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PHARMACOECONOMIC ANALYSIS OF USE OF SPECIALIZED HEALTH FOOD LINE «MDMIL PKU» IN CHILDREN FROM BIRTH COMPARED WITH DIET THERAPY, STARTED IN LATER PERIODS

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Abstract: Phenylketonuria is a hereditary disease associated with a metabolic disorder of amino acids in the organism, the prevalence of which in the Russian Federation is 1:10000. Currently, the main treatment of phenylketonuria is diet therapy with specialized health food (a mixture of amino acids without phenylalanine). This research presents the results of a comparison of diet therapy with medicinal mixtures of MDmil PKU line taken from the first month of life of a child compared to food of other producers, taken in later periods. Efficiency analysis is based on data provided by the major regional genetics specialists from 24 regions of the Russian Federation on treatment of 1088 children suffering from phenylketonuria. Cost analysis of treatment of patients with PKU until their majority reveals least expensive diet therapy initiated from the first month of life with specialized health food of MDmil PKU line compared with diet, started in later periods with specialized products of different manufacturers. During the "cost-effectiveness" analysis and the "cost-utility" analysis indicators of CER and CUR are identified showing that when used from the first month of life diet therapy with MDmil PKU line compared with diet, started in later periods with various manufacturers, it is easy to determine treatment of the first group of children as dominant. Budget impact analysis shows that diet therapy with specialized health food of MDmil PKU line in treatment of phenylketonuria can achieve cost savings of 34% to 38% depending on periods of commencement of the diet.

Keywords: specialized health food, MDmil PKU, phenylketonuria, normal mental development, mental retardation, quality-adjusted life years gained, QALY, efficiency analysis, utility analysis, cost analysis, "cost-effectiveness" analysis, "cost-utility" analysis, budget impact analysis.

Introduction

Phenylketonuria (PKU) is a hereditary disease associated with a metabolic disorder of amino acids in the organism, the prevalence of which in Russia is 1:10000. The minimum prevalence of PKU is observed in the Republic of Tuva (1:18000), while the maximum - in Kursk Region (1:4725) [16]. In accordance with the RF Government Decree dated on April 26, 2012 No. 403 all forms of PKU are included in the list of life-threatening and chronic progressive rare (orphan) diseases, that can shorten life expectancy of citizens or lead to disability [8].

The clinical picture of the disease has been developing for 2-3 weeks after birth and until the age of six months in the child irreversible changes are formed in the central nervous system. Patients with PKU are characterized by progressive mental retardation, epileptic syndrome and other Neuropsychiatric disorders [4].

The Order of the Ministry of Health and Social Development of the Russian Federation in 2006 has approved the mass screening of newborns for hereditary diseases, which lead to start of diet therapy in the earliest possible periods and to prevent occurrence of mental retardation in the child [11].

Basics of diet during PKU is a diet with low contain of phenylalanine, source of which is a low-protein food. Therapeutic diet during PKU includes specialized products (a mixture of amino acids without phenylalanine), one of which is a line of medical products MDmil PKU, representation of different forms of release for certain child's age (Table 1) [28].

Table 1. Range of Health Food of MD-Mil PKU line for PKU patients

Age	Name	Weight, g.	Protein Equivalent (g) in 100 g.
0-1 year	MDmil PKU-0	350	13
from 1 year to 3 years	MDmil PKU -1	400	20
from 3 to 7 years	MDmil PKU -2	400	40
older than 7 years	MDmil PKU -3	400	69,1
	MDmil PKU Premium	400	69,1
	MDmil PKU MAXI	500	75

The main regional genetics specialists during assessment of the effectiveness range of health food of MDmil PKU line on the basis of long-term use of mixtures have come to conclusions on compliance of organoleptic properties, good tolerability by children of these products, as well as the

absence of allergic reactions. On the contrary, an attempt to replace the mixture into another has led to dyspeptic, allergic and other disorders, as well as to the complete abandonment by children from receiving the medical mixture that has evolved unfavorably on the state of children and has led to a decrease in school performance, fatigue and irritability.

In accordance with the RF Government Decree dated on 09.04.2015 No. 333 "On Approval of the Regulations for Formation of the List of Specialized Products of Dietetic Therapy for Children with Disabilities" there is a prerequisite for the provision of pharmacological and economic studies, that show the feasibility of the inclusion in the list of specialized products that will further allow the patient within program receive medical care at the expense of budgetary funds [9].

Due to the fact, that the line of MDmil PKU is not included in the list of specialized health food for children with disabilities, conducting pharmacological and economic evaluation in terms of the Russian Federation to compare the use of diet therapy with MDmil PKU taken from an early age and diet, started in later periods, is relevant.

The Purpose of the present research is to determine the terms of pharmacological and economic analysis of preferential schemes of diet therapy used in treatment of patients with PKU by comparing the ratio between cost and efficiency / usefulness, safety during diet therapy with specialized mixtures in three groups analyzed, which started taking it from different ages.

Materials and Methods

This research has compared treatment regimens of children suffering from Phenylketonuria, divided on the basis of data provided by the Chief Specialist of Geneticists, into three groups:

First group – diet therapy with specialized health food of MDmil PKU line in children taking from the first months of life before the onset of adulthood (724 children). Strict adherence to the diet. Over the entire period of treatment in this group children get:

1. during the first year of life specialized health food MDmil PKU-0;
2. from 1 year to 3 years - MDmil PKU-1;
3. from 3 to 7 years - MDmil PKU-2;
4. older than 7 years - MDmil PKU-3, MDmil Premium PKU, MDmil PKU MAXI.

Thus, children in the study group during treatment up to 18 years receive specialized health food according to their age group.

Second group – diet with medicinal mixtures of various manufacturers taken from 3-4 months before the major age (117 children). Getting specialized health food according to age group. Interruptions of supply, change of product supply.

Third group – diet with medicinal mixtures of various manufacturers taken from 1 year to the major age (247 children). Getting specialized health food according to age group. Interruptions of supply, change of product supply.

As a result of the research horizon of more than one year discounting has been used at the rate of 3% [29]. It should be noted that the research horizon of the first and second groups has corresponded to 18 years of treatment, and in the third group - 17 years, due to the start of the diet in the group from 1 year after birth.

For pharmacological and economic assessment an analytical model of decision-making has been developed in Microsoft Office Excel 2010 by using: effectiveness analysis, cost analysis, cost-effectiveness analysis, cost-utility analysis, budget impact analysis.

Effectiveness Analysis

During the analysis of effectiveness the data has been submitted by 24 major Russian regions of geneticists, the main results are presented in Tables 2, 3 and 4. On the basis of the data three comparison groups are identified, and a detailed analysis of statistical data for each group of patients has been conducted, the final results are presented in Table 5. [1,2,5-7]

During the information retrieval it has been found that the basic criteria of efficiency when comparing the three treatment groups, which differ by the initial age of compliance of dietetics and used therein therapeutic product, is the data of the normal children's intellectual development and the absence of seizures.

Table 2. Regional statistical data on effectiveness of treatment of patients with PKU, who started dieting at the age of 1 month

Region	Quantity, persons	Mental development, persons				Spastic syndrome, persons	
		N	D	Im	Id	+	-
Altai Krai	102	90	10	2	0	4	98
Belgorod Region	7	7	0	0	0	0	7
Bryansk Region	36	35	1	0	0	-	-
Vladimir Region	21	21	0	0	0	0	21
Vologda Region	5	5	0	0	0	0	5
Zabaykalsky Krai	21	21	0	0	0	-	-
Ivanovo Region	18	18	0	0	0	0	18
The Karachay-Cherkess Republic	28	28	0	0	0	-	-
Krasnodar Krai	126	126	0	0	0	0	126
Kurgan Region	17	14	3	0	0	0	17
Lipetsk Region	19	19	0	0	0	0	19
Murmansk Region	22	21	1	0	0	0	22
Omsk Region	34	32	2	0	0	-	-
Penza Region	11	11	0	0	0	0	11
Primorsky Krai	38	37	1	0	0	0	38
The Republic of Bashkortostan	26	26	0	0	0	0	26
The Republic of Mordovia	18	14	4	0	0	1	17
Smolensk Region	8	8	0	0	0	0	8
Stavropol Krai	23	18	5	0	0	0	23
Tambov Region	16	15	1	0	0	0	16
Tula Region	14	11	3	0	0	0	14
Tyumen Region	43	37	3	3	0	12	31
Chelyabinsk Region	41	41	0	0	0	0	41
Yaroslavl Region	30	30	0	0	0	0	30
TOTAL	724	658	34	5	0	17	588

Note: N – norm, D – debility, Im – imbecility, Id – idiocy

Table 3. Regional statistical data on effectiveness of treatment of patients with PKU, who started dieting at the age of 3-4 months

Region	Quantity, persons	Mental development, persons				Spastic syndrome, persons	
		N	D	Im	Id	+	-
Bryansk Region	8	5	3	0	0	2	6
Vladimir Region	17	12	4	1	0	4	13
Zabaykalsky Krai	10	0	8	2	0	-	-
Ivanovo Region	8	8	0	0	0	0	8
The Karachay-Cherkess Republic	15	0	10	5	0	-	-
Kurgan Region	8	0	3	5	0	0	8
Penza Region	10	6	3	1	0	1	9
Primorsky Krai	4	0	2	2	0	1	3
The Republic of Mordovia	10	7	3	0	0	0	10
Stavropol Krai	6	1	3	2	0	1	5
Tula Region	4	0	4	0	0	2	2
Chelyabinsk Region	17	5	9	3	0	2	15
TOTAL	117	44	52	21	0	13	79

Note: N – norm, D – debility, Im – imbecility, Id – idiocy

Table 4. Regional statistical data on effectiveness of treatment of patients with PKU, who started dieting at the age of 1 year

Region	Quantity, persons	Mental development, persons				Spastic syndrome, persons	
		N	D	Im	Id	+	-
Altai Krai	52	8	32	12	0	2	50
Belgorod Region	1	0	0	1	0	1	0
Bryansk Region	6	1	4	1	0	-	-
Vladimir Region	41	10	23	6	2	12	29
Zabaykalsky Krai	1	0	1	0	0	-	-
The Karachay-Cherkess Republic	13	0	5	8	0	-	-
Kurgan Region	2	0	1	1	0	1	1
Lipetsk Region	23	18	3	2	0	1	22
Penza Region	15	7	4	2	2	4	11
Primorsky Krai	18	2	11	2	2	5	13
The Republic of Mordovia	24	2	16	6	0	1	23
Smolensk Region	1	0	0	1	0	0	1
Stavropol Krai	6	0	4	2	0	0	6
Tula Region	2	0	0	2	0	2	0
Chelyabinsk Region	42	4	14	20	4	12	30
TOTAL	247	52	117	65	10	40	185

Note: N – norm, D – debility, Im – imbecility, Id – idiocy

Table 5. Results of the analysis of effectiveness of specialized health food in children with PKU in the three groups being compared for 1 year

	General number of patients	Normal mental development		Absence of seizures	
		%	ratio	%	ratio
First group	724	94,6	0,95	97,2	0,97
Second group	117	37,6	0,38	85,9	0,86
Third group	247	21,1	0,21	81,4	0,81

Table above shows efficiency criteria for each comparable group. An assumption has been made, that efficiency in children with PKU is characteristic for the first and subsequent years of diet therapy and yet, when determining efficiency of the compared methods of diet therapy for 18 years, it is necessary to determine their value in the future to the present moment, which requires discounting of efficacy (Table 6, 7).



Table 6. Results of the analysis of efficiency of specialized health food in children with PKU of three groups for 18 years compared, taking into account discount (efficiency criterion - normal mental development)

Normal mental development	First group		Second group		Third group	
	Year	%	ratio	%	ratio	%
1	95	0,95	38	0,38	-	-
2	91,77	0,92	36,48	0,36	21	0,21
3	89,02	0,89	35,38	0,35	20,42	0,20
4	86,35	0,86	34,32	0,34	19,81	0,20
5	83,76	0,84	33,29	0,33	19,21	0,19
6	81,25	0,81	32,29	0,32	18,64	0,19
7	78,81	0,79	31,33	0,31	18,08	0,18
8	76,45	0,76	30,39	0,30	17,54	0,18
9	74,15	0,74	29,47	0,29	17,01	0,17
10	71,93	0,72	28,59	0,29	16,50	0,17
11	69,77	0,70	27,73	0,28	16,00	0,16
12	67,68	0,68	26,90	0,27	15,52	0,16
13	65,65	0,66	26,09	0,26	15,06	0,15
14	63,68	0,64	25,31	0,25	14,61	0,15
15	61,77	0,62	24,55	0,25	14,17	0,14
16	59,91	0,60	23,81	0,24	13,74	0,14
17	58,12	0,58	23,10	0,23	13,33	0,13
18	56,37	0,56	22,41	0,22	12,93	0,13

Table 7. Results of the analysis of efficiency of specialized health food in children with PKU of three groups for 18 years compared, taking into account discount (efficiency criterion – absence of seizures)

Absence of seizures	First group		Second group		Third group	
	Year	%	ratio	%	ratio	%
1	97	0,97	86	0,86	-	-
2	94,27	0,94	83,29	0,83	81	0,81
3	91,45	0,91	80,79	0,81	79,05	0,79
4	88,70	0,89	78,37	0,78	76,68	0,77
5	86,04	0,86	76,02	0,76	74,38	0,74
6	83,46	0,83	73,74	0,74	72,15	0,72
7	80,96	0,81	71,53	0,72	69,98	0,70
8	78,53	0,79	69,38	0,69	67,89	0,68
9	76,17	0,76	67,30	0,67	65,85	0,66
10	73,89	0,74	65,28	0,65	63,87	0,64
11	71,67	0,72	63,32	0,63	61,96	0,62
12	69,52	0,70	61,42	0,61	60,10	0,60
13	67,43	0,67	59,58	0,60	58,30	0,58
14	65,41	0,65	57,79	0,58	56,55	0,57
15	63,45	0,63	56,06	0,56	54,85	0,55
16	61,55	0,62	54,38	0,54	53,20	0,53
17	59,70	0,60	52,75	0,53	51,61	0,52
18	57,91	0,58	51,16	0,51	50,06	0,50

Thus, the data above shows that efficiency value in both criteria above in the first group as compared with the second and third, what shows the highest efficiency of treatment by specialized health food of MDmil PKU line at early diet therapy.

Utility Analysis

When analysing utility the information research has been carried out, aimed at the definition of the QALY indicator ("quality-adjusted life year" - saved years of quality of life), because the criterion of efficiency is the end point with the greatest conviction. When calculating QALY incidence of mental retardation has been taken into account, as well as the time horizon of the research [30,31]. Results of utility analysis are shown in Table 8.

Table 8. Results of the analysis of utility in children with PKU in two comparable groups for the entire period of treatment till their major age

	First group	Second group	Third group
QALY	15,13	13,10	11,57
QALY (discounted result)	8,26	7,15	6,31

Note: QALY – quality adjusted life years

Table 7 shows that the results of the analysis of utility point the highest rate of saved years of quality of life of children of the first group, in which strict adherence to diet therapy started from the first month to 18 years with health food of MDmil PKU line in accordance with the age of the child.

Cost Analysis

The present research considers both direct medical and nonmedical, and indirect costs (Table 9) [1].

Table 9. Results of the analysis of utility in children with PKU in two comparable groups for the entire period of treatment to their major age

Direct costs	Indirect costs
Diet therapy	Related to disability
Medical Services	Payment for incapacity certificate
Emergency medical services in event of seizures	GDP loss

In the first stage of cost analysis calculation of the cost of diet therapy in each of the groups being compared is carried out, which is dependent on the initial weight of children and their age. It has been assumed that the average weight of the child from 0 to 2 months is about 4.3 kg, then the average body weight of the child for each year up to 18 years has been calculated, and rates of consumption of protein and Phenylalanine per day are identified.

When calculating the cost of diet therapy the cost of medicinal food is established, on the basis of which equivalent of the daily value of protein and diet therapy costs for each year of treatment with discounting have been obtained. By adding the cost of diet therapy for each year of treatment, the total cost of treatment for 18 years of children with PKU has been received.

The total amount of the cost of diet therapy of PKU patients of the first group is about 6,457,058 roubles for 18 years of dieting using a dedicated food of MDmil PKU line for different ages. For one child of the second group - about 9,104,877 roubles for 18 years, and for the third – about 8,974,425 roubles for 17 years dieting using specialized health food of different manufacturers (Table 11).

The next step of the analysis is calculation of the cost of expenses for medical services (MS) for diagnosis and treatment of PKU, which are included in the standard of care for patients with PKU, where is a list of MS, frequency and frequency of their use. Price information is taken from the tariff of the Federal Mandatory Medical Insurance Fund (FMMIF) of Moscow [12,14].

Thus, the cost of MS is about 47,401 roubles per child for the first group and second group, and 46,153 roubles for the third group in treatment of PKU till the major age. It has been agreed that MS, as reflected in the standard of care, each patient has received 1 time per year. Hence, the cost of MS for children of the first and second groups are the same, since treatment has been started in the first year of life. In the third group therapy has been performed in children older than 1 year, which reduces the cost of MS since in the first year of life the child has not received medical care in accordance with the standard delivered later due to lack of diagnosis.

According to the data presented by leading specialists in genetics from different regions of the Russian Federation, ratio of children with the presence

of seizures has been determined. In this research work, each child has been assumed to be in need of emergency medical care once a year in accordance with the standard treatment of acute conditions in children with seizures [13]. These costs include the costs of medical emergencies, MS and pharmaceuticals (PH).

The costs of drugs have been calculated on the basis of prices taken from the state register of limiting selling prices for VED as of November 23, 2015 [21]. For drugs that are not included in the list of VED, the weighted average retail selling prices for Moscow have been used as of November 23, 2015 [22].

When calculating the costs the incidence of seizures in children with PKU in the two groups have been taken into account. As a result, it has been found that the cost of emergency medical care has amounted to about 133,858 roubles, 673,142 roubles, and 824,581 roubles for the first, second and third groups, respectively, during treatment period till 18 years (Table 11).

In this research work all indirect costs are associated with disabled children with PKU due to manifestations of mental retardation, which is the basis for assigning the category of "disabled child" according to the Government Decree dated on 20.02.2006 No. 95 [10,23].

For calculation of direct costs incidence of children with disabilities in each comparison group has been found, which is presented in Table 10.

Table 10. Incidence of mental retardation, heavy and severe degree in the analysed groups

	Imbecility (heavy), %	Idiocy, %	General incidence, %
First group	0,35	0	0,35
Second group	8,9	0	8,9
Third group	13,2	4,1	17,3

The costs associated with disability include: monthly payments, pensions and disability payments to persons caring for disabled children, which together in terms of money is 6,998 roubles for the first group, 181,887 roubles - for the second and 342,315 roubles - for the third group in treatment of PKU patient till the majority age (Table 11) [15,17,18].

Next is calculation of the cost of paying incapacity certificate (IC), the result of which has showed, that for the first group the costs are about 403,035 roubles, for the second - 429,716 roubles and for the third - 451,870 roubles per child for the entire research period (Table 11) [19].

In the next stage of cost analysis calculating of GDP losses has been taken, that are associated with disability of patients, i.e., to the inability of a parent to work, and pay SL. Total losses of GDP have amounted to 716,056 roubles for the first group of children, 1,324,416 roubles - for the second and 1,848,224 roubles - for the third group (Table 11).

Thus, by adding up all costs previously obtained the total cost has been calculated of treating of one patient with PKU until his majority in each comparison group (Table 11).

Table 11. The total cost of treatment of one child up to the age of majority

Costs	from 1 month MDmil PKU	from 3-4 months	from 1 year and later
	First group	Second group	Third group
Diet therapy	6 457 058	9 104 877	8 974 425
Medical services	47 401	47 401	46 153
Medical care in event of seizures	133 858	673 142	824 581
Payments of disability pensions	3 868	100 530	189 199
Monthly cash payments	686	17 833	33 562
Payments for those caring for children with disabilities	2 444	63 524	119 554
Payment for incapacity certificate	403 035	429 716	451 870
GDP loss	716 056	1 324 416	1 848 224
TOTAL	7 764 406	11 761 439	12 487 568

Table above shows that the cost per case of treatment of PKU in the first group with health food of MDmil PKU line is about 7,764,406 roubles, in the second and third groups with the use of health food from different manufacturers - 11,761,439 roubles, and 12,487,567 roubles respectively. The obtained results are shown graphically in Figure 1.

Note: DP – disability pension, MP – monthly payments, PP – payments to persons caring for disabled children, IC – payment for incapacity certificate, GDP – gross domestic product, MS – medical services, MC – medical care in event of seizures.

Cost-effectiveness analysis

Cost-effectiveness analysis determines the preferential treatment among the compared in terms of pharmacological economics, given the values of the Cost-effectiveness ratio (CER), which reflect the cost of one efficiency unit to compared methods of diet therapy [24,25].

Using the previously obtained data Cost-effectiveness ratio has been calculated by efficiency criteria in each study group. Calculation is made taking into account the discounting both costs and efficiency. The results are shown in Tables 12-13 and Figures 2,3.

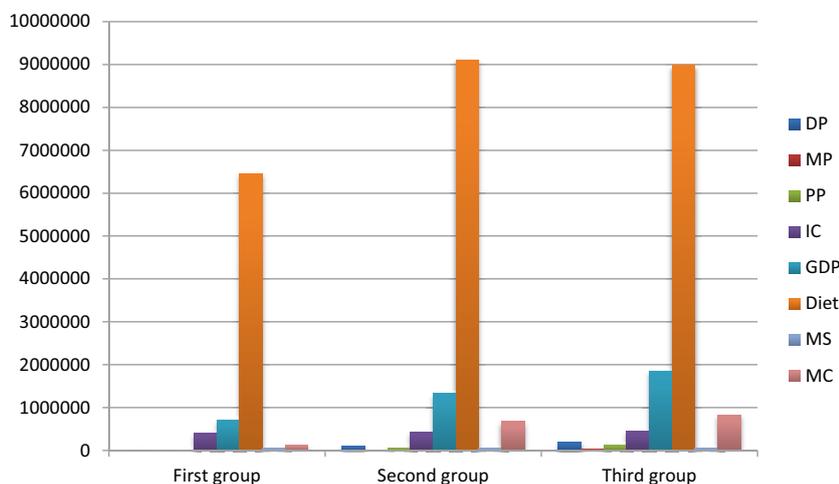


Figure 1. Total costs for treatment of PKU child before his 18th birthday



Efficiency criterion: normal mental development

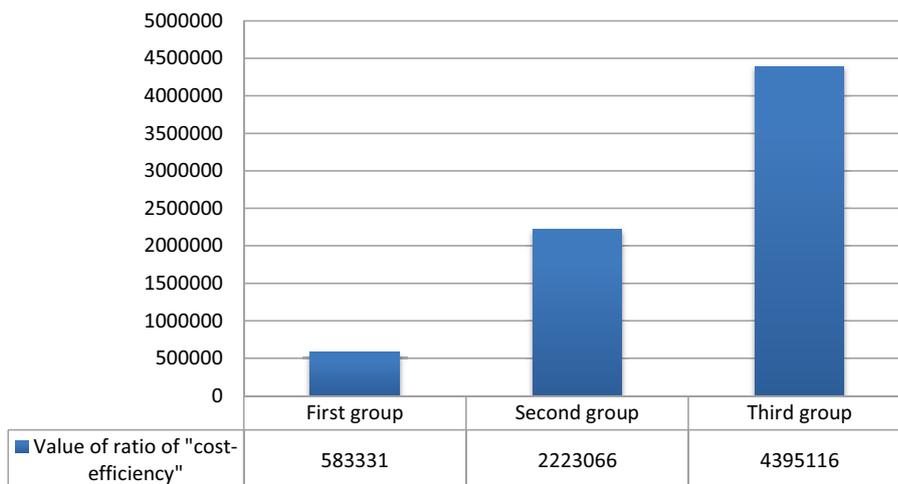


Figure 2. Values of ratio of “cost-effectiveness” for treatment compared using as an efficiency criterion of normal mental development of the child

Efficiency criterion: absence of seizures

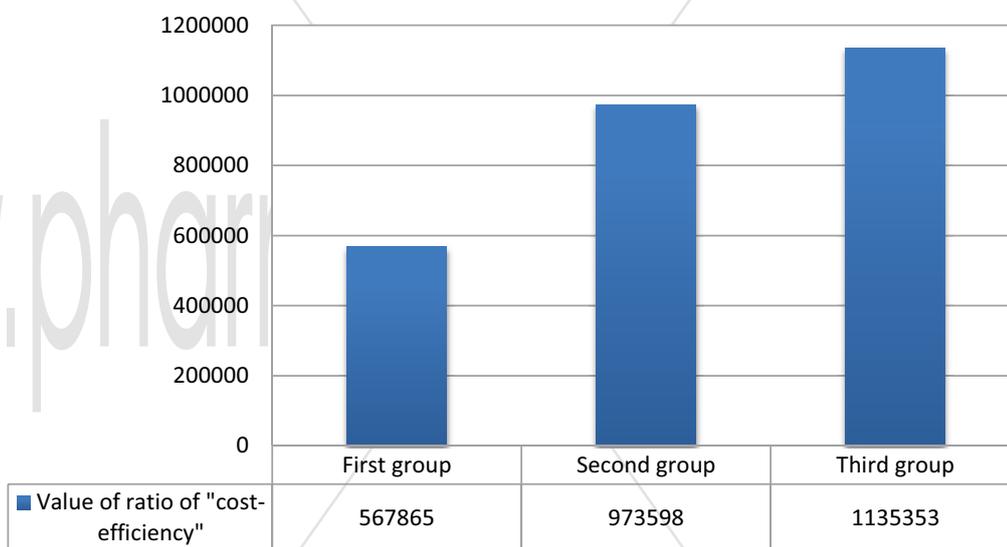


Figure 3. Values of ratio of “cost-effectiveness” for treatment compared, using as an efficacy criterion of absence seizures in children

Table 12. Results of the cost-effectiveness analysis based on efficiency criterion - normal mental development

Efficiency criterion: normal mental development	First group	Second group	Third group
Costs, rub.	7 764 406	11 761 439	12 487 568
Efficiency for 1 year	0,95	0,38	0,21
Efficiency for 18 years	13,31	5,29	2,84
CER ₁	583 331	2 223 066	4 395 116

Note: CER₁ – cost-effectiveness ratio

The cost-effectiveness analysis of treatment compared with the use of efficiency criterion of normal mental development of the child has showed the following values of CER for the first group - 583,331 roubles, for the second - 2,223,066 roubles, for the third - 4,395,116 roubles.

Thus, value of CER is lower in the first group than the second and third, which suggests, that treatment with health food of MDmil PKU line of the first group, where it has been applied from the first month of life, is the dominant method of treatment in terms of pharmacological economics as with respect to the second and the third group.

Table 13. Results of the cost-effectiveness analysis based on efficiency criterion – absence of seizures

Efficiency criterion: Absence of seizures	First group	Second group	Third group
Costs, rub.	7 764 406	11 761 439	12 487 568
Efficiency for 1 year	0,97	0,86	0,81
Efficiency for 18 years	13,67	12,08	10,98
CER ₂	567 865	973 598	1 135 353

Note: CER₂ – cost-effectiveness ratio

Utility Criterion: QALY

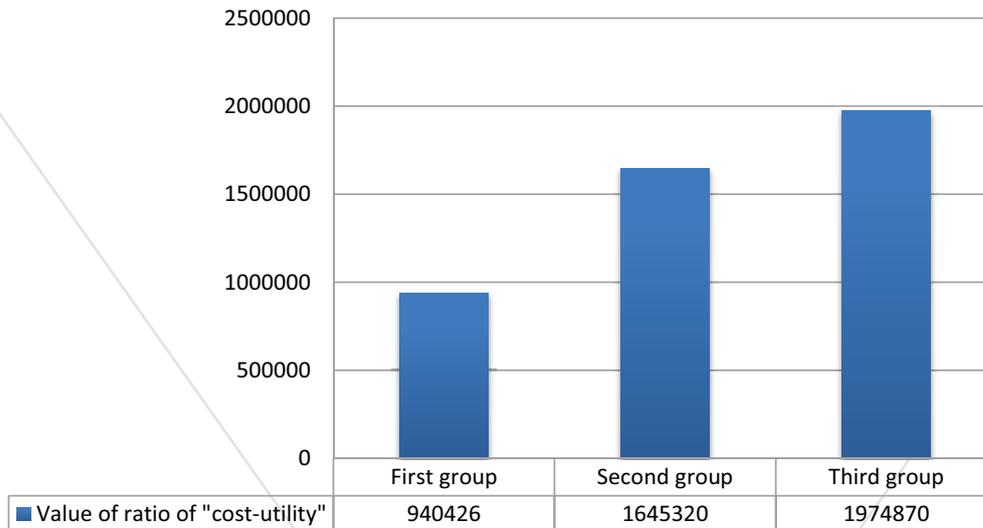


Figure 4. Values of ratio of “cost-utility” of groups of patients compared, using as a utility criterion the data on saved years of quality of life per patient

The cost-effectiveness analysis of treatment compared with the use of efficiency criterion of absence seizures in the child, has showed the following values of CER for the first group - 567,865 roubles, the second - 973,598 roubles, for the third - 1,135,353 roubles.

Thus, value of CER is lower in the first group than the second and third, which suggests, that treatment with health food of MDmil PKU line of the first group, where it has been applied from the birth, is the dominant method of treatment in terms of pharmacological economics as with respect to the second and the third group.

“Cost-Utility” Analysis

During the pharmacological and economic research cost-utility analysis has been carried out on the basis of treatment of one child suffering from PKU. The results of the cost-utility analysis are expressed in the form of relevant factors, the evaluation of which allows to choose preferential treatment in terms of the clinical and economic analysis [27].

The analysis has found the values of cost-utility ratio for each of the analysed group in treatment of PKU children, where the criterion is the value of utility of quality life years saved. The results are shown in Table 14 and Figure 4 [20].

Table 14. Results of the cost-utility analysis, conducted for the compared groups of patients, using as a criterion of usefulness of the data on saved years of quality of life

	First group	Second group	Third group
Costs, rub.	7 764 406	11 761 439	12 487 568
QALY (discounted result)	8,26	7,15	6,31
CUR	940 426	1 645 320	1 974 870

Note: QALY – quality adjusted life year, CUR – ratio of “cost-utility”

The analysis of “cost-utility” of treatment compared with the use of utility criterion the data on saved years of quality of life in the child, has showed the following values of CUR for the first group – 940 426 rub., for the second – 1 645 320 rub., for the third – 1 974 870 rub.

Thus, value of CUR is lower in the first group than the second and third, which suggests, that treatment with health food of MDmil PKU line of the first group, where it has been applied from the birth, is the dominant method of treatment in terms of clinical and economic analysis, both in relation to the second and the third group.

Budget impact analysis

This analysis allows to predict the impact on the health budget and to determine the economic impact, which is expressed either by saving money or requires additional costs during the transition from treatment of comparison to the evaluated therapy [26].

The results of the budget impact analysis for the child with PKU during treatment with the diagnosis of the disease before the age of majority are shown in Table 15.16 (Figure 5.6).

Table 15. Results of budget impact analysis when comparing the first and second groups

Costs	General costs, rub.	Costs difference, rub.	Costs decrease
First group	7 764 406	3 997 033	34%
Second group	11 761 439		

According to the budget impact analysis it can be concluded, that treatment of children with PKU from the first month of life to their majority age by specialized health food of MDmil PKU line, compared with the beginning of a diet from 3-4 months with health food of different manufacturers, savings of budgetary funds appear in the amount of 3,997,033 roubles per child, which may reduce costs by 34%.

Table 16. Results of the budget impact analysis when comparing the first and third groups

Costs	General costs, rub.	Costs difference, rub.	Costs decrease
First group	7 764 406	4 723 162	38%
Second group	12 487 568		

According to the budget impact analysis it can be concluded, that treatment of children with PKU from the first month of life to their majority age by specialized health food of MDmil PKU line, compared with the beginning of a diet from 1 year with health food of different manufacturers, savings of budgetary funds appear in the amount of 4,723,162 rub. per one child, which may reduce costs by 38%.

Results

1. During the information retrieval two main criteria of efficiency have been identified: normal mental development, absence of seizures. Efficiency, presented by the data on normal mental development of the child, for the first group of children, who have used health food of MDmil PKU line, has corresponded to 95%, for the second group - 38% and third - 21% per year of treatment of PKU. Efficiency, presented by the data on absence of seizures, has been 97%, 86% and 81% for the first (health food of MDmil PKU line), second and third (health food from different manufacturers) group of children, respectively, for the year of treatment of PKU.

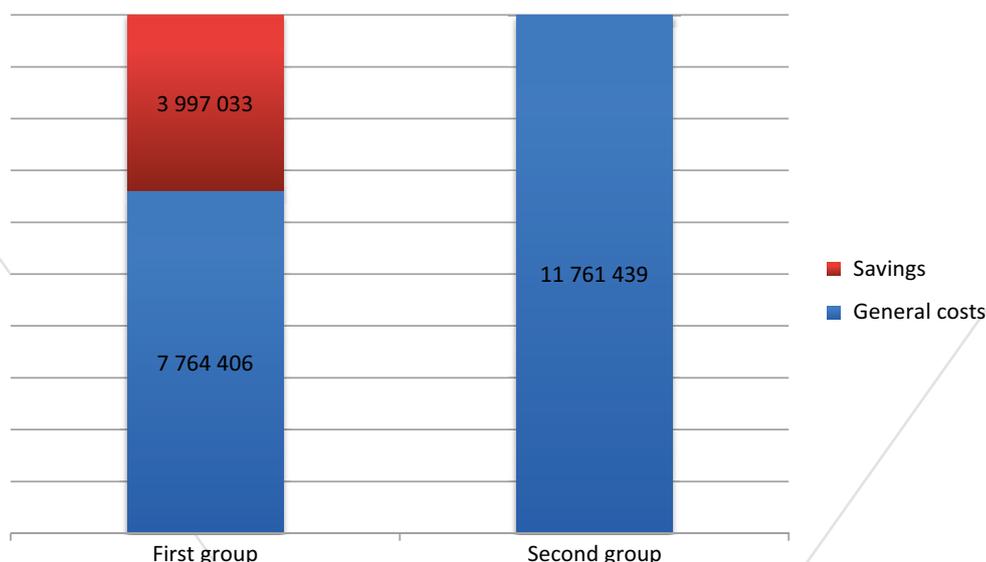


Figure 5. Results of budget impact analysis when comparing treatment of PKU children in the first and second groups

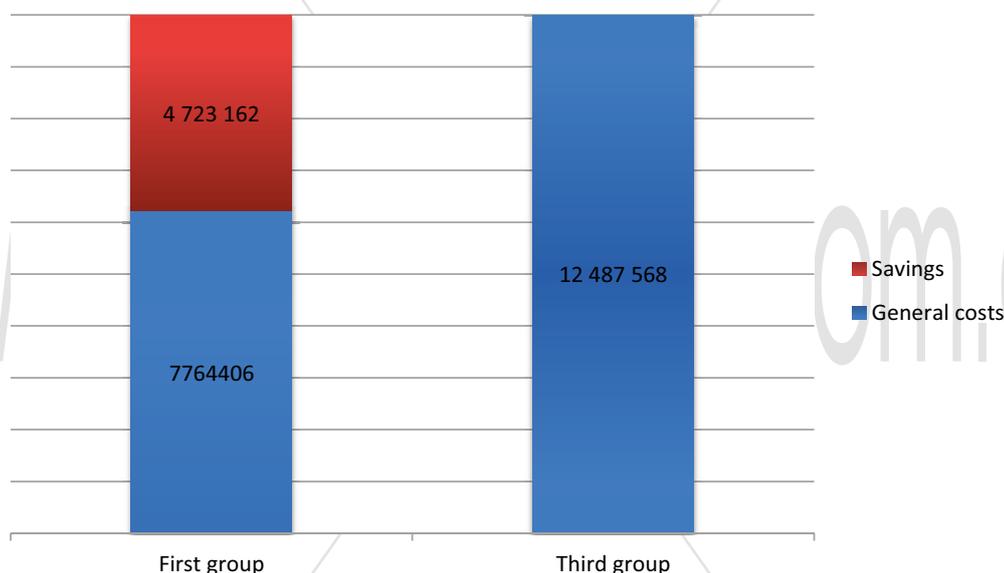


Figure 6. Results of budget impact analysis when comparing treatment of PKU children in the first and third groups

- Utility analysis has showed, that value of QALY is 8.26 for the first group of children, which has been applying health food of MDmil PKU line according to age, 7.15 - for the second, 6.31 for the third group for the entire period of treatment of PKU to adulthood children, taking into account a discount rate of 3%.
- Cost analysis has showed, that the total cost of treating a child with PKU is about 7,764,406 roubles if the therapy has begun from the first month of life to 18 years with using health food of MDmil PKU line in accordance with the patient's age, 11,761,439 roubles - in treatment of children from 3-4 months to 18 years with medicinal food of various manufacturers and 12,487,568 rub. - in treatment of children from 1 year to 18 years with medicinal food of various manufacturers.
- The cost-effectiveness analysis has determined, that value of CER for efficiency according to normal mental development of children for the first group of patients, who have been using health food of MDmil PKU line for 18 years in accordance with the needs of age, is 583,331 roubles, the second group, that has been applied a variety of health food of other manufacturers for 18 years - 2,223,066 roubles, and the third group, that has been using health food of manufacturers for 17 years - 4,395,116 roubles, and on efficiency according to absence of seizures 567,865 roubles, 973,598 roubles and 1,135,353 roubles, respectively.
- The cost-utility analysis has derived value of CUR of 940,426 roubles for the first group of patients, 1,645,320 - for the second group and 1974,870 roubles - for the third in treatment of children with PKU from the time of diagnosis of the disease before the major age.
- The budget impact analysis has demonstrated, that nutritional therapy with health food of MDmil PKU line from the first month of life and till 18 years would save about 3,997,033 roubles, compared with diet, started from 3-4 months of life with health food various manufacturers. When comparing the diet started from the first month of life with health food of MDmil PKU line and after 1 year of health food of different manufacturers, it has been found, that at the earliest diet therapy medicinal mixtures of MDmil PKU line saves 4,723,162 roubles.

Conclusions

Based on the data obtained in the course of pharmacological and economic research, comparing the two groups of children with PKU, who have complied with diet therapy from the first month of life with specialized health food of MDmil PKU line, from 3-4 months and 1 year of medicinal mixtures of different manufacturers till 18 years, we have made the following conclusions:

- Efficiency analysis has found, that based on efficiency criterion of the presented data on normal mental development of the child, the highest

- efficiency is achieved when diet therapy with specialized health food of MDmil PKU line is taken from the first month of life and till 18 years (the product of this line varies depending on age) and in the diet, started in later periods with the use of clinical nutrition from different manufacturers, efficiency drops sharply. On efficiency criterion of the presented data on absence of seizures in the child, the same pattern is saved.
- Value of QALY, reflecting the quality of life years saved, shows the greatest value at the beginning of diet therapy from the first month of life with specialized health food of MDmil PKU line and then applying in the appropriate age till 18 years.
 - According to cost analysis of treatment of patients with PKU to their majority least expensive is diet therapy, initiated from the first month of life with health food of MDmil PKU line (use of food with the appropriate equivalent of protein, depending on the child's age) compared with the diet, started in more later periods, using specialized food from different manufacturers.
 - The cost-effectiveness analysis has defined value of CER, reflecting the cost of achieving one efficiency unit, the lowest value of which, according to the data on normal mental development, and on absence of seizures, diet therapy has, initiated from the first month of life with specialized health food of MDmil PKU line, that in terms of pharmacological economics defines it as dominant.
 - The cost-utility analysis has showed, that the cost of one saved year of quality of life is lower when used from the first month of life with health food of MDmil PKU line compared with a diet, started in later periods with nutrition from different manufacturers, which allows to determine treatment of the first group of children as dominant in terms of pharmacological economics.
 - The budget impact analysis shows that diet therapy with specialized health food of MDmil PKU line in treatment of Phenylketonuria, starting from the first month of life using specialized health food of MDmil PKU-0 for children with Phenylketonuria from the first year of life to their major age: on the basis of the continuing use of specialized health food of MDmil PKU line: MDmil PKU-1 for pre-school children aged from 1 to 3 years; MDmil PKU-2 for preschool children from 3 to 7 years; and MDmil PKU-3, MDmil PKU Premium, MDmil PKU MAXI for children of primary school age from 7 to 11 years, secondary school pupils from 11 to 14 years of age, adolescents between 14 and 18 years and older - may save budgetary funds resulting decrease of costs by 34%, compared with a group of patients, initiating treatment from 3-4 months and by 38% at the beginning of the diet, where medicinal mixtures of different manufacturers have been applied.

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