PSY83

COST-EFFECTIVENESS ANALYSIS OF RESTRICTED PROTEIN DIET IN PATIENTS WITH PHENYLKETONURIA IN THE CZECH REPUBLIC

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BACKGROUND AND OBJECTIVES

Restricted protein diet (RPD) is the only effective and safe treatment in patients with phenylketonuria (PKU) along with amino acids supplementation excluding phenylalanine. If untreated, PKU leads to severe mental retardation and wide range of other health complications.[1–4] Although specialized low-protein foods (LPF) are substantially more expensive than regular food, they are not reimbursed from public health insurance which may consequently lead to non-compliance with RPD. The main objective was to assess the cost-effectiveness of reimbursed RPD (i.e. basic LPF) versus not reimbursed RPD in patients with PKU from healthcare payer's perspective.

METHODS

We developed a life-time Markov cohort cost-utility model with yearly cycle length and 3 health states, i.e. on diet (normal health; all patients begin in this state), non-compliance to diet (mental retardation) and death. The model structure is shown in Figure 1 and model settings in Table 1. In order to estimate compliance with diet and cost of RPD, we conducted our own cost-of-illness study (COI) including approximately half of Czech PKU patients.[5] We assumed that reimbursement of basic LPF (flour, pasta, milk (dried and liquid), rice and eggs)) would decrease non-compliance from 34.1% (i.e. COI result) to 15.0% based on income distribution in society.[6] Non-compliance with diet causes a whole range of health complications. In the model we focus on the disutility associated with mental retardation. The non-compliance with diet is assumed to be affecting a patient in the first 25 years of patient age due to the development of the main brain functions (Table 2).[7]

The costs of RPD and given food categories are shown in Table 3. The average monthly costs of RPD is equal to €57.6.[5] In the scenario analysis, we assume additional costs of €480.1/year for patients with intellectual disability (ID).[8,9]

In compliant patients, the age-dependent utility was assumed.[10] In non-compliant (mentally retarded) patients utility for patients with ID was equal to 0.64 (based on Monte Carlo simulations of each domain[11] and the UK value set). Other utility sources were modelled in scenario analysis (Table 4).

Probability of death was derived from Czech mortality tables and in scenario analysis for non-compliant patient adjusted by standardized mortality ratio (SMR) for patients with ID (SMR=2.8).[12,13]

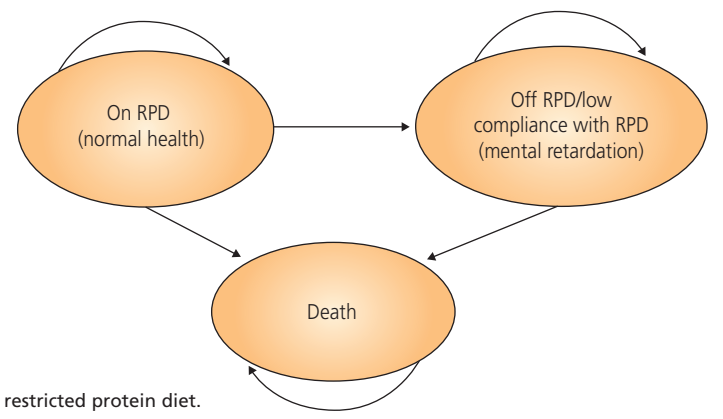
Costs and outcomes were discounted by 3%.

Probabilistic sensitivity analysis (PSA) with 3000 iterations using a willingness-to-pay (WTP) threshold equal to 3-times GDP per capita (€47,000) in the Czech Republic was performed. Table 5 shows the PSA setting. One-way sensitivity analysis (OWSA) and scenario analysis (SA) explored the impact of all considered variables and several assumptions on the base-case result (Figure 4).

RESULTS

Over a life-time horizon, reimbursement of RPD (i.e. basic LPF) compared to no reimbursement of RPD brings additional 0.81 QALY (23.16 vs. 22.35). The total life-time incremental costs are €16,235 (€16,235 vs. €0). ICER is thus equal to €19,955 per QALY gained (Table 6). The results of PSA show that reimbursement of basic LPF is cost-effective with probability of 95% at the WTP threshold and increases with increasing WTP (Figure 1 & 2). OWSA and SA consequently showed that probability of non-compliance has the biggest impact on the results along with the cost of RPD and utilities, other parameters had negligible impact (Figure 4). Sensitivity analyses confirmed high robustness of the base-case CE result.

Figure 1. Markov model structure



Note: RPD – restricted protein diet.

Figure 2. Incremental cost-effectiveness scatter plot (Assessed intervention vs. Comparator)

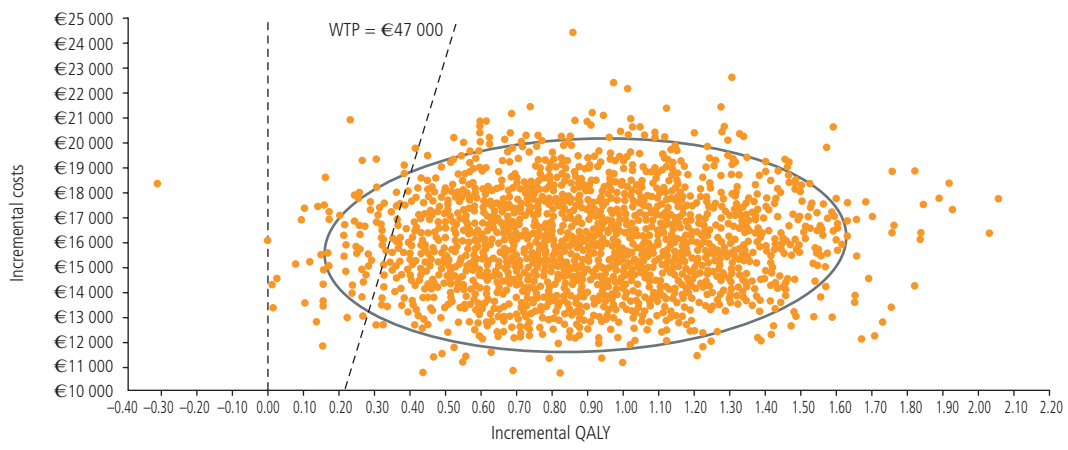


Figure 3. Cost-effectiveness acceptability curve

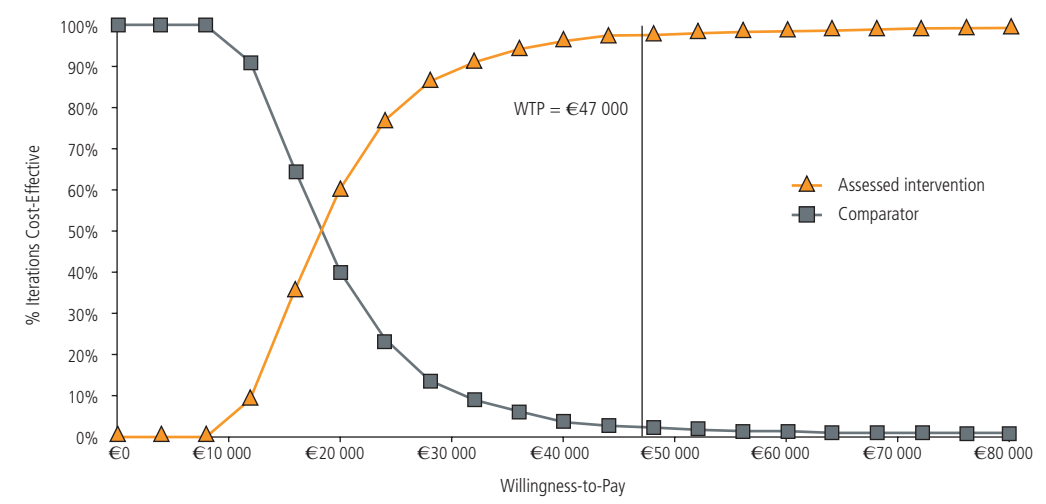


Table 1. Summary of the model settings

Perspective	Healthcare payer's (public health insurance)
Analysis type and model type	Cost-utility analysis, Markov model
Software	TreeAge Pro 2016
Time horizon	Life-time (50 years)
Cycle length	1 year
Discount rate	3% for costs and outcomes
Patient population	Patients with PKU requiring life-time restricted protein diet
Assessed intervention	Basic low-protein foods necessary for RPD reimbursed from public health insurance (i.e. low-protein flour, milk (dried and liquid), pasta, rice and eggs)
Comparator	Standard of care, i.e. no basic low-protein foods reimbursed from public health insurance
Outcomes	Quality-adjusted life-years
Discount rate	3% for costs and outcomes
Sensitivity analysis	One-way, probabilistic and scenario analysis

Table 2. Probability of non-compliance with RPD[5]

	Assessed intervention	Comparator
Probability of non-compliance with RPD (over 25-year time horizon)	15.00%	34.10%
Yearly probability of non-compliance with RPD*	0.64%	1.65%

*The yearly probability was recalculated using exponential distribution and probtoprob function in TreeAge Pro 2016.

Table 3. Cost and consumption of LPF categories[5]

Low-protein food category	Average monthly costs	Average monthly consumption per consumer	Number of consumers	Kcal/100g	Kcal/day
Flour	€22.6	4111g	181	348	470 kcal
Pasta	€15.0	1848g	179	359	218 kcal
Milk total	€12.1	2072g	-	-	-
Dried milk	€6.9	343g	110	466	53 kcal
Liquid milk	€5.2	1728g	85	49	28 kcal
Egg substitute	€4.0	195g	140	442	28 kcal
Rice substitute	€3.9	562g	89	354	65 kcal
Total costs per month	**€57.6**	–	–	–	–

Table 4. Utilities for non-compliant patients (mental retardation)

Utility source	Value
Intellectual disability (children)[11] (base-case utility value)	0.64
Fragile X syndrome (children)[14] (scenario analysis)	0.46
Fragile X syndrome (adults)[15] (scenario analysis)	0.52
Mild mental retardation (children)[15] (scenario analysis)	0.62

Table 5. PSA setting

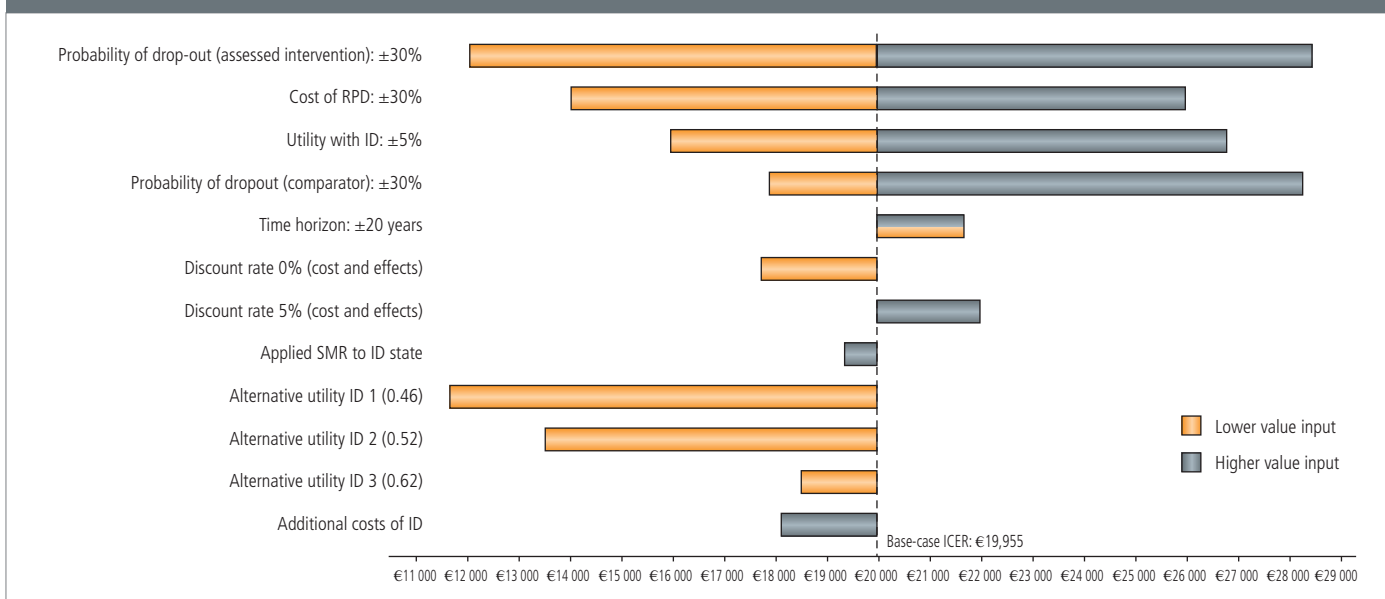
Variable	Distribution	S.E. (range)
Cost of RPD	Gamma	€2.7[5]
Age-dependent utilities	Beta	5%*
Utility with ID	Beta	0,0246[11]
Non-compliance with RPD (both treatment arms)	Beta	20%*

*Assumption

Table 6. The results of cost-effectiveness analysis

	Reimbursed RPD	Not reimbursed RPD	Difference
Total costs of RPD	€16,235	€0	€16,235
QALY	23.16	22.35	0.81
On diet	21.60	18.72	2.88
Off diet	1.56	3.63	-2.07
ICER (CZK/QALY)			**€19,955**

Figure 4. Tornado diagram (OWSA and SA)



CONCLUSIONS

Reimbursement of basic LPF proved its favourable cost-effectiveness in patients with PKU and therefore it represents good value for money. To our knowledge, this is the first cost-effectiveness analysis of RPD and it clearly shows a potential for cost-effective improvement in PKU patients.

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