values

The threshold values used to define cost-effectiveness were DKK300,000/QALY (€40,268/QALY) for Denmark³⁸ and SEK500,000/QALY (€55,370/QALY) for Sweden³⁹. As no published values were available for Finland, a value of €40,000/QALY was used for Finland (local equivalent of the £30,000/QALY National Institute of Clinical Excellence (NICE) threshold) and a value of NOK500,000/QALY (€64,103/QALY) for Norway, based on generally accepted threshold values in Norway⁴⁰.

Sensitivity analyses

One-way sensitivity analyses were performed for all four countries to assess the impact of individual parameter uncertainty. Sensitivity analyses were performed for the baseline rates of non-severe hypoglycaemic events (event rates from the clinical trial²³ and UKHSG event rates for T2DM patients on insulin treatment for more than five years⁴¹), the impact of changes in utility decrements associated with hypoglycaemia ($\pm 50\%$), and the impact of using the utility decrement of 0.0052 as referenced by NICE⁴². Utility decrements associated with BMI changes were tested by using the utility estimate from the CODE-2 study of 0.0061⁴³. The impact of changes in the cost of NPH insulin ($\pm 20\%$) was also estimated. To assess the uncertainty associated with the trial data on the hypoglycaemia relative rates and weight gain, upper and lower confidence intervals for the RR estimate (0.44:0.61) and weight gain (-0.1; -0.53 kg/m²) were utilised²³.

Probabilistic sensitivity analysis was performed to assess the joint uncertainty of input parameters. All input parameters were defined by their probability distributions using the same ranges of uncertainty as used in the one-way sensitivity analyses. Monte Carlo simulation techniques were used to propagate the parameter uncertainty using 1000 iterations.

Results

Incremental cost-effectiveness: base case analysis

The health-related quality of life gain associated with initiating treatment with insulin detemir compared with NPH insulin based on the benefit of reducing the number of non-severe hypoglycaemic events and the weight benefit was 0.010 QALYs per patient per year. The incremental cost was DKK1709 (€229) in Denmark, €284 in Finland, NOK1698 (€218) in Norway and SEK2267 (€251) in Sweden. The incremental cost-effectiveness ratio (cost/QALY) was DKK170,852 (€22,933) for Denmark, €28,349 for Finland, NOK169,789 (€21,768) for Norway and SEK226,622 (€25,097) for Sweden (Table 2). Figure 1 shows the incremental costs and incremental QALYs for insulin detemir and NPH insulin for each of the four countries in the study. Insulin detemir was a cost-effective or dominating (better outcomes at a lower cost) treatment alternative in most simulations in the four countries. For Denmark, 68% of the simulations were below a cost/QALY threshold value of DKK300,000 (€40,268), in Finland 63% were below a cost/QALY threshold value of €40,000, in Norway 85% were below a cost/QALY threshold value of NOK500,000 (€64,102) and in Sweden 80% were below a cost/QALY threshold value of SEK500,000 (€55,370).

Sensitivity analyses

One-way sensitivity analyses were performed for key input parameters (Figure 2). Results were most sensitive to the relative rate of hypoglycaemic events using insulin detemir instead of NPH insulin but they were generally robust to changes in individual input parameters. For example, if the utility decrement associated with hypoglycaemia was reduced by 50%, this resulted in the largest increases in the calculated incremental cost-effectiveness ratio, but in all four countries remained below the threshold values used to define cost-effectiveness (Figure 2).

Discussion

The health economic analysis performed in the current investigation focused on statistically significant differences in rates of non-severe hypoglycaemia and weight gain observed in a clinical trial using either insulin detemir or NPH insulin for the initiation of insulin treatment in insulin naïve people with T2DM²³. The results suggest that insulin detemir can be considered a cost-effective treatment alternative to NPH insulin over a one year period in all four countries analysed. These findings are consistent with long-term modelling studies that have compared the economic benefit of insulin analogues and NPH insulin in the treatment of T2DM⁴⁴⁻⁴⁶.

Randomised clinical trials comparing the efficacy of long-acting insulin analogues generally follow the treat-to-target study design⁴⁷, in which the aim is to treat patients to a pre-defined target level of glycaemic control. Given this commonly used trial design it is relevant to compare the safety profile associated with achieving the HbA_{1c} target, i.e., the rate of hypoglycaemic events and weight gain for comparable treatment regimens. A short-term modelling approach was therefore used to capture those relevant differences in outcome parameters. Basing the analyses only on differences in short-term outcomes may be a conservative approach as weight differences are also associated with differences in long-term complications¹⁴. Similarly, the incidence of hypoglycaemia tends to increase with longer durations of insulin treatment and therefore there is a greater potential for reducing the number of hypoglycaemic events over longer time-horizons.

The analyses show that economic benefits of insulin detemir in patients with T2DM are consistent across the four Nordic countries, with very similar results between the sensitivity analysis across Denmark, Finland, Norway and Sweden which were robust to changes in individual input parameters.. Efficacy and safety data used in the analyses were derived from a head-to-head clinical trial reflecting current clinical treatment practices using a once-daily basal insulin treatment regimen. Pooling of data from different clinical trials reflecting different treatment regimens of once- and twice-daily dosing was avoided since the heterogeneity of data would be too great.

One-way sensitivity analysis demonstrated that results were most sensitive to changes in the relative rate of hypoglycaemia between treatment strategies, and the utility decrement associated with non-severe hypoglycaemic events and baseline risk of hypoglycaemic events. The crude rate ratio of 0.52 was derived from the head-to-head trial²³. A similar risk reduction has been observed in another head-to-head trial comparing twice daily basal insulin detemir treatment with NPH insulin²⁴. Hypoglycaemia rates from an observational study were used for the analysis as this was considered to be a better approximation of the actual event rate in 'real-world' treatment settings⁴⁸ compared with the rates observed in clinical trials. Similar or higher rates of non-severe hypoglycaemia have been observed in other observational studies⁴⁹⁻⁵¹. The applied baseline rate of hypoglycaemic events reflects people that have been on insulin therapy for less than two years. As the frequency of hypoglycaemia increases with longer disease duration and longer use of insulin therapy, the applied baseline rate of non-severe hypoglycaemia is likely to be a conservative estimate for a T2DM population that has been receiving insulin for more than two years⁴¹. Furthermore, we used overall rates of hypoglycaemia and did not separate into daytime and nocturnal hypoglycaemia rates. However, nocturnal hypoglycaemia is a major issue and concern for people with diabetes and is feared more than any other type of hypoglycaemia⁵². Future analysis should also include the cost-effectiveness of insulin analogue regimens on the reduction of nocturnal hypoglycaemia.

In this study, a utility decrement of 0.0035 per non-severe hypoglycaemic event was used. In comparison, a utility decrement of 0.0052 per hypoglycaemic event avoided was applied in a health technology assessment performed for NICE⁴², and in a study from Sweden a disutility of 0.07 was reported in a group of T2DM patients experiencing symptoms of hypoglycaemia during the last month in comparison to a patient group not experiencing these symptoms⁵¹. Hence, the utility decrement estimate used in these analyses was lower than utility decrement estimates used elsewhere and may also be considered a conservative estimate. Non-severe hypoglycaemic events are associated with considerable direct and indirect costs due to additional healthcare contacts and absence from work¹⁰. Indirect costs related to work time lost were not included in these analyses. However, with the reduced number of hypoglycaemic events in the insulin detemir treatment arm, it

is expected that insulin detemir would be even more cost-effective if indirect costs were also included in the analyses.

Possible limitations of the study are that data on hypoglycaemia and relative weight benefits from a clinical trial were combined with hypoglycaemia incidence data from observational studies. These populations may not be readily comparable. We also cannot rule out the possibility that the risk reduction in real world clinical practice may be higher or lower than observed in the trial population. Furthermore, the rate of hypoglycaemia was derived from the UKHSG study and applied as the baseline risk in the NPH insulin treatment group. As data in the UKHSG study were not presented by treatment group, we cannot be certain that all the patients were treated with NPH insulin. However, as the incidence rates used reflected a T2DM patient group on insulin for less than two years, it may be assumed that the majority of patients were on a basal (e.g. once daily long acting) insulin plus oral antidiabetes drug treatment regimen. This assumption is supported when comparing with data from other observational studies in people with T2DM where hypoglycaemia incidence rates were higher⁴⁹⁻⁵¹.

Conclusions

This cost-effectiveness analysis shows that the reduction in non-severe hypoglycaemic events and relative weight benefits associated with the use of the long-acting insulin analogue insulin detemir in the initiation of insulin treatment of T2DM provide economic benefits over a one-year period compared with using NPH insulin. Even in the short term, the intervention represents good value for money in the countries analysed.. This analysis highlights the importance of considering short-term treatment differences from a health economic perspective.

Transparency

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Table 1: Healthcare cost input data for each country

Country	Drug costs (per pack – 1500 IU)		Cost of HCP contact	Assumptions for modelling:
	IDet	NPH		
Denmark ³⁰	DKK 500* (€67.11)	DKK 318 (€42.68)	DKK 126.86 (€17.03)	25% of a GP consultation (10 min) – DKK 32 (€4.30)
Finland ³¹	€72.64	€40.60	€57.83 ³¹	25% of a GP consultation €14.46
Norway ³²	NOK 456** (€58.46)	NOK 275 (€35.26)	NOK 137 (€17.56)	25% of normal tariff for a private specialist – NOK 34 (€4.36)
Sweden ³³	SEK 597*** (€66.11)	SEK 324 (€35.88)	Physician visit SEK1201 (€133.00) Nurse visit SEK 375 (€41.53)	25% of the average cost of a GP and a primary care nurse contact (assuming a 50% split between the two types of contacts). SEK 197 (€21.8)

Abbreviations: HCP=health care professional; IDet=insulin detemir; NPH=neutral protamine Hagedorn; DKK=Danish Krone; NOK=Norwegian Krone; SEK=Swedish Krona; €=euro.

Conversion factors; *DKK7.45=€1; **NOK7.80=€1; ***SEK9.03=€1.

Prices are pharmacy selling price (PSP) excluding VAT, obtained from public sources on 21 March 2012.³⁰⁻³³

Table 2. Cost-effectiveness analysis, base case

Country	Annual total treatment cost			Incremental effectiveness (QALYs)	ICER	ICER (€)
	Insulin detemir*	NPH insulin*	Incremental cost			
Denmark	DKK 4,935* (€662)	DKK 3,226 (€433)	DKK 1,709 (€229)	0.010	DKK170,852	€22,933
Finland	€738	€454	€284	0.010	€28,349	€28,349
Norway	NOK 4,511** (€578)	NOK 2,813 (€361)	NOK 1,698 (€218)	0.010	NOK169,789	€21,768
Sweden	SEK 6,224*** (€689)	SEK 3,957 (€438)	SEK 2,267 (€251)	0.010	SEK226,622	€25,097

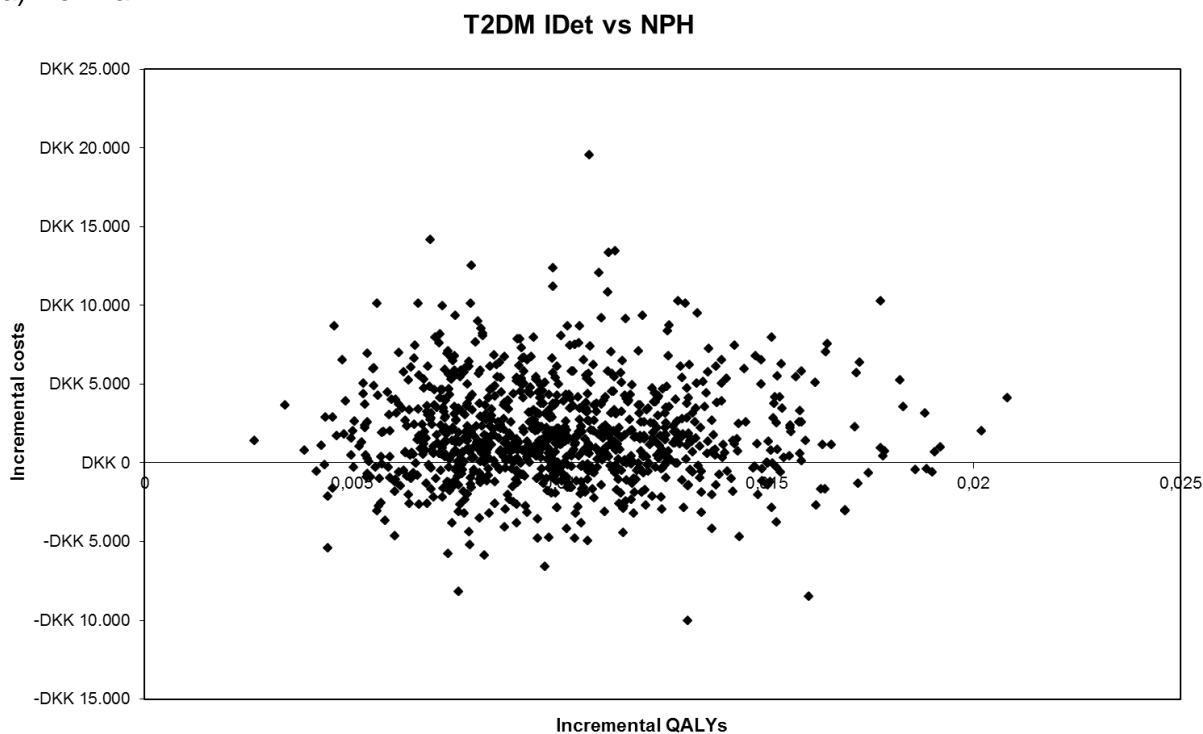
* Based on dose of 40 international units/day multiplied by price per unit derived from pharmacy selling price (excluding VAT) obtained from public sources on 21 March 2012.³⁰⁻³³.

Abbreviations: ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year; NPH = neutral protamine Hagedorn; DKK=Danish Krone; NOK=Norwegian Krone; SEK=Swedish Krona; €=euro.

Conversion factors; *DKK7.45=€1; **NOK7.80=€1; ***SEK9.03=€1.

Figure 1. Incremental costs for insulin detemir versus NPH insulin in (a) Denmark, (b) Finland, (c) Norway and (d) Sweden

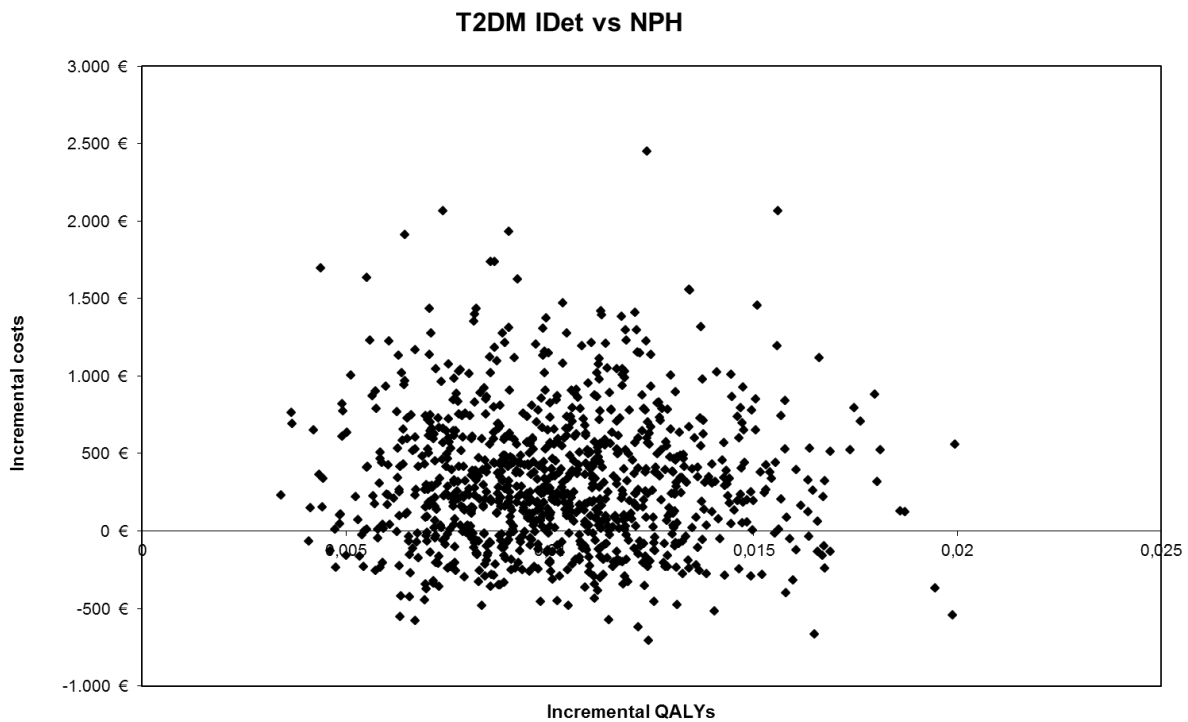
(a) Denmark



Scatterplot results of the probabilistic sensitivity analysis for Denmark. In 68% of the simulations, insulin detemir was a cost-effective or dominating treatment strategy (better health outcomes at a lower cost) compared with NPH insulin.

Abbreviations: QALYs = quality-adjusted life-years; iDET=insulin detemir; NPH = neutral protamine Hagedorn; DKK=Danish Krone; NOK=Norwegian Krone; SEK=Swedish Krona.

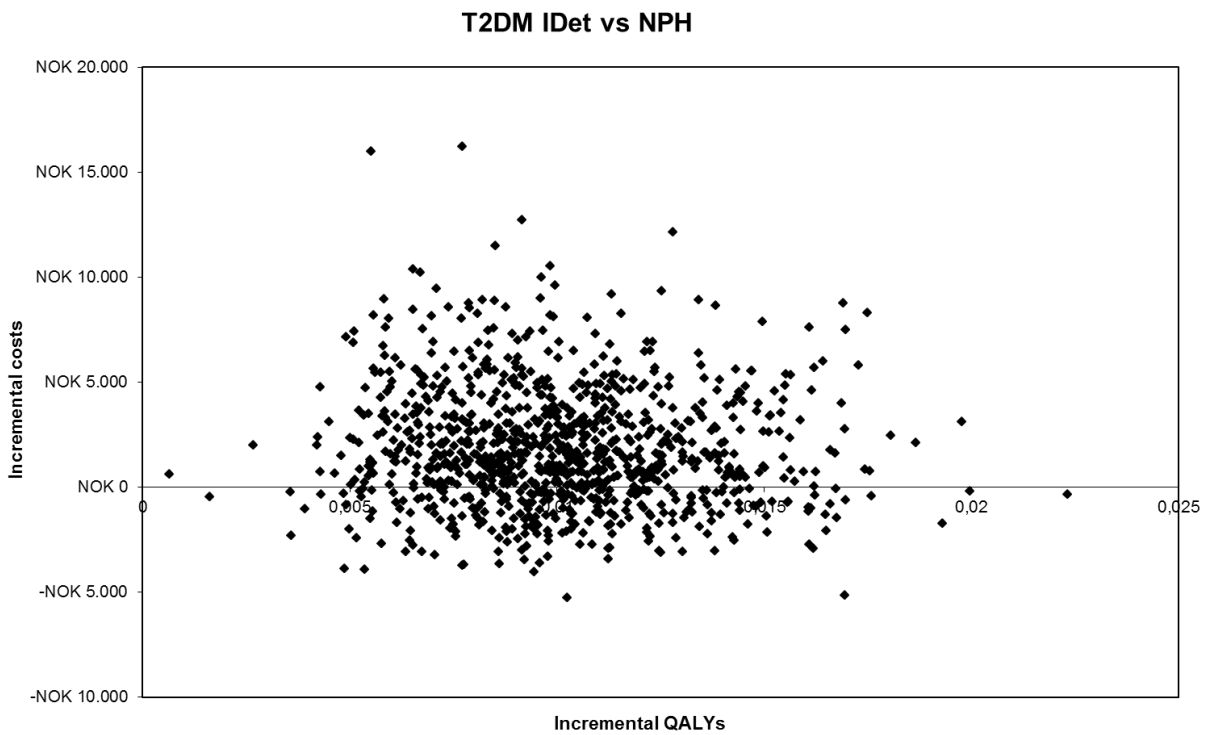
(b) Finland



Scatterplot results of the probabilistic sensitivity analysis for Finland. In 63% of the simulations, insulin detemir was a cost-effective or dominating treatment strategy (better health outcomes at a lower cost) compared with NPH insulin.

Abbreviations: QALYs = quality-adjusted life-years; iDET=insulin detemir; NPH = neutral protamine Hagedorn; DKK=Danish Krone; NOK=Norwegian Krone; SEK=Swedish Krona.

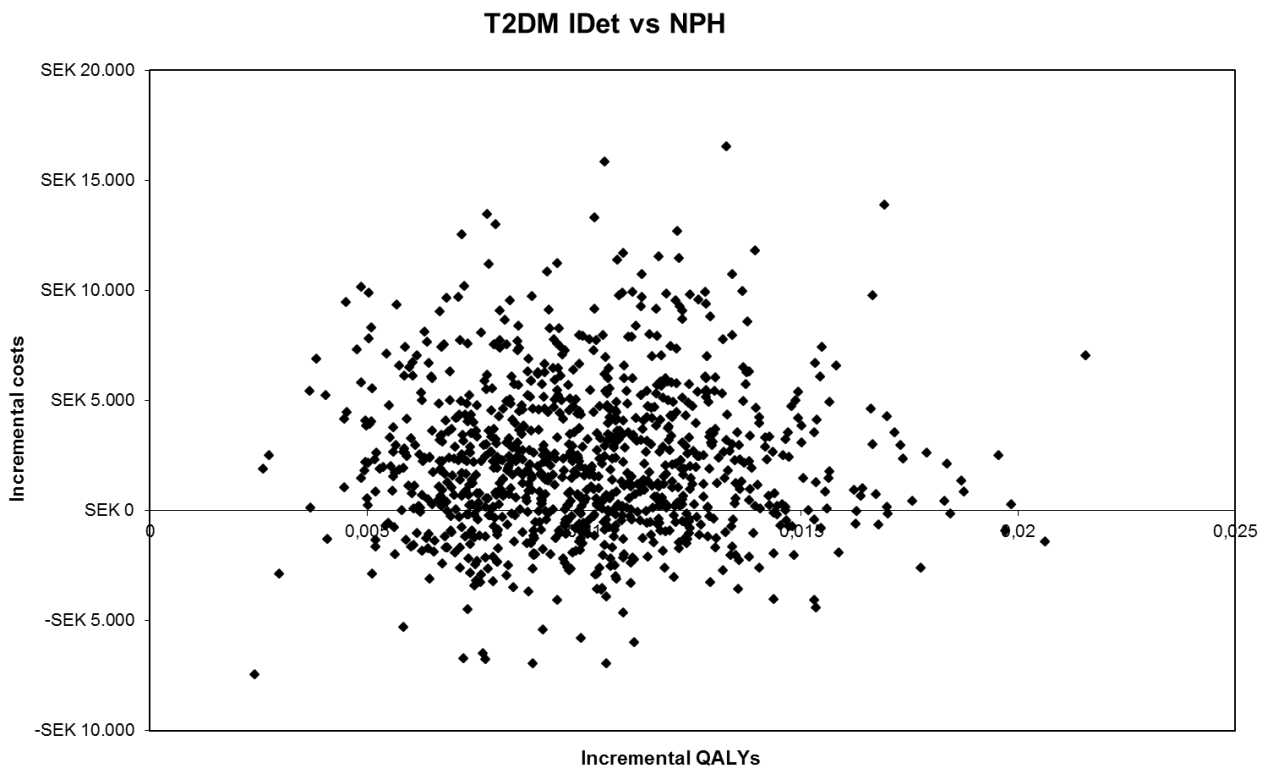
(c) Norway



Scatterplot results of the probabilistic sensitivity analysis for Norway. In 85% of the simulations, insulin detemir was a cost-effective or dominating treatment strategy (better health outcomes at a lower cost) compared with NPH insulin.

Abbreviations: QALYs = quality-adjusted life-years; iDET=insulin detemir; NPH = neutral protamine Hagedorn; DKK=Danish Krone; NOK=Norwegian Krone; SEK=Swedish Krona.

(d) Sweden

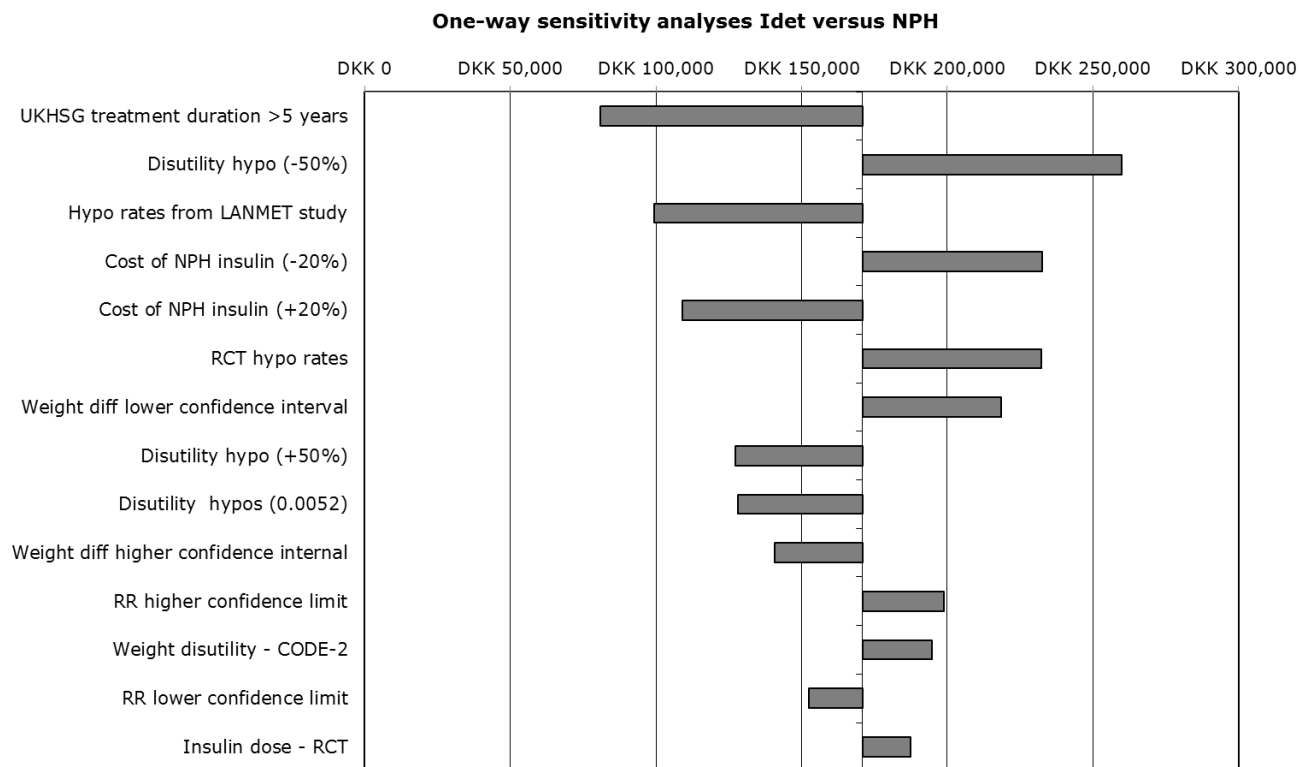


Scatterplot results of the probabilistic sensitivity analysis for Sweden. In 80% of the simulations, insulin detemir was a cost-effective or dominating treatment strategy (better health outcomes at a lower cost) compared with NPH insulin.

Abbreviations: QALYs = quality-adjusted life-years; iDET=insulin detemir; NPH = neutral protamine Hagedorn; DKK=Danish Krone; NOK=Norwegian Krone; SEK=Swedish Krona.

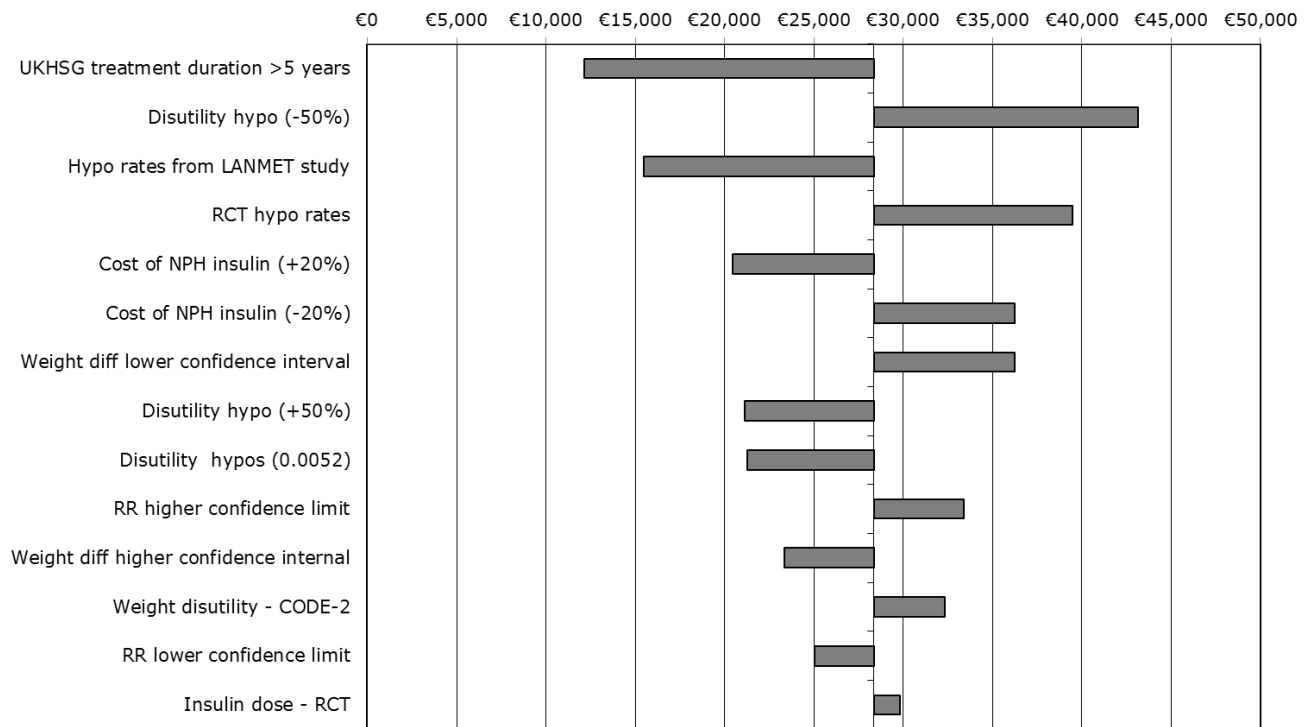
Figure 2. One-way sensitivity analyses for insulin detemir versus NPH in people with type 2 diabetes for (a) Denmark, (b) Finland, (c) Norway and (d) Sweden.

(a) Denmark



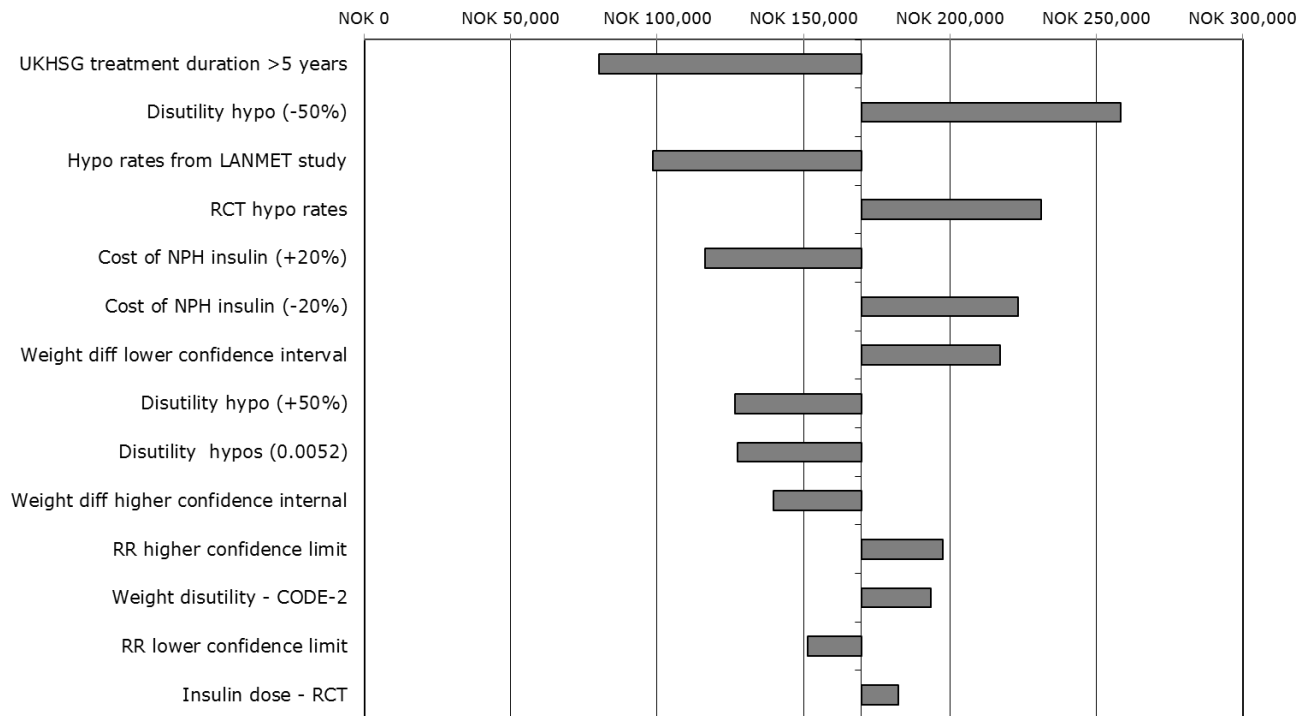
(b) Finland

One-way sensitivity analyses Idet versus NPH



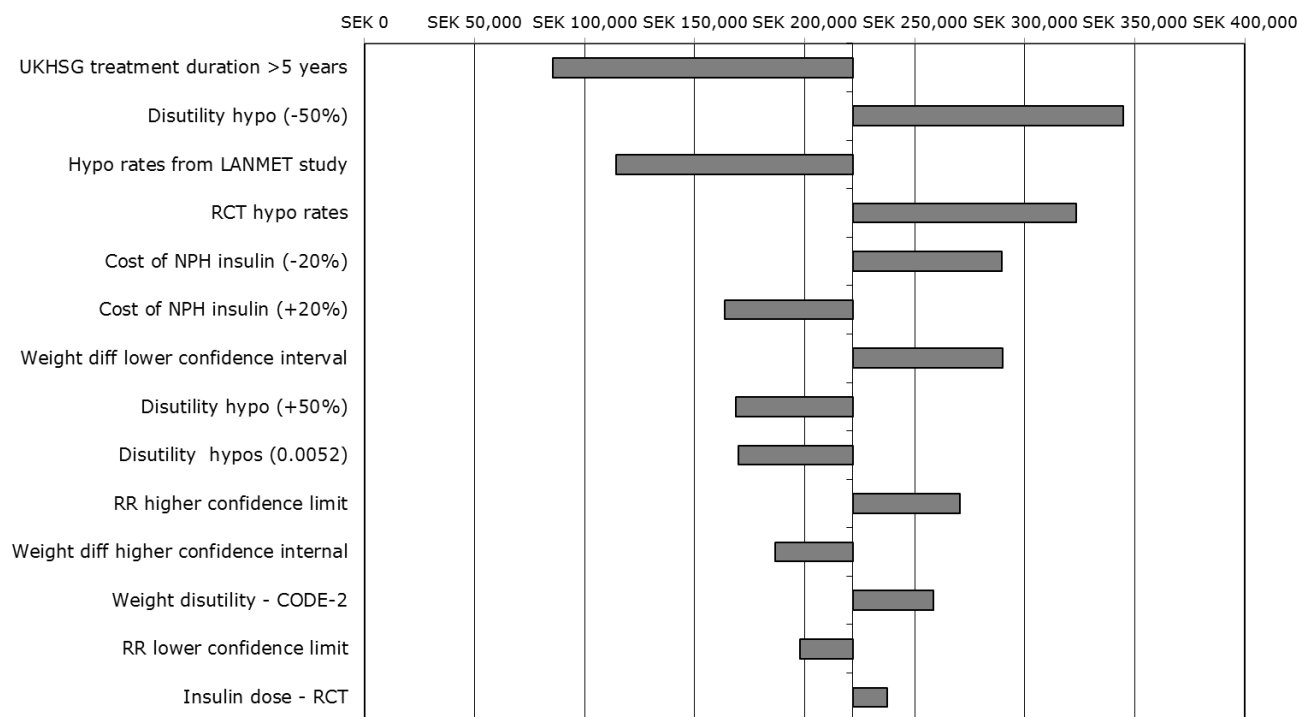
(c) Norway

One-way sensitivity analyses Idet versus NPH



(d) Sweden

One-way sensitivity analyses Idet versus NPH



Abbreviations; IDet=insulin detemir; NPH=neutral protamine Hagedorn; RR=rate ratio; RCT=randomised controlled trial; hypo=hypoglycaemia.

Upper and lower confidence interval values were used for the sensitivity analyses. That is RR of hypoglycaemic events (0.44 – 0.61), weight difference (Δ BMI 0.1 – 0.53), hypoglycaemia rate in UKHSG group with >5 y treatment duration (10.02), LANMET hypoglycaemia rate (8).