# COST-EFFECTIVENESS ANALYSIS OF BASAL INSULIN-SUPPORTED ORAL THERAPY USING HUMAN OR ANALOGUE INSULIN TYPE 2 DIABETES IN HUNGARY

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## Background

The prevalence of diabetes is reaching epidemic proportions worldwide, with type 2 diabetes (T2DM) being the most expressive form of the disease, accounting for 90% of all cases. There are currently 425 million people affected by the condition globally, although as population grows and societies grow old, this number is expected to reach 629 million by 2045 [1a, 1b]. Care of T2DM imposes a huge financial burden on health systems partly due to direct prescription costs, and indirect expenditure associated with costly micro-, and macrovascular complications. As a consequence, long-term cost effectiveness of diabetes therapies is becoming a public health priority. The main objectives of the present study were to investigate long-term health outcomes and costs for patients initiated on Basal Supported Oral Therapy (BOT) using human or analogue insulins in the Hungarian setting.

Although there is a notable price difference between human and analogue basal insulins, extra costs can be offset by reduction in complication costs, as robust medical evidence suggests lower risk of complications with analogue insulins compared to human insulins [2a, 2b]. Furthermore, reduced risk of developing such comorbid events could result in much higher compliance with therapy. On a broader perspective, the aim of the present study was to establish an analytical framework for the better monitoring of the quality, efficiency and financing aspects of diabetes care. Establishment of such evaluation process of data analysis and statistical methodologies helps survey tasks and assist decision makers in providing an appropriate supply structure for a cost-effective and value-based healthcare system.

## Methods

**Study Population**

The study was based on the Claims Database of the National Health Insurance Fund of Hungary which covers all publicly financed inpatient and outpatient events in Hungary (e.g. diagnoses, medication use, medical aids and devices).

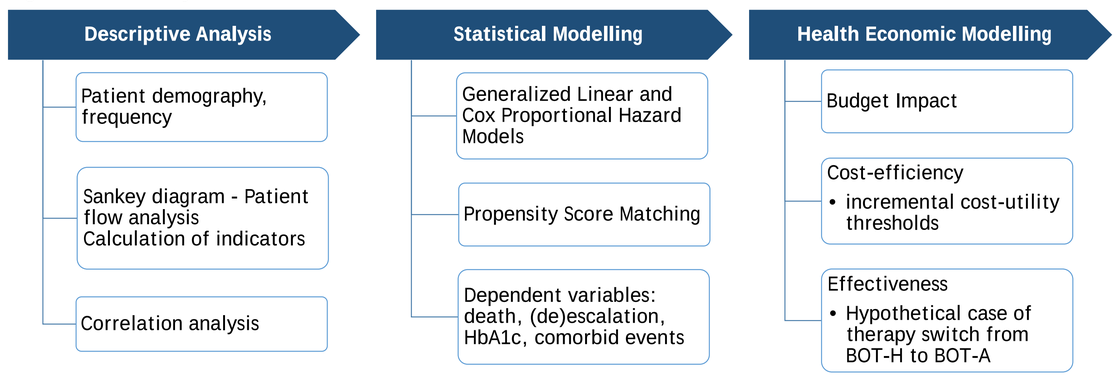
For the current analyses, we created cohort study of all T2DM patients initiated on BOT (long acting insulin plus OAD) and followed them up between 01.01.2009 and 12.31.2016. The first two years were used as baseline period, hence the study period spanned from 1st January 2011 to 31st December 2016. Patients were excluded if they had any drug dispensation with relevant ICD codes (E10/E11/E14) between 01.01.2009 and 31.12.2009. Two patient sub-groups, BOT-A and BOT-H were identified, depending on the first theraputic approach including analogue or human BOT.

**Study Design:**

To observe differences between appointed patient pathways of human and analogoue insulin therapies, comprehensive descriptive, correlation and statistical modelling analyses were conducted (*Figure 1*). **Sankey diagram** is a special type of flow diagram, where the focus of analysis is on the sequence of events. This helps map therapeutic patterns and provides valuable insight into the occurence of comorbid events and costs incurred during specific treatment stages. Indicators can be computed on the basis of mean values of such measures during specific treatment stages in order to identify possible patient subgroups for the therapy switch simulation. **Generalized Linear Models** and **Cox Proportional Hazard Models** were used to measure the difference in the effect of human and analogue insulin therapies on the expected occurence and relative risk of appointed events, respectively.

**Propensity Score Matching (PSM)** method was applied to separate the effect of analogue and human insulin therapies from the effect of the covariates that predict receiving that treatment. The **Health Economic Simulation** works by generating pairs of patients: one of them belonging to the BOT-H patient arm and the other to the BOT-A arm. Variables on demography, date of therapy initiation and retrospective (baseline) comorbid events related to a particular arm were included in the Individual Sampling Model using the results of the statistic models above. In case of cost calculations 320 EUR/HUF FX rate was applied.

***Figure 1*. The Analytical Evaluation Framework**




## Results

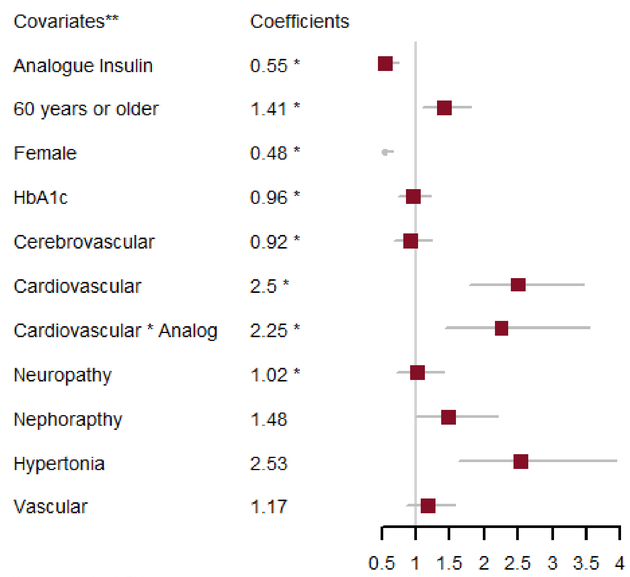
### I. COMPARATIVE ASSESSMENT OF ANALOGUE AND HUMAN THERAPIES

***Table 1*. Number of Patients Included In the Analysis**

| Patients with Type 2 Diabetes N= 295 679 ( 69,5%) | |
|---|---|
| Patients Treated with Insulin Therapy N= 31 012 ( 10,5%) | |
| Analogue BOT Therapy N= 7 315 (23,6%) | Human BOT Therapy N= 6 823 (22%) |

- There were a total of 425,576 newly diagnosed patients (no treatment received during 2009): 295,679 DM patients were diagnosed as type 2, while 25,754 patients as type 1.
- 7,315 and 6,823 patients were categorised as BOT-A and BOT-H, respectively, based on the first therapy received.
- After the PSM 6752 patients were included in the modelling.

***Table 2:* Results of the Cardiovascular GLM model**




* Significant at 5%

** Comorbid events during the baseline period were included, in case of cardiovascular events only pharmacy drug costs were considered.

*The propensity adjusted GLM models revealed the advantage of BOT-A therapy compared to BOT-H* in the following cases:

- As seen in *Table 2*, the incidence of cardiovascular complications (RR=0.55, CI: 0.4 – 0.75, p=0.01) for patients free of cardiovascular complications (in-, and outpatient care events) at baseline (n=6 752, 60%).
- Incidence of cerebrovascular complications (RR=0.71, CI: 0.57 – 0.89, p=0.01) for patients free of cerebrovascular complications (in-, and outpatient care) at baseline (n=6 872, 90%), and younger than 60 years.

### II. COST-EFFECTIVENESS ANALYSIS

Patient pathways were clustered based on appointed dimensions (average daily costs and number of avoided comorbid events). Each cluster can be evaluated as an individual patient subgroup based on the chosen value pairs (*Figure 2*). Cluster analysis enables specific risk groups of patients and predictive factors to be identified for the selection of the most preferred therapy.

***Figure 2:* Cluster Analysis**

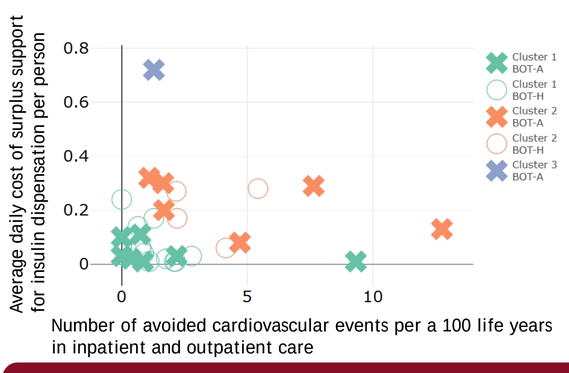



***Figure 3: Cost-effectiveness Analysis***

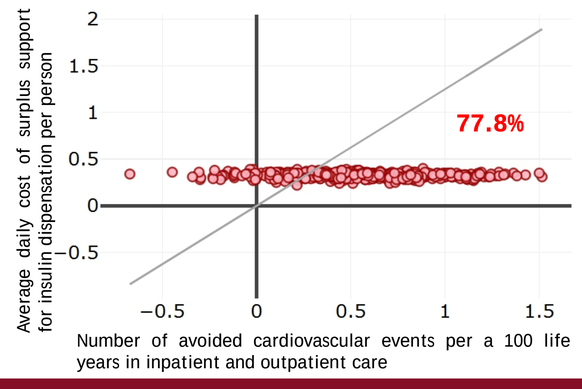



*Figure 3* shows the evalutaion of cost-effectiveness for the appointed dimensions: if we are willing to spend an additional daily reimbursement expenditure of 1.25 EUR per patient for one prevented cardiovascular event per 100 patient-years for the initiation of BOT-A therapy we would have a *77.8 % chance for the treatment to be cost-effective*.

### III. MULTICRITERIAL ASSESSMENT

The cost-effectiveness ranking of therapy switches between BOT-H and BOT-A depends on the the chosen rate of efficiency: *expected saving, expected efficiency and expected cost-effectiveness*. Based on the aformentioned criteria, the *weighted evaluation of therapy switches can be used during decisio*n-making.

### IV. HEALTH ECONOMIC MODELLING

Analysed patient subgroup: patients who were free of cardio-, and cerebrocascular complications at baseline.

Method: What-If analysis based on Simulated Patient-Level Decision Tree Model. The propensity adjusted GLM models revealed that the incidence of cardio-, and cerebrovascular comorbid events are lower for patients initiated on analogue insulin therapy compared to human (*RR=0.55 and RR=0.71*). With the application of our simulation model we are able to determine the extra costs incurred per one avoidable complication in the hypothetical case of having *k* patients initiated on analogue insulin therapy instead of human. The model works by multiplying average daily ratio (of events /costs) per patient with 365 days and the respective patient ratio and RR numbers. When determining the costs, different RR numbers have been applied for patients below and above the age of 60.

Results: In the hypothetical case of having 500 patients initiated on BOT-A therapy instead of BOT-H between the ages of 40 and 59: 6.65 cardiovascular events prevented for an additional expenditure of 46,460 EUR; 3.48 cerebrovascular events for an additional 50,680 EUR.

### V. BUDGET IMPACT ANALYSIS

Taking into account the number of patients initiated on BOT therapy in 2016 and the amount of reimbursement for analogue and human insulin we can conclude the following:

- If a patient was initiated on analogue BOT therapy, it would mean an extra, daily expenditure of 0.77 – 1.91 EUR for the insurer depending on the reimbursement rate (*Figure 4*).
- In the hypothetic case of having all patients treated with analogue insulin, it would mean an additional expenditure of 582 – 1 444 thousand EUR yearly (*Table 3*).
- If we restrict the number of patients who receive analogue insulin treatment to be in line with relevant clinical guidelines, it would mean a rate of access of about 50-70 % which could translate to an additional expenditure of about 625 – 937,5 thousand EUR.

***Figure 4:* Daily Reimbursement Costs of Insulin Therapies**

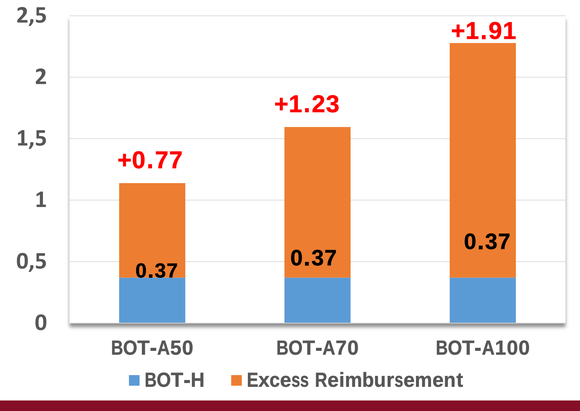



***Table 3:* Excess Expenditure for Patients Initiated on BOT-A Therapy**

| Patient numbers | | | Excess Expenditure (EUR) | | |
|---|---|---|---|---|---|
| Range | BOT-H | BOT-A50 | BOT-A50 | BOT-A70 | BOT-A100 |
| : 94 | 352 | 223 | 16 688 | 26 566 | 41 387 |
| 95 : 184 | 307 | 245 | 36 400 | 57 950 | 90 278 |
| 185 : 274 | 256 | 241 | 48 060 | 76 516 | 119 200 |
| 275 : 364 | 245 | 297 | 63 720 | 101 450 | 158 044 |
| 365 : 365 | 1486 | 2480 | 417 316 | 664 403 | 1 035 038 |
| **Total** | **2646** | **3486** | **582 184** | **926 884** | **1 443 947** |

## Conclusions

Despite the higher medication costs of analogue based BOT, this theraputic approach was associated with a substantial reduction in the occurence of macrovascular complications after therapy initiation and an acceptable cost-effectiveness compared to human insulin based BOT. Although the primary requirement for the initiation of more expensive therapies is usually not to prevent complications, but to avoid further deterioration of patients already at risk of exposure, our study draw on valuable clinical and health-economic conclusions which confirm the need for the broader use analogue insulin products by providing greater financial support. In the Hungarian setting, the introduction of higher reimbursement rates from 50% to 100% for BOT-A therapies are of principal importance for patients with rapid growth- and sustained levels of HbA1c. Further investigations are needed to describe patient subgroups that would gain the most benefit from the analogue BOT approach.

## References

[1a] International Diabetes Federation [IDF Diabetes Atlas Eighth edition 2017]. International Diabetes Federation; 2007

[1b] World Health Organization {WHO Global Report on Diabetes}. World Health Organization; 2016. http://apps.who.int/iris/bitstream/handle/10665/204871/9789241565257_eng.pdf;jsessionid=2EA23BE9C7FE559C8703C3392F08E981?sequence=1

[2a] Cornell S. [Exploring The Quality-Of-Life Benefits With Insulin Analog Use]. The Internet Journal of Family Practise. 2009; V9 N1. https://print.ispub.com/api/0/ispub-article/9405

[2b] Gordon J, Evans M, McEwan P, Bain S, Vora J. [Evaluation of Insulin Use and Value for Money in Type 2 Diabetes in the United ingdom]. Diabetes Therapy. 2013 Jun; 4(1):51-66. doi: 10.1007/s13300-012-0018-3. pmid:23296753

Disclosure of authors

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