COST-UTILITY OF BIPHASIC INSULIN ASPART AS COMPARED WITH PREMIX HUMAN INSULIN

IN TREATMENT OF TYPE 2 DIABETES MELLITUS IN POLAND

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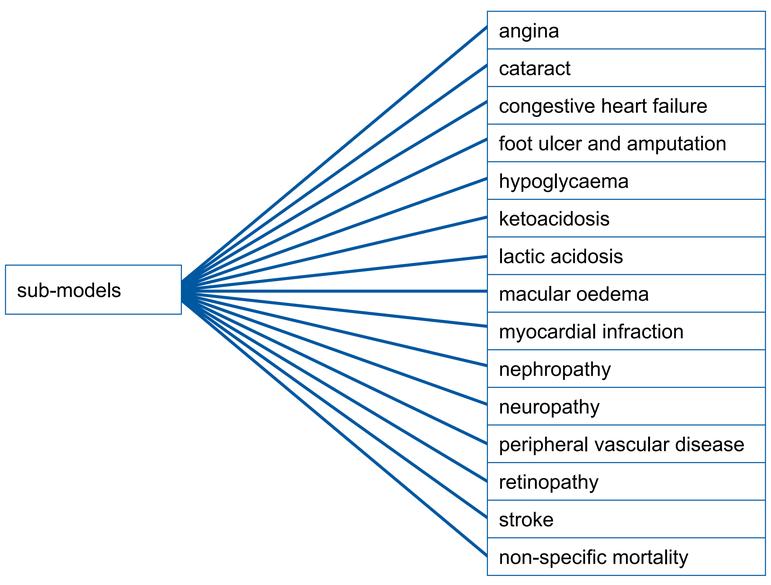
*A study conducted by **HTA Consulting** **www.hta.pl***

Objectives

The aim of this analysis was to evaluate cost-utility of biphasic insulin aspart (BiAsp) as compared with premixed human insulin (Premix) in type 2 diabetes mellitus in Poland.

Methods

- A cost-utility analysis based on The CORE Diabetes Model (www.core-diabetes.com) was conducted, resulting in estimation of total direct costs incurred by the National Health Fund and patients, life years gained (LYG) and quality-adjusted life years (QALY).
- The CORE Diabetes Model is a complex tool allowing for evaluation of long term health and economic outcomes of different treatment options in diabetes mellitus. It implements Markov modeling techniques, Monte Carlo and bootstrap simulations in a series of interconnected sub-models representing diabetes complications. Results are evaluated throughout a course of microsimulations, where defined number of patients is run through the model. Transition probabilities between sub-model states depend on cohort baseline characteristics as well as patient's health status changing over time (i.e. developing complications changes transition probabilities). The risk of events in the model changes also according to whether or not patients are on ACEI, statin or aspirin treatment. In addition, for DM type 2 simulations comparison of treatment sequences rather than single-line treatment can be made.
- The CORE Diabetes Model is based on data from published trials (The Framingham Heart Study, Diabetes Control and Complications Trial), but all crucial parameters may be changed by the user.
- Effectiveness of specific treatments was expressed as change in the HbA1c level and hypoglycaemia rates.
- Costs were calculated from the public payer (NHF – National Health Fund) + patient perspective.
- The time horizon in the model was set to 30 years in order to calculate estimates of costs and outcomes in a life-time period. Taking into account baseline cohort age, it is unlikely that patients will outlive assumed period of time and therefore time horizon can be referred to as life-time.
- Incremental cost per QALY and per LYG gained were calculated.
- In order to estimate the probability of BiAsp being cost effective in Polish settings (a threshold of ca. 91,000 PLN), bootstrap simulations were performed.
- Costs and outcomes were discounted according to the Polish HTA Agency guidelines. The discount rates used were 5%.
- One-way sensitivity analyses were conducted in order to assess the influence of assumptions regarding input parameters on final results. The following parameters were included in one-way sensitivity analysis: discount rates (0% for both costs and outcomes, 5% for costs and 0% for outcomes), complication costs (+/-25%), hypoglycaemia rates (+/-10% and no difference between BiAsp and Premix), HbA1c change from baseline (no difference between BiAsp and Premix).



Data collection

- Cohort baseline characteristics and baseline distribution between states in the model were derived from published Polish sources. Literature search was conducted in order to gather information on characteristics of Polish cohort. All data were meta-analyzed so that estimates would be based on the best evidence available. Baseline characteristics include age, sex, duration of diabetes, smoking status as well as clinical parameters: HbA1c, systolic blood pressure, total cholesterol, HDL, LDL, triglycerides level, BMI. Distribution of patients between the states was dependent on the percentage of the following comorbidities: cardio-vascular diseases, renal diseases, retinopathy, macular edema, cataract, foot ulcer and neuropathy.
- Interventions were defined in means of change in baseline HbA1c and frequency of hypoglycaemia episodes. Efficacy and safety data were derived from studies identified in the course of a systematic review of RCTs. BiAsp was associated with slightly greater change in baseline HbA1c than Premix and with greater reduction of hypoglycaemia rates.
- Costs of interventions included only insulin costs and were calculated on the base of April 2009 prices. Annual cost of treatment per patient was 1,760 PLN for BiAsp vs. 1,111 PLN for Premix.
- Polish diabetes complication costs collected by other researchers and allowed for public access in the CORE Diabetes Model were updated according to the Consumer Price Index and used in the analysis.
- Default Model settings regarding transition probabilities and health states utilities were kept.

Table 1. Cohort baseline characteristics

Parameter	Mean (SD)	Parameter	Mean (SD)
Age	63.83 (1.36)	Myocardial infraction	18.95%
Duration of diabetes	12.43 (0.72)	Peripheral vascular disease	6.48%
Proportion of male patients	50%	Stroke	3.11%
HbA1c [%]	7.75 (0.40)	Congestive heart failure	15.51%
SBP [mmHg]	138.71 (3.35)	Atrial fibrillation	3.30%
T-CHOL [mg/dl]	212.82 (2.98)	Microalbuminuria	19.14%
HDL [mg/dl]	62.50 (6.15)	Background diabetic retinopathy	31.01%
LDL [mg/dl]	114.15 (7.11)	Proliferative diabetic retinopathy	1.65%
TG [mg/dl]	143.02 (19.01)	Severe vision loss	1.12%
BMI [kg/m2]	30.29 (0.62)	History of amputation	3.94%
Proportion of smokers	31%	Neuropathy	5.11%

Table 2. Efficacy and safety

Parameter	BiAsp	Premix
Change in baseline HbA1c [%], mean (SD)	-0.51 (0.31)	-0.49 (0.17)
Minor hypoglycaemia event rate [per 100 patients per year]	419	606
Major hypoglycaemia event rate [per 100 patients per year]	3	14

Table 3. Annual treatment cost per patient

Perspective	BiAsp	Premix
Payer (NHF)	1,149 PLN	1,075 PLN
Patient	611 PLN	35 PLN
NHF + Patient	1,760 PLN	1,111 PLN

Results

In a 30 years horizon both treatments are comparable in terms of LYG (7.47 for BiAsp and 7.46 for Premix), but BiAsp yields higher QALY then Premix (5.06 vs. 4.95). Lifetime cost per patient treated with BiAsp and Premix is 30,079 PLN and 24,970 PLN, respectively. Incremental cost per QALY for BiAsp compared with Premix is 49,425 PLN and per LYG is 455,778 PLN.

Table 4. Cost and effectiveness comparison, ICERs

Category	BiAsp	Premix
QALY	5.06	4.95
LYG	7.47	7.46
Costs	30,079 PLN	24,970 PLN
ICERs		
ICER QALY	49,425 PLN	
ICER LYG	455,778 PLN	

Table 5. Breakdown of direct costs

Category	BiAsp	Premix
Treatment	14,188 PLN	8,944 PLN
Hypoglycaemia	59 PLN	258 PLN
Renal complications	403 PLN	384 PLN
Cardio-vascular diseases	13,445 PLN	13,397 PLN
Ulcer / amputation / neuropathy	1,217 PLN	1,221 PLN
Other costs	767 PLN	766 PLN
Total cost per patient	30,079 PLN	24,970 PLN

Figure 1. PSA results for QALY

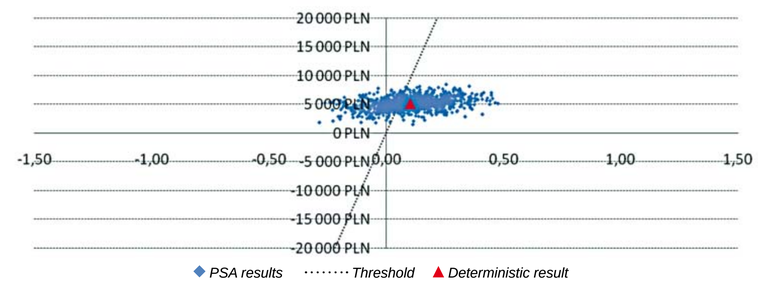


Figure 2. PSA results for LYG

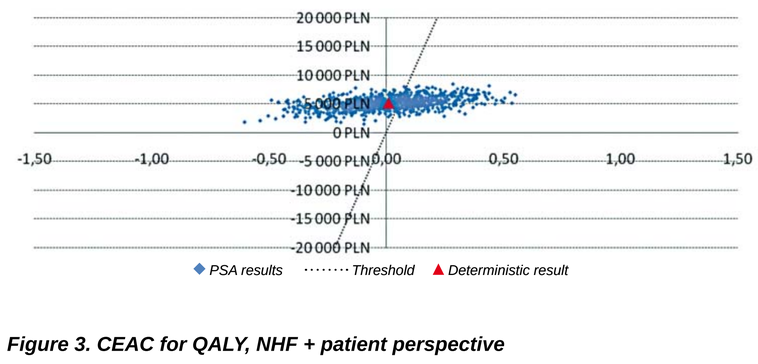


Figure 3. CEAC for QALY, NHF + patient perspective

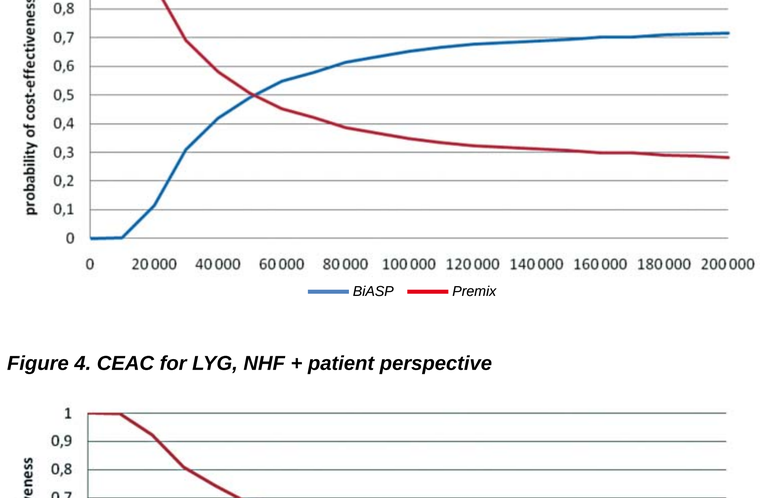
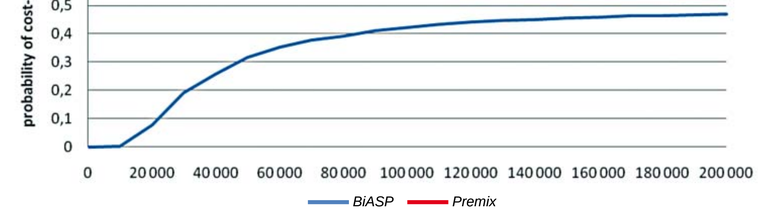


Figure 4. CEAC for LYG, NHF + patient perspective



Summary

Objectives: To evaluate cost-utility of biphasic insulin aspart (BiAsp) as compared with premixed human insulin (Premix) in type 2 diabetes mellitus.

Methods: A cost-utility analysis based on The CORE Diabetes Model was conducted, resulting in estimation of total direct costs incurred by the National Health Fund and patients, life years gained (LYG) and quality-adjusted life years (QALY). The CORE Diabetes Model is a complex tool allowing for evaluation of long term health and economic outcomes of different treatment options in diabetes mellitus. It is designed as a Markov model using Monte Carlo simulations and is based on a series of interconnected sub-models representing diabetes complications. Cohort baseline characteristics and baseline distribution between states in the model were derived from published literature. Effectiveness of specific treatments was expressed as change in the HbA1c level and hypoglycaemia rates calculated on the base of a systematic review of RCTs. CORE default data were used for transition probabilities and health states utilities. Costs were calculated from the NHF+patient perspective. The time horizon in the model was 30 years. In order to estimate the probability of BIAsp being cost effective in Polish settings (a threshold of ca. 91,000 PLN), bootstrap simulations were performed.

Results: Both treatments were comparable in terms of LYG (7.47 for BIAsp and 7.46 for Premix), but BIAsp yielded higher QALY (5.06 vs. 4.95 for BHI). Costs generated by BIAsp were 30,079 PLN and by premixed insulin 24,970 PLN. Incremental cost per QALY for BIAsp compared with Premix was 49,425 PLN. Probability of BIAsp cost effectiveness over Premix was 63% for QALY and 41% for LYG.

Conclusions: Biphasic insulin aspart improves quality of life reflected by higher QALY values. Despite higher treatment-associated costs, biphasic insulin aspart is cost-effective in Polish settings.

Conclusions

- BiAsp is more effective in terms of QALY than Premix, although it does not extend life expectancy more than Premix.
- Lower rates of hypoglycaemia events in case of BiAsp compared to Premix are the main reason of higher QALY for patients treated with BiAsp than for patient treated with Premix..
- BiAsp and Premix are comparable in terms of LYG.
- The difference in total costs is mainly due to the difference in treatment costs.
- It was assumed that while experiencing major hypoglycaemia episode only 2,4% of patients required hospitalization and the rest was only given a dose of glucagon. Therefore, difference in major hypoglycaemia rates did not have a great impact on the difference in total costs.

Table 6. Abbreviations

BiAsp	Biphasic insulin aspart
CI	Confidence Interval
DM	Diabetes Mellitus
HbA1c	Glycosylated hemoglobin
ICER	Incremental cost-effectiveness ratio
LYG	Life years gained
NHF	National Health Fund
Premix	Premixed human insulin
QALY	Quality-Adjusted Life Years