COST-EFFECTIVENESS OF SOMATROPIN ADMINISTRATION WITH INCREASED ADHERENCE DUE TO MONITORING COMPARED TO NON-MONITORED ADMINISTRATION IN PATIENTS WITH GROWTH HORMONE DEFICIENCY

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Introduction

- Somatropin (recombinant human growth hormone, rhGH) is currently the only available treatment for growth failure in children with growth hormone deficiency (GHD), Turner syndrome, CRI, Prader-Willi syndrome, and in children born small for gestational age.[1]
- All rhGHs have the same molecular structure, therefore providing equal efficacy and safety, and they are granted the same reimbursement in the Czech Republic (CR).
- RhGHs are currently administered subcutaneously once a day, differing only in applicators.
- Easypod™ is the only applicator that enables monitoring the dose, time and date of each injection and allows feedback control by doctors.
- Long-term, continuous adherence is essential to achieve optimal therapeutic results of rhGH treatment. International studies have shown that lower adherence (or the frequency of injection) is associated with poor growth response. [2-7]
- Omission of two or more injections per week has considerable impact on the growth rate during growth hormone treatment.

Objective

- The objective was to assess the cost-effectiveness of monitored rhGH treatment administered by easypod™ compared to the standard, non-monitored rhGH administration in CR.

Methods

- Deterministic cohort model estimated the long-term costs and benefits development of rhGH treatment.
- The interim results (n = 596) of an ongoing multicenter, non-comparative, observational, longitudinal study (ECOS[8]) were used as the model inputs.
- The model evaluation was based primarily on the relationship between the monitoring of treatment and the patient adherence to the treatment as detailed in ECOS.
- Increased adherence of monitored patients was transferred to the increased effectiveness of the treatment (height velocity), based on the study published by Kapoor et al.[3]
- Model further transformed the long-term treatment benefits to the increased quality of life, taking QALY as the target parameter using empirical transformation.
- Empirical study of the relation between the height and the EQ-5D in the general UK population[9] was used to convert the achieved height standard deviation score (HSDS) to QALY (Figure 3).
- Evaluation was done from a lifetime perspective. Discount rate was 3% for both costs and outcomes. Costs were expressed from the payer's perspective. Exchange rate was EUR/CZK 25.635.
- Model assumptions: rhGH treatment starts at the age of 2-15; patients' age at the start of rhGH treatment is normally distributed; rhGH treatment is discontinued at the age of 18 in boys and 16 in girls; adherence rate of monitored patient in subsequent years is calculated as the average of the values measured from the time period observed so far (=93.8); patients can reach maximum HSDS=0; if patients reach HSDS=0, the treatment continues, but HSDS stays at the constant value=0; side effects are not considered.

Figure 1: Adherence rates depending on the presence of monitoring (interim analysis from ECOS[8])

Time period	Number of patients		Adherence Rate (Median)		interquartile range (Q1 ;Q3)	
	Non-monitored	Monitored	Non-monitored	Monitored	Non-monitored	Monitored
3 months	199	216	94.5	94.9	82.4; 98.8	85.7; 98.7
12 months	102	26	84.8	94.9	44.0; 95.6	77.7; 97.8
18 months	64	NA	66	NA	28.2; 88.4	NA
24 months	44	NA	52.3	NA	36.6; 81.7	NA

Figure 2: Adherence rate and corresponding height velocity (* in SDS/year)

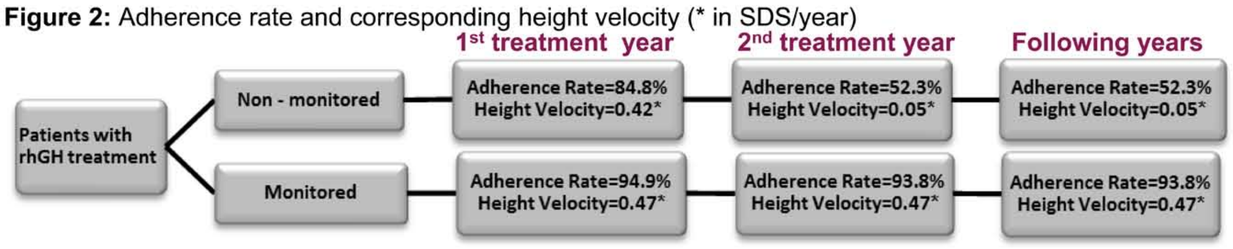
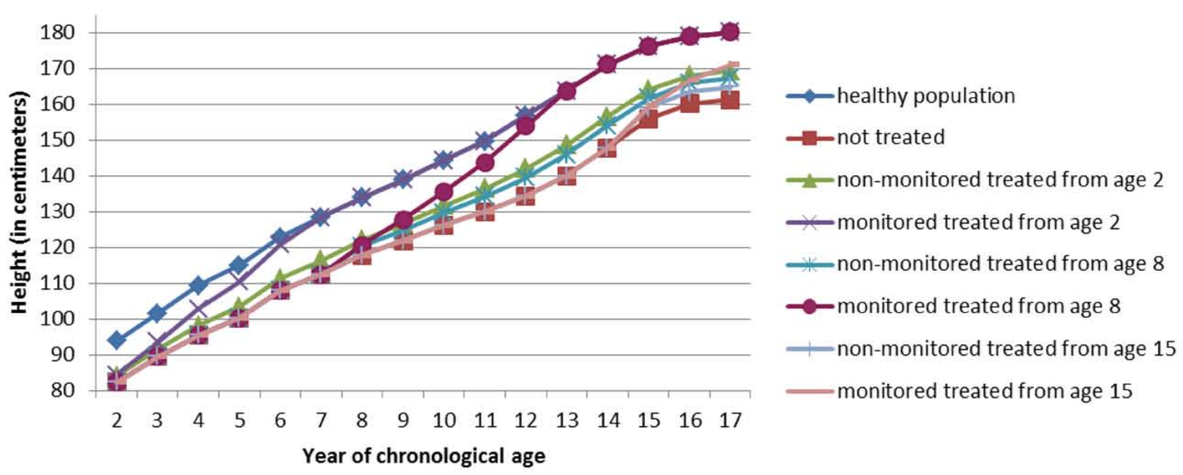


Figure 3: Relationship between HSDS and EQ-5D score[9]

The range of individual HSDS	EQ-5D score improving factor for unit decrements in HSDS
HSDS < -2	0.061
HSDS between -2 and 0	0.010
HSDS > 0	0.002

Results

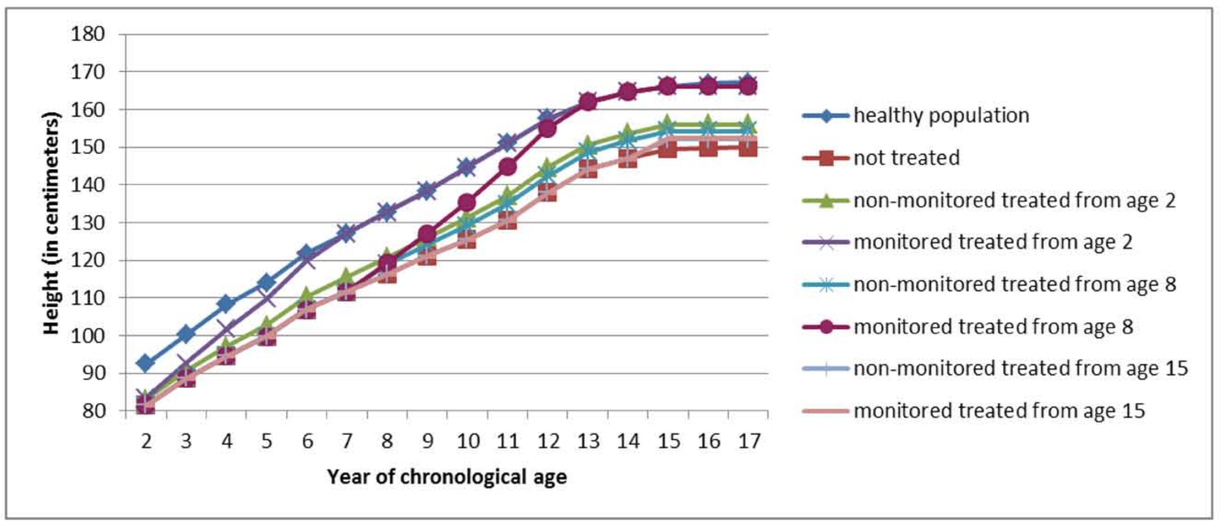
Figure 4: Modeling of height development (in centimeters), in boys



Results

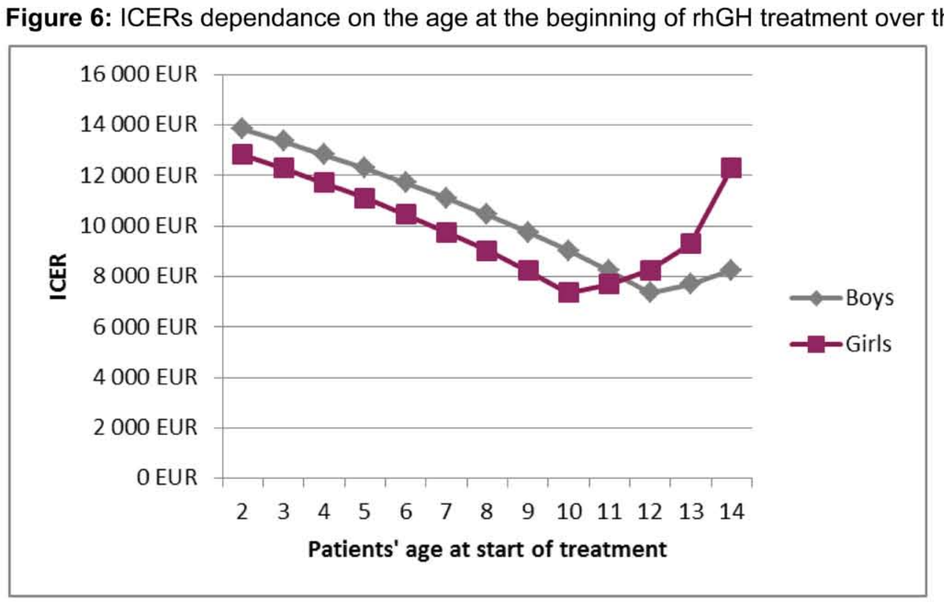
- Based on the assumed starting HSDS (-2.7) and the empirical relationship between the adherence rate and HSDS, the patients' height throughout the treatment was modeled. Examples of growth development for patients starting rhGH treatment at the age of age 2, 8 and 15 years compared to non-treated patients and healthy population are shown in Figures 4 and 5.

Figure 5: Modeling of height development (in centimeters), in girls



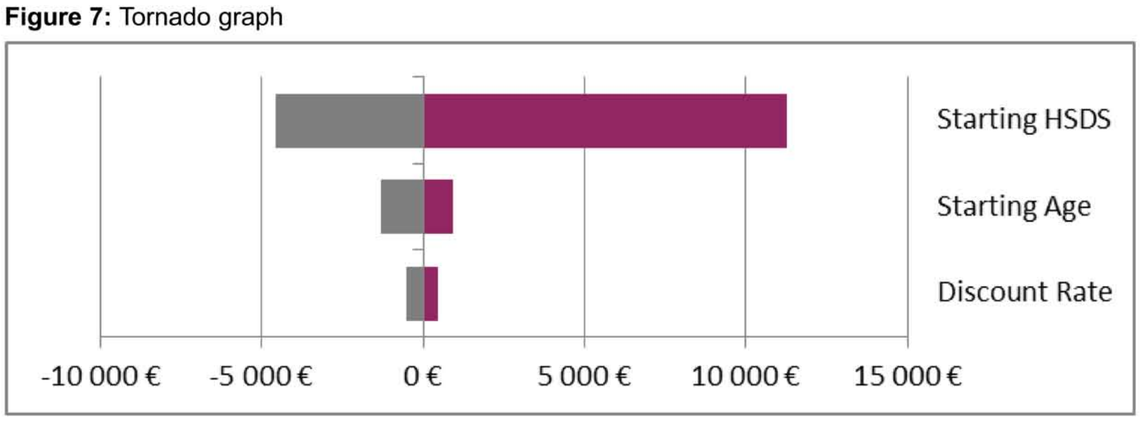
- The acquisition cost of standard rhGH treatment was approximately EUR 7,370 per year. An increase in the acquisition cost (10% bonus) for rhGH treatment administered by easypod™ therefore led to the acquisition cost of EUR 8,112 per year. Other direct medical costs (quarterly endocrinological examinations, yearly blood tests to observe thyroid hormones levels and yearly radiographs to assess bone age of patients) were same in both model arms.
- The ICERs were modeled separately for boys and girls, depending on the patients' age at the start of rhGH treatment (Figure 6).

Figure 6: ICERs dependance on the age at the beginning of rhGH treatment over the treatment horizon



- Due to an increased adherence and consequent improvement of HSDS and thus EQ-5D score, the hypothetical cohort of 10,000 monitored boys generated 9,517 of incremental QALY in total, and the hypothetical cohort of 10,000 monitored girls generated 11,504 incremental QALY in the lifetime horizon.
- In addition, monitored boys generated EUR 63.8 million (CZK 1.6 billion) incremental costs and monitored girls generated EUR 52.8 million (CZK 1.35 billion) incremental costs in the lifetime horizon.
- The average cost per QALY (ICER) for an average patient (boys and girls) with GHD was calculated to be approximately EUR 6,120 (CZK 157,000) in a lifetime horizon.

Figure 7: Tornado graph



- One-way sensitivity analysis was performed by modifying the main input parameters by ±20% from the base case values. For the considered uncertainty of the age and HSDS score at the beginning of rhGH therapy and the discount rate, the ICER does not exceed EUR 17,550 (CZK 450,000) in the lifetime horizon.
- The starting HSDS indicated a major effect on the ICER followed by the starting age at treatment onset and the discount rate .

Conclusions

- Facilitated by easypod™, monitoring of rhGH administration may lead to an increased adherence and thus more effective treatment at relatively low cost, hence being considered cost-effective. Sensitivity analysis showed that ICER does not exceed EUR 17,550 upon the considered uncertainty in the lifetime horizon.

 # PND27

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