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- ФАРМАКОЭКОНОМИКА ТУБЕРКУЛЕЗА: МЕТОДОЛОГИЧЕСКИЕ ОСОБЕННОСТИ ПРОВЕДЕНИЯ ИССЛЕДОВАНИЙ
- ФИНАНСИРОВАНИЕ СИСТЕМЫ ЗДРАВООХРАНЕНИЯ НА РЕГИОНАЛЬНОМ УРОВНЕ. ВЗАИМОСВЯЗЬ КАЧЕСТВЕННЫХ И КОЛИЧЕСТВЕННЫХ ПОКАЗАТЕЛЕЙ С ВЕЛИЧИНОЙ ФИНАНСИРОВАНИЯ ЗДРАВООХРАНЕНИЯ

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# THE ECONOMIC BURDEN OF CHRONIC KIDNEY DISEASE IN THE RUSSIAN FEDERATION

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## Summary:

For the first time in Russia, economic burden of chronic kidney disease on a national scale was determined. The economic burden of chronic kidney disease was calculated based on the methodology of a special kind of pharmacoeconomic analysis, the «cost of illness» analysis. The analysis included both direct and indirect costs associated with the disease in question. In the course of the study, the cost of individual stages of chronic kidney disease per patient per year was determined. The most expensive stages were those, at which the patients received renal replacement therapy. At the same time, the cost of illness analysis based on the entire population carried out at the next stage revealed that most of the cost falls on the early stages of chronic kidney disease as a result of a significant number of patients at these stages. The cumulative economic burden of chronic kidney disease in Russia exceeded 451 billion rubles.

**Keywords:** chronic kidney disease, economic burden, the «cost of illness» analysis, pharmacoeconomics, direct costs, indirect costs, renal replacement therapy, chronic kidney disease stages.

This publication provides the results of the study aimed at assessment of the economic burden of chronic kidney disease (CKD) in the Russian Federation. Before proceeding to the detailed description of the study subject, the authors would like to note that no previous integrated economic evaluation of CKD in Russia has been conducted, or its results have been not published, as the literature search in specialized databases (Federal electronic health library and others) and universal search engines (Yandex, Google etc.) carried out by us in the preparatory phase of the study has not revealed any reports of this kind. However, the demand for data on the economic burden of CKD in Russia from all parties interested in the problem of the CKD treatment; both the professional community and officials responsible for the formulation of health policy in the field of CKD, and patient organizations, and commercial companies - is very high. Thus, the absence of a clear quantitative description of the economic problem of CKD in the country available to decision-makers and, as a consequence, the impossibility of a well-grounded feasibility study make adoption of federal or regional health programs for treatment of CKD unlikely<sup>1</sup>. Thus, the above provisions necessitate a study for estimating the economic burden of CKD in the Russian Federation.

## Materials and methods.

Estimation of economic burden of CKD in Russia was conducted based on the

methodology of pharmacoeconomic analysis with a time horizon of one year. The choice of this approach to achieve the aim has been predetermined by the presence of a well-developed methodological apparatus adapted to the conditions of our country that has been previously successfully tested in a number of other studies, for example, in assessing the economic burden of alcohol and smoking in Russia [1, 2]. In particular, we have used a special kind of pharmacoeconomic analysis; the «cost of illness» analysis of, which aims to solve the problem of determining the economic burden of the illness. The «cost of illness» analysis considers the economic burden of the disease as the sum of direct and indirect costs associated with the disease, calculated taking into account the local epidemiological, demographic and clinical data, as well as local peculiarities of treatment of the disease under study [3].

The process of analyzing the «cost of illness» was divided into three steps:

- Preparatory step, which included collection and analysis of epidemiological, demographic and clinical data and information on approaches to the treatment of CKD in Russia. Also during this step, a number of interviews with experts\* were carried out. The objective of the preparatory step was to describe the structure of the CKD treatment costs in Russia and to determine the list of information sources that will be used during the later steps of analysis;
- determination of the economic burden of CKD calculated per 1 averaged patient for each of the stages of CKD. During this step, the sum of all direct costs specific to a particular stage of CKD and indirect costs (taking into account the demographic structure of the population) was calculated. Direct costs included the cost of the treatment of CKD per se, treatment of complications (taking into account their incidence) caused by CKD, correction of CKD therapy complications (taking into account their incidence). Indirect costs included one-time disablement payouts, disability pensions (taking into account the disability group) and GDP losses due to disability or premature death;
- calculation of the economic burden of CKD on the entire patient population, which is carried out by adding products of the costs per 1 patient in each stage of CKD by the number of patients in this stage of CKD in the general population.

Table 1 provides formulas, used in the calculations during the analysis.

<sup>1</sup>There are no current government programs in this field in Russia



Table 1. The formulas for analysis of the «cost of illness»

Description	Formula	№
Calculation of the pharmacotherapy cost	$\text{Cost}_{\text{Pth}} = \text{price}_{\text{Pth}} * \text{Dc} * \text{F}_{\text{Pth}}, \text{ where:}$ $\text{Cost}_{\text{Pth}} - \text{the cost of pharmacotherapy, rubles;}$ $\text{Price}_{\text{Pth}} - \text{price for one unit of the active substance of the drug, rubles;}$ $\text{Dc} - \text{course dose of the drug, in terms of the active substance;}$ $\text{F}_{\text{Pth}} - \text{frequency of the drug administration.}$	(1)
Calculation of the cost of medical procedures	$\text{Cost}_{\text{Ser}} = \text{price}_{\text{Ser}} * \text{N}_{\text{Ser}} * \text{F}_{\text{Ser}}, \text{ where:}$ $\text{Cost}_{\text{Ser}} - \text{expences for the medical procedure, rubles;}$ $\text{Price}_{\text{Ser}} - \text{price of 1 medical procedure, rubles;}$ $\text{N}_{\text{Ser}} - \text{number of procedures administered;}$ $\text{F}_{\text{Ser}} - \text{frequency of the procedures.}$	(2)
Calculation of the cost of the standard care	$\text{Cost}_{\text{sd}} = \sum (\text{Cost}_{\text{Pth}} + \text{Cost}_{\text{Ser}}), \text{ where:}$ $\text{Cost}_{\text{sd}} - \text{cost according to standard, rubles}$	(3)
Calculation of the cost of treatment of complications based on the standard	$\text{Cost}_{\text{comp}} = \text{Cost}_{\text{sd}} * \text{F}_{\text{Comp}}, \text{ where:}$ $\text{Cost}_{\text{comp}} - \text{the cost of treating complications, rubles;}$ $\text{F}_{\text{Comp}} - \text{incidence of the complication.}$	(4)
Calculation of the hemodialysis cost	$\text{Cost}_{\text{HD}} = \text{T}_{\text{HD}} * \text{N}_{\text{HD}}, \text{ where:}$ $\text{Cost}_{\text{HD}} - \text{expences for hemodialysis, rubles}$ $\text{T}_{\text{HD}} - \text{price of 1 hemodialysis procedure according to standard rates, rubles}$ $\text{N}_{\text{HD}} - \text{number of hemodialysis procedures per year}$	(5)
Calculation of the peritoneal dialysis cost	$\text{Cost}_{\text{PD}} = \text{T}_{\text{PD}} * \text{N}_{\text{PD}} * 365, \text{ where:}$ $\text{Cost}_{\text{PD}} - \text{expences for peritoneal dialysis, rubles}$ $\text{T}_{\text{PD}} - \text{price of 1 exchange of peritoneal dialysis according to standard rates, rubles}$ $\text{N}_{\text{PD}} - \text{the number of exchanges per day}$ $365 - \text{the number of days per year}$	(6)
Calculation of the cost of treatment per patient in a stage of CKD	$\text{Cost}_{\text{CKD}} = \text{Cost}_{\text{sd}} + \sum \text{Cost}_{\text{comp}} + \text{Cost}_{\text{ind}}, \text{ where:}$ $\text{Cost}_{\text{CKD}} - \text{the cost per 1 patient in this stage of CKD, rubles}$ $\text{Cost}_{\text{ind}} - \text{indirect costs per 1 patient, rubles}$	(7)
Calculation of the total economic burden of CKD	$\text{Cost}_{\text{Total}} = \sum (\text{Cost}_{\text{CKD}} * \text{N}_p), \text{ where:}$ $\text{Cost}_{\text{Total}} - \text{the total economic burden of CKD on the population, rubles}$ $\text{N}_p - \text{number of patients in each stage of CKD in the total population}$	(8)

As reference sources for prices for medical services and drug treatment in our analysis, we used MFOMS (Moscow City Compulsory Medical Insurance Fund) rates and registered prices for the VED drugs [5,6].

**Results of the CKD «cost of illness» analysis study in Russia**

During the preliminary analysis of the data, it was found that currently there are standards of care in force for patients with stage IV and stage V CKD, while no national standards describing the treatment of patients with early-stage CKD (I-III) in Russia. Consequently, it was decided to calculate the treatment cost for patients with CKD at advanced stages (IV-V) based on the respective standards (with a separate calculation of the cost of each of the three types of renal replacement therapy (RRT): hemodialysis (HD), peritoneal dialysis (PD), kidney transplantation (KT)). At the same time, defining methods for calculation of treatment cost for patients in the early stages required further study. Reference to national guidelines for treatment of CKD showed that the main trend of care for patients with early-stage CKD is regular monitoring of renal function (including determination of urine protein, blood creatinine) and regular consultation with a nephrologist. However, the results of interviews with experts revealed that in actual practice, the management of patients with early-stage CKD is inconsistent with national guidelines, and, moreover, patients in this group, in fact, receive no medical care for CKD. Taking into account the opinion of experts, it was assumed in the further analysis that patients with stage I-III CKD receive no target therapy for CKD. Also it should be noted that in the course of studying the literature data for the most accurate and flexible calculations of economic burden of CKD,

patients with the disease in this study were divided into the following groups:

- CKD I - patients with the first stage of CKD;
- CKD II – patients with the second stage of CKD;
- CKD III – patients with the third stage of CKD;
- CKD IV – patients with the fourth stage of CKD;
- CKD VH RRT – patients with the stage five CKD, not receiving RRT;
- CKD VHD start – patients with stage five CKD who started receiving HD this year;
- CKD VHD cont – patients with stage five CKD, who continue HD;
- CKD VPD start – patients with stage five CKD, who started PD in the current year;
- CKD VPD cont – patients with stage five CKD, who continue PD;
- CKD VKT first →→ patients with stage five CKD, who received a kidney transplant in the current year;
- CKD VKT subseq – patients with stage five CKD, with kidney transplantation performed earlier.

The rationale for such a detailed division of patients' models in the study was the fact that the cost structure for patients at the start and at the continuation of the RRT was different. So, at the start of HD and PD, patients required additional hospitalization to prepare for the beginning of the RRT; direct costs for patients

by KT were determined during the first year by the cost of the surgery itself, while in the following year – by the cost of immunosuppressive drug therapy. After studying literature data (national guidelines on CKD, clinical studies reports), as well as interviews with experts, a list of complications to be included in the analysis was identified, comprising those caused by CKD itself and by its therapy in patients (Table. 2). As can be seen from the data presented in Table 2, the CKD complications were presented by a group of cardiovascular events (CVE: myocardial infarction (MI), stroke, angina pectoris, arterial hypertension (AH)), anemia and secondary hyperparathyroidism (SHPT). Complications of CKD therapy (RRT) resulted into costs for treatment of peritonitis caused by the PD and costs of treatment of sepsis caused by HD.

**Table 2.** Complications of CKD and CKD therapy included in the «cost of illness» analysis

CKD complications			CKD therapy complications	
CVE:	Anemia	SHPT	Sepsis (during HD)	Peritonitis (during PD)
AH				
MI				
Angina pectoris				
Stroke				

Information on the incidence of anemia and SHPT in various stages of CKD was taken from the reports of the Russian Dialysis Society (RDS) [7] (Table. 3), while no data on the incidence of CVE in different stages of CKD in the domestic sources were found, therefore this information was taken from the publication of Lori A. et al. 2011. [8] (Table. 3). The incidences of complications caused by different types of RRT were taken from a foreign study by Ai-Hua Zhang et al. 2007. [9] (Table. 3). However, as follows from the data provided in Table 3, due to the lack of available information, it has been assumed in this study that incidences of certain complications are constant over time and do not differ between patients starting RRT in the current year, and patients who are on RRT for a long time.

**Table 3.** Incidences of CKD complications and of CKD treatment complications

CKD stage	I	II	III	IV	VH RRT	VHD	VPD	VKT
Complication:								
Anemia	0	0	0	0	0,875*	0,915	0,875	0
SHPT	0	0	0	0	0	0,89	0,95	0
AH	0,241	0,353	0,465	0,516	0,94	0,94	0,94	0,94
MI	0,0324	0,0372	0,06	0,06	0,12	0,12	0,12	0,12
Angina pectoris	0	0	0	0	0,107	0,107	0,107	
Stroke	0,00036	0,00036	0,00036	0,00036	0,00072	0,00072	0,00072	0,00072
Sepsis	-	-	-	-	-	0,102	-	-
Peritonitis	-	-	-	-	-	-	0,141	-

\*It has been assumed that the frequency of anemia in patients with stage V CKD not receiving RRT is equal to that in patients on PD.

patients to HD or PD (table 5). It was assumed that during the year, patients on PD must attend clinics for routine examination, which included experts' consultation and laboratory tests; while routine examination of patients on HD was conducted during their visit to the dialysis centers for the HD procedure. In this regard, the routine examination of patients on PD was calculated as a separate item of costs while the cost of the routine examination for HD patients was considered to be included in the cost of HD itself. The structure of the cost of the scheduled examination for PD patients was based on medical and economic standards. The cost of the HD and PD procedures was calculated in accordance with formulas 5-6 based on the MFOMS rates and data on RRT regimens, according to which the patients on HD underwent the procedure 3 times a week, while the patients on PD underwent 4.5 exchanges daily on average (Table. 5). Price for KT in FGBU «V.I. Shumakov Federal Research Center of Transplantation and Artificial Organs» of Russian Ministry of Health served as data source on the cost of this operation. The cost of immunosuppressive drug therapy was calculated by the formula 1, wherein it has been assumed that tacrolimus was used as the immunosuppressive drug (Table. 5).

Data on the treatment cost, included in the analysis of CKD complications (CVE, anemia and SHPT), were obtained from previously conducted pharmacoeconomic studies in the field of nephrology [10, 11]. In these studies, the cost of CVE treatment was calculated based on the respective standards of care; the cost of anemia treatment was determined by the sum of the costs of erythropoietin and iron drugs, the cost of SHPT - as the sum of the cost of its drug therapy and of drug therapy caused by its complications. The cost of sepsis and peritonitis treatment was also calculated based on the standards of care according to the formulas 1-3. The data on the cost of therapy of CKD and its complications used in this study are presented in Table 4.

**Table 4.** The cost of treatment of CKD and its complications

Cost item	Cost, rubles per case (patient per year)
MI	340483
Stroke	108936
Angina pectoris	44344 (per patient based on the incidence)
Sepsis	187000 (per patient based on the incidence)
Peritonitis	93000 (per patient based on the incidence)
SHPT	427337 (5% with calcium mimetics); 45536 (95% without calcium mimetics)
Anemia	160000
AH	28748

Based on the standards of care and formula 1-3, we calculated the cost of therapy for patients with stage IV-V CKD, as well as preparation of these groups of

**Table 5.** Costs of various types of RRT in patients with CKD

Cost item	Cost, rubles per case (patient per year)
HD	707533
PD	1264889
Routine examination during PD	10488
Preparing for HD	94513
Preparing for PD	86636
The cost of KT	3148000
The cost of immunosuppressive therapy	291270



**The calculation of indirect costs was performed only for patients with stage V CKD.**

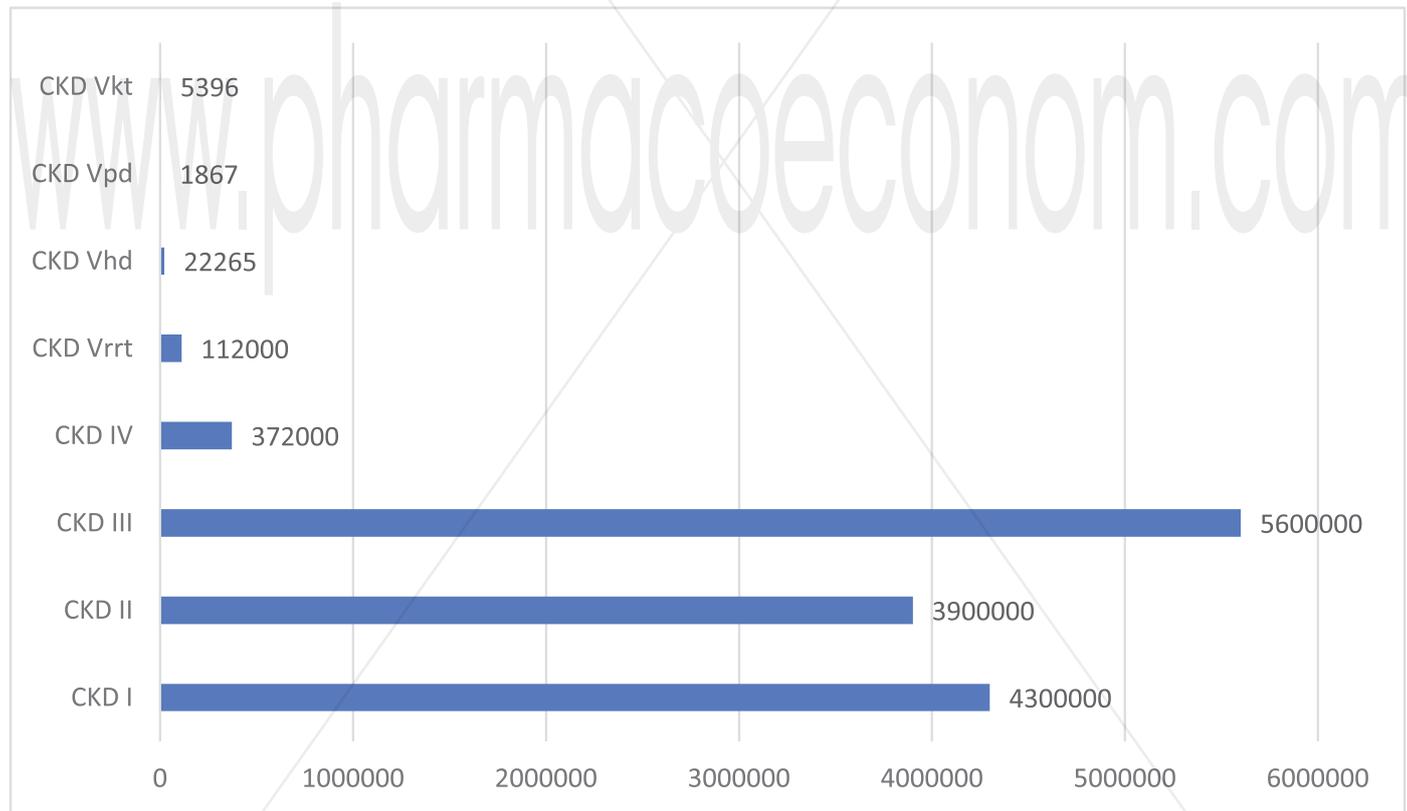
At the first stage of indirect costs estimation, costs associated with payments of disability pension and monthly payments (MP) were estimated. The amount of disability pension and MP depends on the disability group [12]. Due to lack of information, we have made the assumption that one half of the patients with stage V CKD were assigned the first group of disability, while the other - the second group of disability. It is also necessary to note that in our study, the MP was taken into account only for patients receiving RRT for the first time or for stage V CKD patients without dialysis, whereas the disability pension was included for all patients on RRT.

In the next step, based on data on the incidence of CKD among the economically active population and the average GDP per capita, GDP losses due to premature mortality and disability among patients with CKD were assessed. Since the average age of patients with CKD on dialysis was 47 years according to RDS, every second patient was considered of economically active age. The source of the value of GDP per capita, which amounted to 437,104 rubles, was data of Rosstat [13] for 2013. Given the above data, we calculated the average loss of GDP for each adult patient, equal to 218,552 rubles per year. It was assumed that patients with stage V CKD after kidney transplantation became able to work again (keeping their disability at the same time), so that the costs associated with the loss of GDP for this group of patients were not calculated.

Search and analysis of epidemiological data revealed that, in fact, in the Russian Federation, only epidemiological information on the later stages of CKD (associated with the RRT administration) taken from the RDS register is available. At the same time, there is no information about the early stages of CKD, including the most general one, for example, the number of patients with stage I-IV CKD in Russia. Therefore, for calculation of the disease burden for the entire CKD population,

data on the number of patients in the singled out groups (CKD VHD start, CKD VHD cont, CKD VPD start, CKD VPD cont, CKD VKTfirst, CKD VKT subseq) were taken from the RDS register. To determine the number of patients in the remaining groups we assumed that the total number of patients with CKD in Russia was 10% of the total population, and the structure of the distribution of patients with CKD between stages I-IV corresponds to that abroad. Based on this, in the analysis of the «cost of illness» at the population level, we have extrapolated data on the distribution of patients by CKD stages reported by Lori A. et al. 2011. According to Lori A. et al. 2011, 30.3% of all patients with CKD are in stage I, 27,2% - in stage II, 39% - in stage III, 2,6% in stage IV, and 1% in stage V. Separately, it should be noted that the number of patients in the CKD VH RRT group was determined as the difference between the total number of patients with stage V CKD (calculated by extrapolating foreign epidemiological data on the Russian patient population) and the number of patients receiving various types of RRT, according to the RDS data. Distribution of the Russian CKD patients population between the separate groups is shown in Figure 1. Differentiation of patients within groups of various RRT kinds between those receiving RRT in the first year and those receiving RRT in the next years was performed as follows: the number of patients who underwent surgery for KT in the current year was taken from the RDS data and amounted to 830 patients. Calculation of the number of patients receiving HD or PD for the first time was based on a number of assumptions. Thus, it was assumed that capacities of HD and PD facilities in Russia are usually limited, therefore the entry into the systematic dialysis program for new patients could occur only upon withdrawal of the other patients, ie, in the event of their death. Based on this, the number of patients receiving first HD or PD was determined as the product of the number of patients on HD or PD by the respective mortality values, amounting to 0,071 for HD, and 0,085 for PD according to RDS.

Figure 1. Distribution of CKD patients among different stages



**Results of calculation of the economic burden of the individual CKD stages**

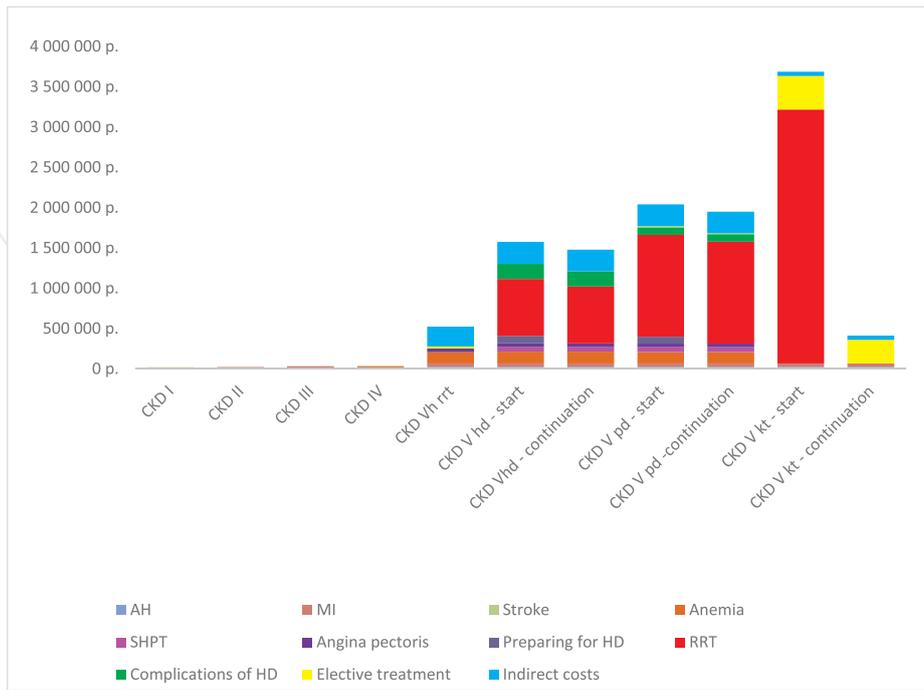
In accordance with the above method of «cost of illness» analysis and the formulas 4 and 7, the cost of various stages of CKD (including direct and indirect costs) per patient was calculated, as presented in Figure 2. As can be seen from the results of the analysis performed, the advanced CKD stages were the most expensive, due to costly RRT administered to the patients. Thus the total cost per patient in the CKD VH RRT, CKD VHD start, CKD VHD cont, CKD VPD start, CKD VPD cont, CKD VKT first, CKD VKT subseq groups were 525268 rubles, 1576180 rubles, 1479365 rubles, 2039311 rubles, 1950374 rubles, 3684959 rubles and

412129 rubles per year respectively. Whereas the costs for patients in the early stages of CKD, I to IV, were 17997 rubles, 22850 rubles, 30958 rubles and 38817 rubles per year respectively. When calculating the cost for CKD patients in the

CKD IV and CKD VH RRT groups, the following assumptions were made:

- according to standards, only every fifth patient met the CKD IV criteria;
- according to standards, every second patient met the CKD VH RRT criteria.

Figure 2. Results of the «cost of illness» analysis per patient per year, by stages of CKD

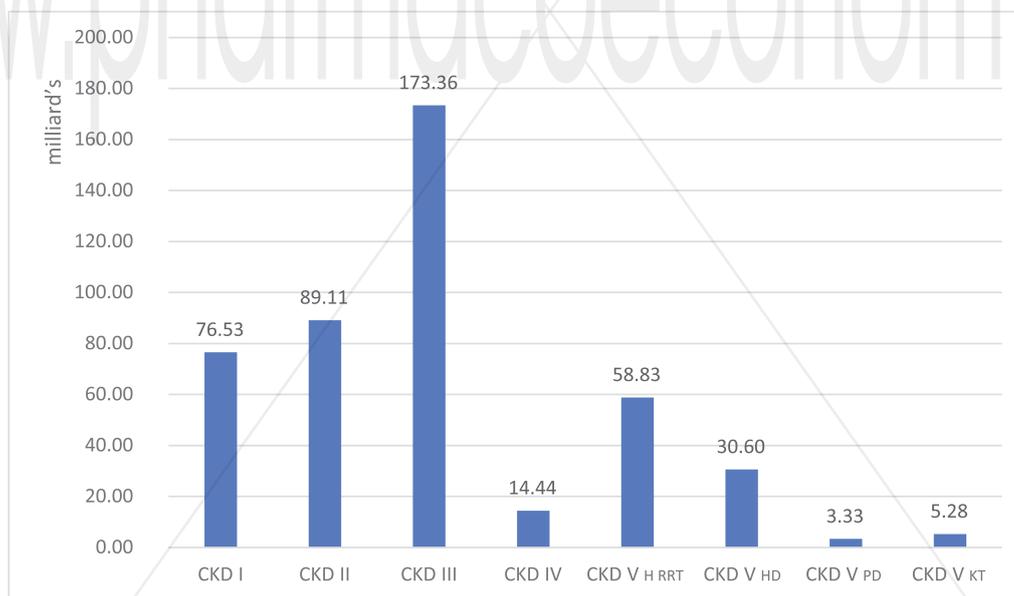


**Results of calculation of the economic burden of CKD on the entire population**

At the final stage of the analysis, in accordance with the formulas 7 and 8, the economic burden of chronic kidney disease on the entire patient population in the Russian Federation was determined. The total cost for all CKD patients, in the stages I to V, per year amounted to (Fig. 3):

CKD I – 76525896000 rubles.; CKD II – 89113830000 rubles.; CKD III – 173362392000 rubles.; CKD IV – 14440035600 rubles.; CKD VH RRT – 58830038400 rubles.; CKD VHD – 30599459343 rubles.; CKD VPD – 3331833657 rubles; CKD VKT – 5282361896 rubles

Figure 3. The economic burden of CKD based on the total population, by stages.



In summary, the total economic burden of all stages of CKD on a national scale was 451,485,846,896 rubles per year. At the same time, special attention should be paid to the fact that despite the high cost of advanced stages of CKD per patient due to the use of expensive RRT, the economic burden of CKD based on the number of patients in each of the stages had a different structure (Fig. 3). So, most of the economic burden of CKD, 75%, falls on its early stages, I-III, which is caused by a large number of patients in these stages. Also, the authors would like to emphasize that in this paper, for the first time in Russia, economic burden of CKD on a national scale was estimated. In the course of the study, a lack of national epidemiological data on the early stages of CKD was identified, as well as of data on the clinical features for various stages of CKD (egg, incidence of complications at different stages of CKD). Due to this, we have been forced to resort to extrapolation of foreign epidemiological data and introduce a number of assumptions that must be considered when assessing the accuracy of the results, which at the same time can be a basis for justification of various organizational initiatives aimed at improving the care of patients with CKD.

**Conclusion**

For the first time in Russia, economic burden of CKD on the entire patient population was estimated, which exceeded 451 billion rubles. The later CKD stages, associated by RRT administration, were the most costly stages per patient; while the analysis of the cost by the CKD stages based on the number of patients, has revealed that the bulk of the cost falls on the early stages of CKD.

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