COST-UTILITY OF INSULIN GLARGINE

IN COMBINATION THERAPY WITH ORAL AGENTS AS COMPARED WITH PREMIX INSULIN WITH OR WITHOUT ORAL AGENTS IN TYPE 2 DIABETES MELLITUS. THE POLISH PERSPECTIVE

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Background

Type 2 diabetes mellitus (T2DM) is a chronic disease associated with substantial morbidity and mortality, including microvascular complications (retinopathy, neuropathy, nephropathy) and macrovascular complications (coronary heart disease, cerebrovascular disease), resulting in high costs and reduced quality of life. [2, 3]

Improved glycemic control (i.e. improved HbA1c level) is correlated with a significantly reduced risk of diabetes-related long term complications. However, the risk of hypoglycaemia increases with lower HbA1c levels. Therefore, patients often choose to settle for suboptimal glucose control in order to prevent hypoglycaemic events. Insulin glargine, the first clinically available basal analogue with prolonged absorption and 24-hour peakless activity profile, has been demonstrated to reduce HbA1c values to a lower level than premix insulin and its use resulted in lower risk of hypoglycaemia compared with premix insulin in parallel. [2, 3]

Therefore, the aim of this analysis was to project long-term complications over the patient's life-time horizon with the DES model for a representative cohort of patients with T2DM in Poland. Being insufficiently controlled by oral antidiabetics (OAD), the cohort was initially treated with either insulin glargine (IGlar) or premix insulin (IMix) added to OAD, or IMix alone. Total costs, effectiveness in terms of QALY and cost-utility of both interventions were assessed.

Summary

Objectives: The objective of this study was to compare the cost-utility of insulin glargine (IGlar) in combination therapy with oral antidiabetic drugs (OAD) versus premix insulin (IMix) added to OAD and IMix alone in patients with type 2 diabetes mellitus.

Methods: A micro-simulation DES model was used to estimate utilities and costs. Costs were calculated from the National Health Fund (NHF) perspective and from the NHF plus patient perspective. Simulation was performed in one year cycles and terminated at the time of the patient's death. Transition probabilities between health states were calculated based on a systematic review of RCTs and supplemented with published literature if necessary. Health state utilities were obtained from published literature. Probabilistic sensitivity analysis was performed to estimate the probability that IGlar with OAD is cost effective in Polish settings (for a threshold of ca. 92,000 PLN).

Results: From the NHF perspective IGlar added to OADs compared with IMix added to OADs was less costly (cost difference PLN 2,496) and more effective (QALY difference 0.19) and from the NHF plus patient perspective incremental costs were PLN 34,662 per QALY gained. When compared with insulin mixtures alone, IGlar added to OADs was from the NHF perspective less costly (cost difference PLN 1,105) and more effective (QALY difference 0.13) and from the NHF plus patient perspective incremental costs were PLN 19,800 per QALY gained. The probability of IGlar+OAD cost effectiveness over IMix+OAD for the defined threshold from the NHF perspective was 96.9%, and that of IGlar+OAD over IMix alone was 95.7%. From the NHF plus patient perspective the probability of IGlar cost effectiveness over IMix with OAD for the defined threshold was 86.7% and IGlar+OAD over IMix alone was 82.8%.

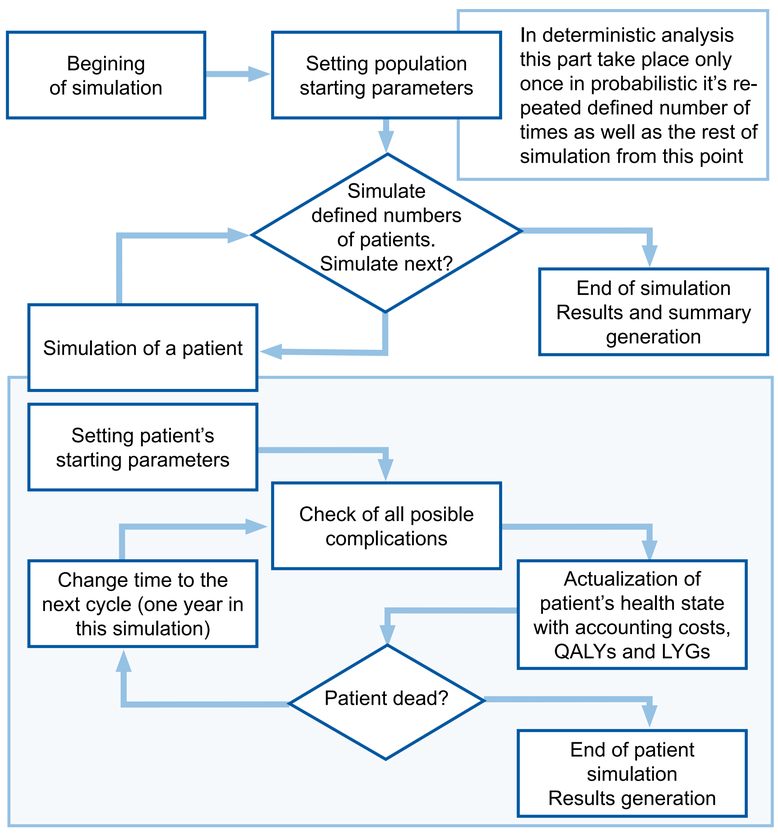
Conclusions: According to this analysis performed in Poland, insulin glargine, when added to OADs, is more cost effective than insulin mixture, either in combination with OADs or alone.

Methods

The model functions as an individual patient simulation, implemented using discrete event simulation (DES) – a modelling technique that permits the course of disease and its management to be conceptualized in terms of the events that happen and the impact these events have on the patients and other components of the system. The simulation was performed in one year cycles and terminated at the time of the patient's death.

A schematic representation of the model structure is provided in Figure 1. At the start, a patient with type 2 diabetes mellitus is assigned characteristics based on pre-specified distributions for demographic and physiologic parameters. The changes in physiologic parameters and diabetes-related complications expected to occur given the patient's assigned treatment are then derived using regression equations and transition probabilities developed from a systematic review of RCTs and supplemented with published literature if necessary. During lifetime period hypoglycaemic, macrovascular and microvascular disease events (i.e. retinopathy, nephropathy, neuropathy, stroke, myocardial infarction (MI), coronary artery disease, diabetic foot and amputation) are counted and management costs and implications of those events for life utility are accumulated. Costs and effects occurring are discounted at 5% per year. The modelling process is replicated for a hypothetical cohort of 100,000 patients. Cost were collected from National Health Fund (NHF) and National Health Fund and patient (NHF + patient) perspectives.

Figure 1. DES model structure



Comparison of clinical effectiveness

Data concerning clinical effectiveness of different treatments compared in the analysis were derived from a systematic review [1]. Detailed information about the parameters obtained is presented in the tables below (Table 1, Table 2, Table 3, Table 4).

Risk of hypoglycaemia

Table 1. Relative Risk of hypoglycaemia IGlar+OAD vs IMix+OAD

Hypoglycaemia	RR in the control group	IGlar+OAD		IMix+OAD		RR [CI95%]	RD [CI95%]	NNT [CI95%]
		n	N	n	N			
All	0.421	151	593	247	587	0.60 [0.47; 0.76]	-0.17 [-0.23; -0.12]	5.83 [4.41; 8.62]
Severe	0.004	2	243	1	245	1.68 [0.22; 12.66]	0.00 [-0.01; 0.02]	ns

Table 2. Relative Risk of hypoglycaemia IGlar+OAD vs IMix

Hypoglycaemia	RR in the control group (IMix)	IGlar+OAD		IMix		RR [CI95%]	RD [CI95%]	NNT
		n	N	n	N			
All	0.686	132	212	140	204	0.90 [0.78; 1.04]	-0.07 [-0.16; 0.02]	ns
Severe	-	0	212	0	204	-	-	-

Reduction of the HbA1c level

Table 3. Mean difference in reduction of the HbA1C level

Treatment	Group size		WMD HbA1c [CI95%]
	IGlar (experimental group)	IMix (control group)	
IGlar+OAD vs IMix+OAD	660	654	0.38 [0.28; 0.49]
IGlar+OAD vs IMix	202	204	-0.33 [-0.50; -0.16]

Body mass gained

Table 4. Mean difference in body mass gained

Treatment	Group size		WMD body mass gained [CI95%]
	IGlar (experimental group)	IMix (control group)	
IGlar+OAD vs IMix+OAD	669	662	-0.90 [-1.57; -0.23]
IGlar+OAD vs IMix	177	187	-0.70 [-1.48; 0.08]

Results

IGlar + OAD vs IMix + OAD

From the NHF perspective IGlar added to OADs compared with IMix added to OADs was less costly (cost difference PLN 2,496) (Table 5, Figure 2). IGlar added to OADs compared with IMix added to OADs was more effective (QALY difference 0.19) (Table 5, Figure 2).

The probability of IGlar+OAD cost effectiveness over IMix+OAD for the defined threshold from the NHF perspective was 96.9% (Figure 4).

From the NHF plus patient perspective incremental costs were PLN 34,662 per QALY gained when comparing IGlar added to OADs with IMix added to OADs (Table 5, Figure 3).

From the NHF plus patient perspective the probability of IGlar cost effectiveness over IMix with OAD for the defined threshold was 86.7% (Figure 5).

IGlar + OAD vs IMix

From the NHF perspective IGlar added to OADs compared with IMix alone was less costly (cost difference PLN 1,105) (Table 6, Figure 6). IGlar added to OADs compared with IMix alone was more effective (QALY difference 0.13) (Table 6, Figure 6).

The probability of IGlar+OAD cost effectiveness over IMix alone for the defined threshold from the NHF perspective was 95.7% (Figure 8).

From the NHF plus patient perspective incremental costs were PLN 19,800 per QALY gained when comparing IGlar added to OADs with IMix alone (Table 6, Figure 7).

From the NHF plus patient perspective the probability of IGlar cost effectiveness over IMix alone for the defined threshold was 82.8% (Figure 9).

Table 5. IGlar + OAD vs IMix + OAD

Perspective	Incremental costs [PLN]	Incremental effects [QALY]	ICUR [PLN]
NHF	-2,295	0.186	IGlar is dominant
NHF + patient	6,444	0.186	34,662

Table 6. IGlar + OAD vs IMix

Perspective	Incremental costs [PLN]	Incremental effects [QALY]	ICUR [PLN]
NHF	-6,190	0.133	IGlar is dominant
NHF + patient	2,638	0.133	19,800

Figure 2. NHF perspective – scatter plot (IGlar + OAD vs IMix + OAD)

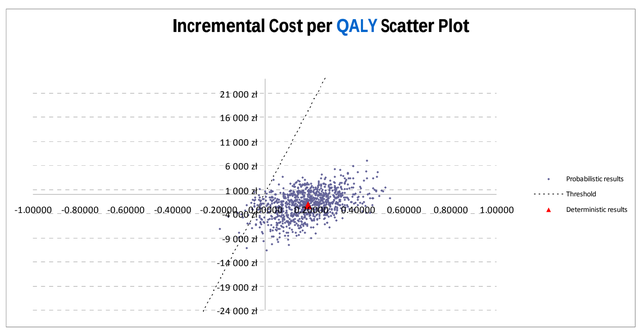


Figure 3. NHF + patient perspective – scatter plot (IGlar + OAD vs IMix + OAD)

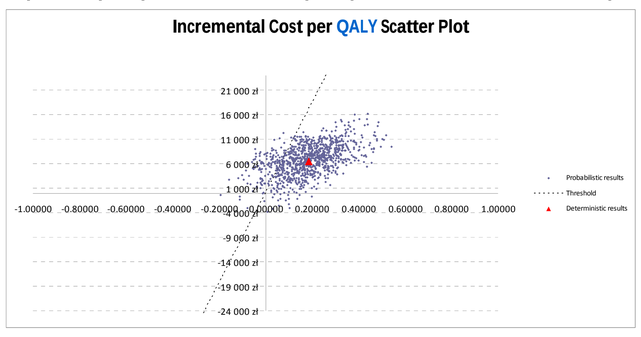


Figure 4. NHF perspective – CEAC (IGlar + OAD vs IMix + OAD)

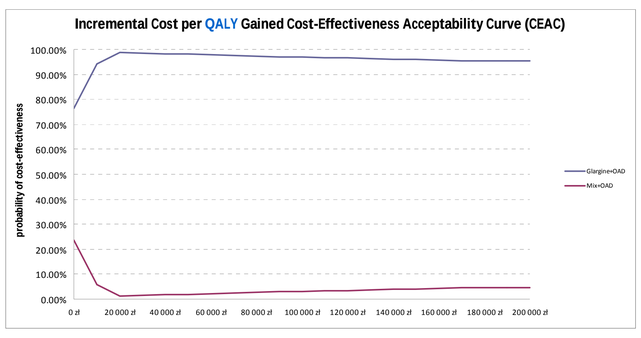


Figure 5. NHF + patient perspective – CEAC (IGlar + OAD vs IMix + OAD)

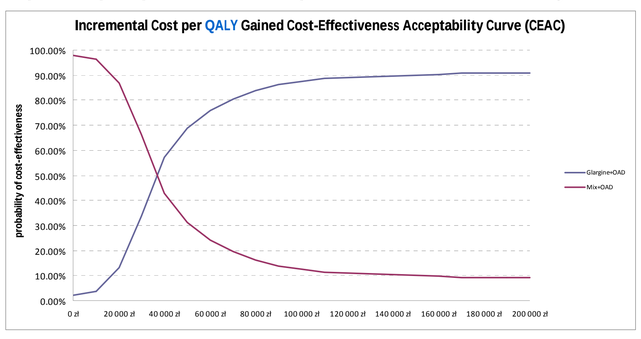


Figure 6. NHF perspective – scatter plot (IGlar + OAD vs IMix)

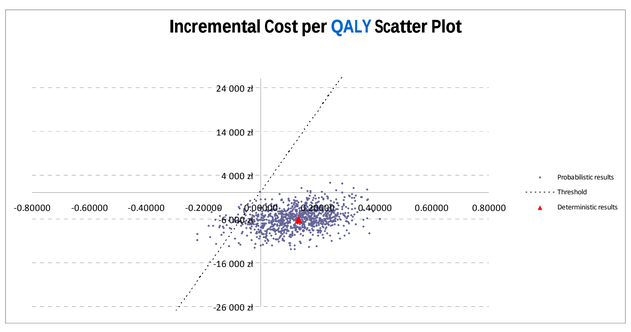


Figure 7. NHF + patient perspective – scatter plot (IGlar + OAD vs IMix)

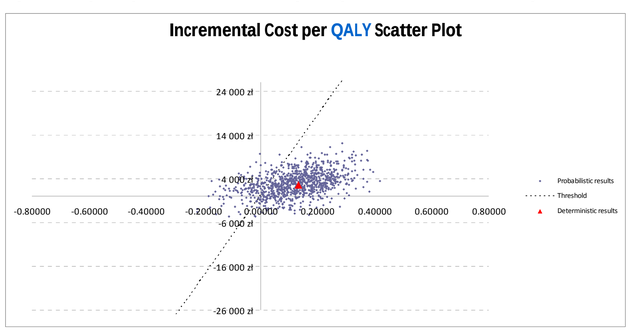


Figure 8. NHF perspective – CEAC (IGlar + OAD vs IMix)

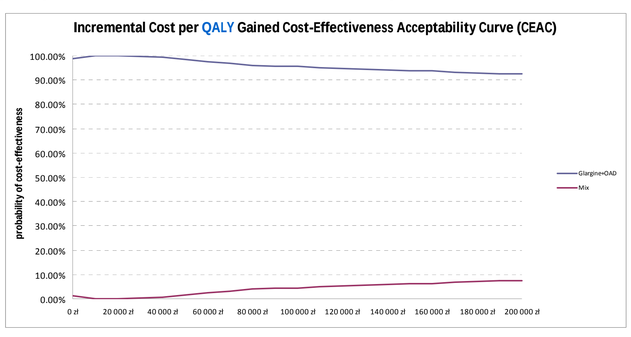
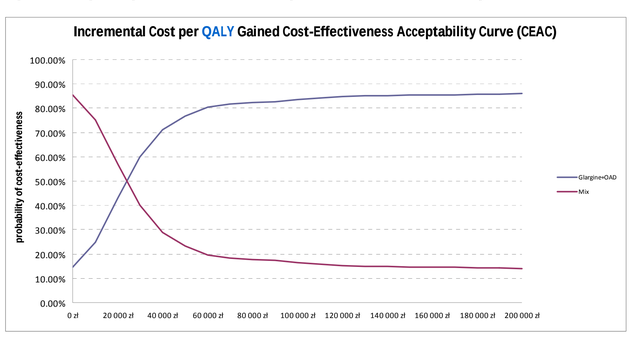


Figure 9. NHF + patient perspective – CEAC (IGlar + OAD vs IMix)



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Conclusion

Insulin glargine is a new basal insulin option for the management of diabetes. It can provide enhanced HbA1c control at a lower rate of hypoglycaemic episodes experienced than premixed insulin. The added cost of insulin glargine therapy (from the NHF + patient perspective) should be weighed against future benefits in the form of reduced long-term diabetes-related complications, such as MI, stroke, retinopathy, nephropathy, neuropathy, coronary artery disease, and amputation. The benefits and cost-effectiveness ratios calculated in this analysis of its long-term use in patients with T2DM provide support for its adoption from the Polish healthcare payer's perspective.