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- РЕПОРТАЖ С X НАЦИОНАЛЬНОГО КОНГРЕССА С МЕЖДУНАРОДНЫМ УЧАСТИЕМ "РАЗВИТИЕ ФАРМАКОЭКОНОМИКИ И ФАРМАКОЭПИДЕМИОЛОГИИ В РОССИЙСКОЙ ФЕДЕРАЦИИ" 4-5 апреля 2016 года В НИЖНЕМ НОВГОРОДЕ

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METHODOLOGY OF COST ANALYSIS

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Abstract: *Cost analysis is an essential step of pharmacoeconomic research. It is the basis for carrying out special methods of pharmacoeconomic analysis: "cost-effectiveness" and "budget impact". This article deals with methodological basis of cost analysis in pharmacoeconomic studies. In particular, the authors describe the classification of costs and various methods of their calculation. In the publication the attention is paid to sourcing prices and cost structure in conducting pharmacoeconomic studies. Thus, the possibilities and limitations of using different types of prices depending on the position of pharmacoeconomic studies. The advantages and disadvantages of cost analysis based on standards of medical care, clinical and statistical groups and evaluation of real clinical practice are also described. The article deals with the features that must be considered when calculating direct and indirect costs. The authors list the problems of accounting the intangible costs.*

Key words: *cost analysis, pharmacoeconomics, direct costs, indirect costs, intangible costs, wholesale prices, retail prices, auction prices.*

The definition of pharmacoeconomics, as a discipline studying in comparative terms the ratio of the results of treatment, prevention, diagnosis, and expended in their use of resources on the one hand, and the content of the second principle of pharmacoeconomics, implying a full accounting of the relevant costs, on the other hand testifies to the fundamental role of cost analysis in pharmacoeconomic studies. In this regard, the importance of development of methodology of cost analysis in conducting pharmacoeconomic studies is difficult to overestimate.

First of all, for a proper understanding of what costs should be included in pharmacoeconomic analysis, it is necessary to have an understanding of classification of costs adopted in pharmacoeconomics.

Classification of costs in pharmacoeconomic analysis

There are different classifications of costs. In the context of the Russian healthcare system the costs used for the pharmacoeconomic analysis can be divided in direct costs (medical and nonmedical), indirect and intangible ones (Fig. 1).

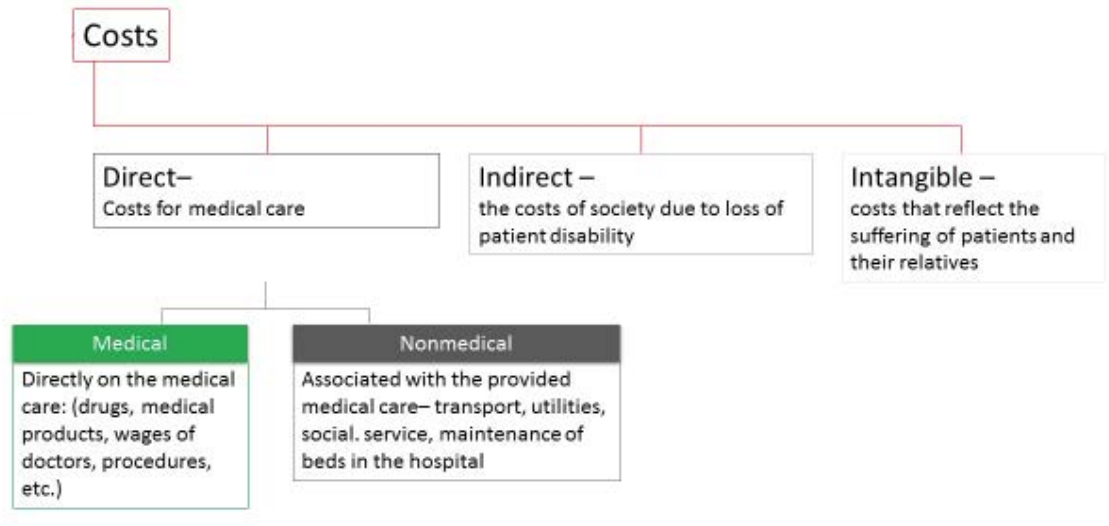

Figure 1. Classification of costs in pharmacoeconomic analysis

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Direct medical costs include ones associated with direct medical care. For example, direct medical costs include the costs of pharmacotherapy (including those associated with drug supply in the hospital and preferential dispensing of medicines (drugs)); blood products; consumables (systems for blood transfusion, syringes, bandages); laboratory and diagnostic studies (for example, total blood analysis); doctor visits; medical procedures (e.g., surgeries) and other medical procedures (e.g., intramuscular injection), etc. Obviously, the cost of correction of side effects of therapy and the costs associated with treatment of complications of the underlying disease, is also an example of direct medical costs.

Direct nonmedical costs include the cost of food of the patient's stay in hospital (i.e. the cost of a bed day), as well as the services of social services and the work of nonmedical personnel. It should be noted that the costs of special medical nutrition or parenteral nutrition should be considered as direct medical costs.

Indirect costs include the economic losses by the state (society) due to the reduction or loss of productivity by the patient and/or caregiver for him. In the group of indirect costs the following costs are highlighted :

- the costs associated with GDP losses arised by reason of the absence disability of patients in the economically active age in the process of GDP formation;
- the costs associated with pay-sheets of temporary disability (for patients in the economically active age);
- costs associated with disability payments for patients;
- other indirect costs, such as costs associated with maintenance of orphans, etc.

Intangible (immeasurable, intangible) costs are assessing various aspects of patient treatment, affecting his health and quality of life. These ones include: pain, suffering, reduction of social activity of the patient (restriction of mobility in joints, inability to drive a car), as well as his relatives and close friends. In other words, the intangible costs take into account the physical, mental, cognitive and sexual as well as emotional and social well-being of the patient. As noted by some authors, in certain cases, the cost of intangible costs in connection with the development of pain associated with the treatment of complications, can reach 30% of the total cost.

During the cost classification in the pharmacoeconomic analysis, in some cases it is advisable to use an additional differentiation of costs to reflect the features of evaluated disease or administered medicinal drug (MD). Thus, they distinguish fixed costs, i.e. costs, which remain constant when changing the number of patients and variable costs which depend on the number of patients

They can distinguish a separate cost element associated with deficit of medical care in conducting pharmacoeconomic analysis. This kind of cost that can be called "implicit", is defined as the costs that the health system can not be held, but it would have to incur in the provision of medical care to needy patients who still have not received it. An example of implicit costs, the ones that may increase the number of doctors (payroll, etc.), if their number is lower than those of normal indicators. The implicit cost also include the cost of increasing the capacity of renal replacement therapy (RRT) (hemodialysis centers), if at the time of the pharmacoeconomic evaluation determined the deficit of RRT capacity.

In general, the costs of pharmacoeconomic analysis can be defined as the product of the nominal value (price) of the unit medical services (or drug) or type of indirect costs and the frequency of this one (Formula 1):

$$Cost_i = Price_i * F_i * N_i$$ where: Formula (1)

$Cost_i$ – costs for cost item, rubles;
$Price_i$ – nominal price of item, rubles;
F_i – frequency of item,%;
N_i – amount of proposed service item.

Thus, the cost value is determined by the parameter value or price (Price), the frequency (F) and the amount (N) of service. The values of these parameters to calculate the costs in pharmacoeconomic analysis obtained by ongoing information retrieval.

From this it follows that the information retrieval, which is devoted to the description of the previous chapter, is also important in conducting cost-benefit analysis.

At the same time the conditions for the health system of the Russian Federation (RF), the following options to find sources for the price (value) and frequency of assignment.

Types of costs (prices) and its sources

Considering the different types of prices it is advisable to allocate separate rates to pharmacotherapy (medicinal drugs); the cost of medical services (such as physician visits, diagnostic or therapeutic procedures, etc.); as well as information about the values needed to calculate indirect costs: the value of GDP, disability pensions, the size of payments to pay for sick leave, etc.

In the pharmacoeconomic analysis, depending on the purpose, the following prices can be used (Figure 2):

- Auction;
- Wholesale;
- Retail

Auction prices for the medicinal drugs should be used, if studied MD are purchased through tenders held in the framework of the state program of drug supply. The main source of information on the auction purchases carried out in the public health system is public procurement portal - http://zakupki.gov.ru/epz/main/public/home.html. During the work with this source it is important to note that the search portal allows you to enter a trade name (TN) of MD and INN. The result of the search portal is a list of ongoing and / or completed and / or rejected auctions for the interest period of time, including information on the amount of purchases in cash and by volume, and, sometimes, the unit value (packaging) of the purchased lot. However, since the purchase of the auction according to the law must be carried out by INN, in the case of several TN single INN in a single auction, often purchased several TN and determine the value of the individual TN it is not possible. The procurement portal does not automatically calculate the average cost of INN of interest on the results of the auction, but it provides an opportunity to generate data to unload the tender in the form of a spreadsheet.

Wholesale prices for the MDs may be used, if the medicinal drugs are procured by the example private hospitals. Retail prices for the MD are used in pharmacoeconomic calculation if MD are purchased at the expense of patients. The main source of data on wholesale and retail prices is a state register of marginal selling prices (http://grls.rosminzdrav.ru/pricelims.aspx). It should be noted that the registry contains only marginal producers' prices; wholesale and retail prices for MD are determined by adding to its maximum selling prices of the relevant manufacturer or wholesale and retail mark-up. This registry contains information on the prices of all trade names of medicinal drugs of vital and essential medicines list. State Register of maximum prices also allows to form a discharge for all the MD in the form of a spreadsheet. If TN of drug is not listed in VED, wholesale price information can be obtained from distributors databases. It should be noted that more often the base price of distributors are the private (non-public) data sources with limited access. Value of retail prices for TN of non-VED drug, can be obtained from open sources of information (with free access), monitors the prices of drugs in pharmacies.

Another type of prices for the MD, which is currently not used in Russia because of lack of legal basis, but it is widely distributed in foreign health systems are price agreements, which are installed between the manufacturer or supplier of the drug and the health system in the private negotiations. Price values at the conclusion of price agreements can be lower than the wholesale, retail and auction prices.

It is extremely important to strictly observe the rule of the comparability of prices during the pharmacoeconomic analysis, which implies that for all the investigated MDs must be the same kind of price - the auction price, or wholesale prices or retail prices.

In case if you use the same kind of price for all comparable MDs it is not possible (for example, if the pharmacoeconomic analysis included an innovative drug that is not yet included in VED list and did not participate the auctions), for conducting pharmacoeconomic studies may be used for price information on the drug from the manufacturer / supplier, but this fact should be reflected in the assumptions of the ongoing pharmacoeconomic evaluation. At the same time, it is absolutely unacceptable to compare to auction / wholesale prices for one drug and retail prices for another one.

Healthcare costs (cost of the visit to the doctor, the cost of blood tests, etc.) can be obtained from various sources, which include:

- Diagnosis-related group (DRG);
- Tariff agreement of compulsory medical insurance (FOMS) funds;
- Prices of individual MDs

In the pharmacoeconomic studies conducted from the public health perspective, you should use the DRG tariffs and tariff agreements of FOMS. Tariff information is posted on electronic resources of FOMS (http://www.ffoms.ru/portal/page/portal/top/index); when it is necessary to take into account the peculiarities of the health care system, according to which each subject of the Russian Federation has a territorial office of FOMS and their collective agreement. It is important to take into account that the DRG tariffs are aggregated, and therefore their use makes inaccessible to perform the depth analysis of the cost of individual items of medical services within the pharmacoeconomic studies.

The use of price lists of selected drug data or received average costs of medical services on the basis of the price lists analysis of several MDs is undesirable in pharmacoeconomic analysis from the perspective of the public health system. However, if there is no other way to determine the cost of medical services, which is essential for the ongoing pharmacoeconomic studies, you can use price lists data provided to reflect this fact in the section of pharmacoeconomic analysis assumptions. Prices tend to be placed on the electronic pages of the medical institution.

The main source of data for the calculation of indirect costs (GDP size, GDP per capita, average wages) in the Russian Federation is the Federal State Statistics Service, the electronic address is http://www.gks.ru/. Data on the size of payments and disability pensions are available on the electronic page of the Pension Fund of the Russian Federation at http://www.pfrf.ru/.

Data on the frequency and amount of medicinal drugs and provision of medical services

As it follows from the general formula (1) the data on the cost and the number of drug administration frequencies (prescriptions) and health services are crucial in calculating the costs. In the conditions of the Russian Federation healthcare, the most relevant and convenient source of data on the frequency and the number of drug prescription and medical services are standards of care. Standards of medical care are official government documents adopted by the Ministry of Health (MOH) and the Russian Federation extending the registration in the Ministry of Justice (MOJ), containing information about the list of medical services and MDs, the average frequency of their appointment and the average amount at different nosology. To date, more than 1000 standards of care are accepted. They are available on the official website of the Ministry of Health of the Russian Federation http://www.rosminzdrav.ru/ministry/61/22/stranitsa-979/stranitsa-983. Thus, it is possible to conduct a detailed analysis of disease-specific cost by multiplying the values contained in the standard frequency and the number of services or the value unit of drug by these services basing on the standard. Setting the frequency of a value from 0 to 1; the frequency of which is equal to 0 means that the medical service or drug is not administered to a patient; at a frequency of 1 medical service or drug are appointed for all patients required; intermediate values of frequency reflect a situation in which a service or DRUG is assigned a certain percentage of patients.

The number of drug prescription refers to course dose of drug, the official source of data used is a leaflet. Leaflets, registered in the Russian Federation, are taken from the State Register of drugs (GRLS) http://grls.rosminzdrav.ru/grls.aspx.

At the same time, it should be noted that in the case of calculating the costs based on the standards of care the use of the DRG as a source of data on the cost of services payment is difficult, since DRG rates include the cost of an aggregated value, without going into detail on the individual items of expenditure.

DRG rates themselves are another official source of information about the frequency and quantity of MDs and medical services, being the maximum value of the finished case of treatment group states. In this regard, as noted above, based on DRG payment is not possible to conduct a detailed cost analysis. Also it should be noted that the rate of DRG, to determine the maximum value of the completed event for the whole group of states makes it difficult to differentiate the value of these states within a predetermined maximum value[1].

In the absence of a suitable standard of medical and DRG data on the frequency and quantity of MDs and medical services, as well as the list of naming can be obtained by analyzing the protocols and treatment guidelines, clinical guidelines and involvement of the expert opinion. The experts presented clinical specialists, while providing information on the drug prescription frequency and health services, which is not contained in the above protocols, manuals and clinical guidelines.

Separately, it should be noted that the possibility of cost estimates based on actual practice, in which data on the frequency and quantity of MDs and health care services from the existing registers of patients or by retrospective analysis of patient records. It should be emphasized that the results of the cost analysis carried out on the basis of evaluation of clinical practice, most accurately reflect reality and therefore have the greatest value to decision-makers by themselves, so they formed on the basis of pharmacoeconomic conclusion (Figure 2).

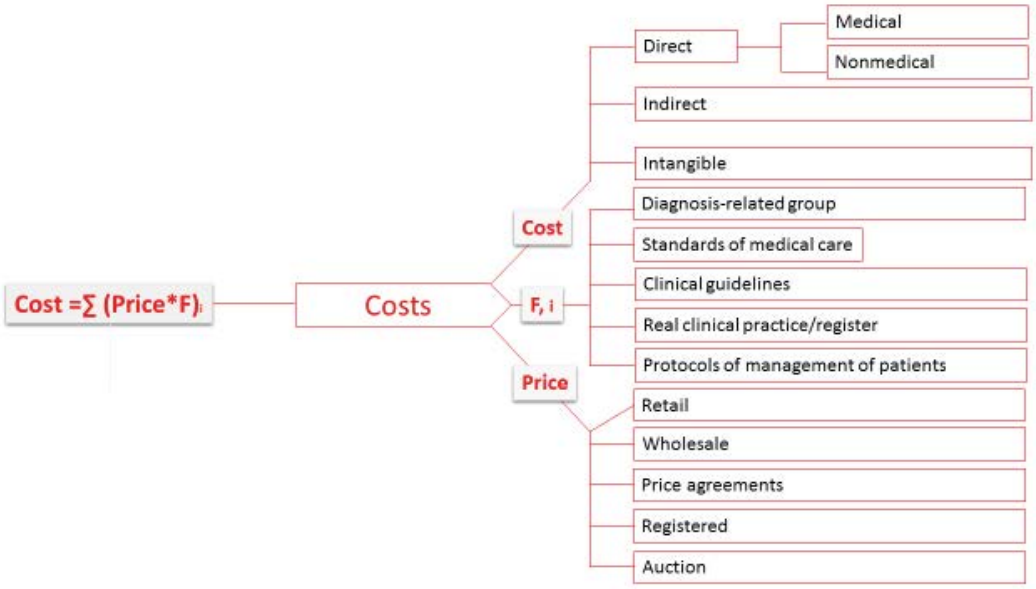

Figure 2. Possible options of direct costs calculation

[1] Although the method of DRG contains correction factors that reflect the particular treatment of a condition features which can reduce or increase the cost because a complete case analysis for cost under study, they do not provide the flexibility of necessary calculation.

Features of calculation of direct costs

Cost analysis during pharmacoeconomic studies is a flexible tool with many options to describe the economic aspects of the problem (disease).

Thus, the calculation of the direct cost of the drug can be done by:
- Number of active ingredient drug;
- The number of units of the dosage form of drug;
- Total drug packages.

In the first method of calculating the cost of the drug course is defined as the product of the unit cost of the active substance of MD by the number of units of the active substance course dose and frequency of drug prescriptions. In the case of calculating the costs of the units on the MD formulation (e.g., tablets or injection) is calculated as the product of the cost value of a unit dosage form, number of units of the dosage form and frequency rate of prescription. In the third case, the costs are calculated as the product of the cost of MD packages, amount of packs for the course and frequency of drug prescriptions. Presented three methods have their own features.

Thus, the first method is based on the MD cost by active ingredient, which is the most simple. However, it involves a number of assumptions, including the main assumption is that the MD dosage form will allow to get the exact dosage equivalent coursework. However, if the costs are defined for MD, which is introduced in the form of injection, and a single dose to the patient is less than the contents of the ampoule, while the MD application instruction does not allow an open vial several times, the calculation of MD costs of active ingredient will be incorrect, and the result of the analysis MD application costs will be lower than the actual cost of its application. Thus, without considering the impact of the MD release form of the outcome, the cost calculation for the active substance is an approximation and in a pharmacoeconomic analysis can be used in the calculation in the accompanying low-cost pharmacotherapy costs.

Calculation of costs by the number of MD units of the dosage form is characterized by the same restrictions as the calculation of the amount of active ingredient, with the only difference that the calculation of the units of the dosage form does not account for the influence factor drug release form. However, this calculation appears to be valid for cost analysis in a hospital where patients typically receive no drug packages but in separate dosage forms.

Calculation of the amount of dosage form units may not be possible for the drugs, issued in the form of ointments, liniments, etc. Calculation of costs of number of packages to be used in the cost analysis of dispensed outpatients, since in this case the patient receives the drug in the form of whole packages. Also, payment of expenses for the PL for packages tied to the structure of the consumption of drug in the context of packages: a change of purchased MD release forms (eg, transition to purchase the LP on the packaging of tablets of 5 mg to 5 N. 10 N. 30 mg) will demand the allocation of costs.

Features of calculation of indirect costs

In calculating the indirect costs, among other things is important to consider the demographic factor: the so-expenditure as a result of foregone GDP; costs associated with the payment for sheets of temporary disability, - apply only to patients who are in the economically active age. Also, the costs associated with payment of sheets of temporary disability depend on the age of the patient, as in the calculation include the factor reflecting the work of the patient experience. When calculating the cost of a one-time disability benefits and disability pension must take into account the distribution of patients by group of disability. The mathematical apparatus for calculation of the direct and indirect costs is presented attached to this article.

Features of calculation of intangible costs

At the moment there is no recognized method of expression of intangible costs in monetary terms, in this regard, this type of costs is not included in the formal part of pharmacoeconomic studies, as a subject for discussion in the section discussion of some pharmacoeconomic publications. Thus, it should be noted that experts do not stop the development of satisfactory methods for calculating the intangible costs. An example of such an approach is the theoretical research "conjoint analysis», conjoint analysis (analysis of intangible costs is a particular case of the methodology "conjoint analysis").

This method is focused on the patient. The essence of the conjoint analysis of the methodology is that after determining the patient assessed the properties and characteristics of the product, the researcher creates profiles (lists of properties and characteristics) of treatment, describing both existing and hypothetical treatment regimens. In the profiles can be drawn up to include such features and characteristics that will take into account the intangible costs. For example, in a simple case - the property of "pain" and its characteristics, "expressed" and "moderate." As a result, research is needed to estimate the relative importance of each individual property compiling a mathematical function of several variables that characterize the studied properties. Thus, knowing the relative importance of each individual property, it is possible to calculate a combined share of utility for all combinations of properties and characteristics, i.e., for each profile treatment of the disease.

For example, in the treatment of gastroesophageal reflux disease as a result of the study a cost factor is received, showing that the increase in the value of one ruble equals 0.01 units of utility. Thus, it can convert units of utility in the monetary equivalent value of patient data by dividing each property by 0.01 ruble per unit of utility. For example, the property "duration of effect after discontinuation of the drug," the characteristic of "high" is estimated at 40 rubles for a single administration of MD. Similarly, you can evaluate in monetary units and the property of "pain", as well as other properties that would allow to calculate the intangible costs.

Features of choice of costs in pharmacoeconomic analysis

The choice of qualifying costs is determined by the disease and medicinal drugs, which were performed or conducted pharmacoeconomic research. The following factors should be considered during analyzing costs if the disease requires inpatient treatment or outpatient only, or both types, if the patients are assigned for rehabilitation, if the disease is accompanied by the development of complications and if the studied drug administration leads to the significant side effects, whether the disease leads to disability of patients or the temporary loss of their working capacity. Another factor influencing the choice of costs in pharmacoeconomic research is the level of conducted pharmacoeconomic research: federal, regional or medical institution.

Conclusion

Cost analysis, as the choice of performance criteria includes information retrieval and it is one of the most time-consuming step in pharmacoeconomic analysis. Adequately performed cost analysis and especially the cost analysis performed basing on data from real clinical practice, builds a solid foundation for the subsequent special methods of pharmacoeconomic analysis and relevant decision-makers demand accurate pharmacoeconomic findings.

Appendix. Formulas for calculation of different types of costs.

Direct costs:

The nominal costs of a course of pharmacotherapy in the calculation on the active substance:

$$Cost(Th)_a = Price(Th)_a \times D(Th)_a \times T(Th),$$ Formula (2)

where:

$Cost\ (Th)_a$ – cost for course of drug therapy, calculated using active ingredient, rubles;

$Price(Th)_a$ – mean cost of a unit of medical drug (calculated as active ingredient mean arithmetic of cost of active ingredient of different pharmaceutical forms of this medicinal drug) or the cost of pack (during the calculation on packs), rubles;

$D(Th)_a$ – single dose of medicinal drug, units of active ingredient;

$T(Th)$ – the length of treatment course with medicinal drug.

Nominal costs for treatment course during the calculation during the calculation using dosage form:

$$Cost(Th)_t = Price(Th)_t \times D(Th)_t \times T(Th),$$ Formula (3)

where:

$Cost\ (Th)_t$ – cost for course of drug therapy, calculated using dosage form, rubles;

$Price(Th)_t$ – mean cost of a unit (tablet, ampoule, syringe, etc) of medical drug (calculated as mean arithmetic of cost of a unit of different pharmaceutical forms of this medicinal drug), rubles;

$D(Th)_t$ – single dose of medicinal drug, units of pharmaceutical form;

$T(Th)$ –the length of treatment course with medicinal drug.

Nominal costs for treatment course during the calculation using packs:

$$Cost(Th)_p = Price(Th)_p \times D(Th)_p, \quad \text{Formula (4)}$$

where:

Cost $(Th)_p$ –cost for course of drug therapy, calculated using packs, rubles;
Price $(Th)_p$ – mean cost of pack of drug, rubles;
$D(Th)_p$ – course dose of drug in packs;

Costs of medical services:

$$Cost(S) = Price(S) \times Q(S) \times F(S), \quad \text{Formula (5)}$$

where:

Cost (S) – cost for medical service, rubles;
Price(S) – price of medical service, rubles;
Q(S) – mean quantity of presented medical service;
F(S) – frequency of medical service.

Cost for side effect treatment:

$$Cost(C) = Price(C) \times F(C), \quad \text{Formula (6)}$$

where:

Cost (C) – cost of treatment of side effect, rubles;
Price(C) – price of treatment of side effect, rubles;
F(C) – frequency of side effect.

Indirect costs:

Indirect costs due to temporary disability.

Considered indirect costs include costs resulting from the loss of GDP due to temporary disability and payments for temporary disability leaves:

$$Cost(ID) = (GDP_d + TDL)*n, \quad \text{Formula (7)}$$

where:
Cost(ID) – cost for temporary disability, rubles
GDP_D *– GDP per capita per day, rubles;*
TDL – payment for temporary disability lists, rubles;
n – number of days with disability.

The first stage is determination of average annual GDP:

Average annual GDP per capita:

$$GDP_d = GDP/P \quad \text{Formula (8)}$$

where:
GDP – annual total GDP, rubles;
GDP_d *– annual GDP per capita , rubles;*
P – number of able-bodied population, people.

GDP per capita per day:

$$GDP_{day} = GDP_d/365 \quad \text{Formula (9)}$$

where:
GDP_{day} *– GDP per capita per day, rubles;*
GDP_d *– annual GDP per capita, rubles;*
365 – number of days per year.

In the next step, they calculate benefits payable under the temporary disability leaves (per day), which is 80% of the daily income. Daily income is determined by the formula:

$$I_d = I_m / 30 \quad \text{Formula (10)}$$

where:
I_d *– income per day per capita, rubles;*
I_m *– income per month per capita, rubles;*
30 – number of days in month.

Payment for temporary disability lists:

$$TDL = I_d \times (80/100) \quad \text{Formula (11)}$$

where:
TDL – payment for temporary disability lists, rubles;
I_d – income per day per capita, rubles;

Indirect costs due to disability.

$$Cost\ (i) = PI*m + GDP_{day}*n, \quad \text{Formula (12)}$$

where:
Cost(i) – indirect costs due to disability, rubles
GDP_{day} *– GDP per capita per day, rubles;*
PI – disability payments per month, rubles
m – life expectancy, months.;
n –the number of days after onset of the disability until the retirement age.

References:

1.Khabriev R.U., Kulikov A. Yu., Arinina E. E. Methodological basis of pharmacoeconomic analysis. MOSCOW: Meditsina. – 2011. – 128 pp.
2. Kulikov A.Yu., Litvinenko M.M. Theoretical basis of new pharmacoeconomics analysis: conjoint analysis. Pharmacoeconomics.Modern pharmacoeconomics ans pharmacoepidemilogy 2009. T. 2. № 2. P. 15-19.