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- VIII конгресс с международным участием «Развитие фармакоэкономики и фармакоэпидемиологии в Российской Федерации»
- Методологические основы моделирования при проведении фармакоэкономических исследований: разные уровни сложности и разная ценность полученных результатов

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METHODOLOGICAL BASICS OF MODELING IN THE PHARMACOECONOMIC STUDIES: DIFFERENT LEVELS OF COMPLEXITY AND DIFFERENT VALUE OF THE RESULTS OBTAINED

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Summary: *Pharmacoeconomic analysis is a flexible tool for the decision-making on different levels in the healthcare system: from the individual patient level to the regional and federal levels. The actuality of such an analysis becomes more and more apparent in the healthcare marked by the annual increase in the implemented and published studies in this area. However, such an increase in evaluations doesn't guarantee the proportional growth in terms of their quality and complexity. This article focuses on the opportunities of pharmacoeconomic researches, as well as on the usual inaccuracies in the pharmacoeconomic studies in Russia.*

The actuality of pharmacoeconomic studies, the results of which are used on different levels of the healthcare management, becomes more and more evident. In recent years, there's a general trend on the increase in number of the pharmacoeconomic studies on different levels of complexity worldwide. To identify the corresponding trends in Russia we have conducted an analysis focusing on the structure and dynamics of pharamacoeconomic studies in the Russian Federation. The analysis is based on the information search process of the electronic database of the Central Scientific Library of Medicine, the First Moscow State Medical University named after I.M.Sechenov under the auspices of the RF Ministry of Health. The keywords (with appropriate endings) of the search process have been the following: "pharmacoeconomics*" and "pharmacoeconomic*".

In the scopes of the analysis, the dynamics of publications on the methodology and normative regulations in pharmaceoconomic studies, including publications on the results of studies carried out in the RF or translations from foreign languages have been taken into account and evaluated. The time interval is 18 years – from 1995 to 2012. The total number of publications for the mentioned period of time achieves to 336. The figure 1 illustrates the dynamics of publications for each year.

According to the graph illustrated on the Figure 1, up to 2000 the annual number of publications didn't exceed 4, whereas in 2000 an abrupt increase was registered and the total average number of publications became 20-30 per year. Since 2006 the necessity of pharmacoeconomic studies has been legally adopted by the document of the RF Ministry of Healthcare and Social Development – the Decree № 96 of February 15, 2006 dedicated to the issues in regards to the formation of medicine lists in the scopes of programs of providing additional and free of charge medical care to the certain categories of citizens.According to the annex of the Decree, there's a regulative procedure of forming the list of preferential medicaments, as well as there's a package of necessary documents applied for the justification in the process of including new medicines in the lists. The description of results of pharmacoeconomic analysis is among the mentioned documents. The revised Regulation on the procedure of drafting the list of vital and essential medicaments was enshrined in the Decree (of May 27, 2009, N276н)of the RF Ministry of Health care and Social Development "On the procedure of drafting the list of vital and essential medicines" and contained the necessity of providing the results of pharmacoeconomic analysis, including the "cost-effectiveness" analysis. There was some decline in the number of publications in 2012, which can be explained bythe untimely receipt of sources in the Central scientific medical library and their late inclusion into the electronic database.

Further we have analyzed the structure of publications released and included in the electronic database of the Central Scientific Medical Library from 2007 to 2012. The results of the analysis are illustrated on the Figure 2.

Figure 1. Dynamics of the publications in the sphere of pharmacoeconomic studies in Russia from 1995 to 2012

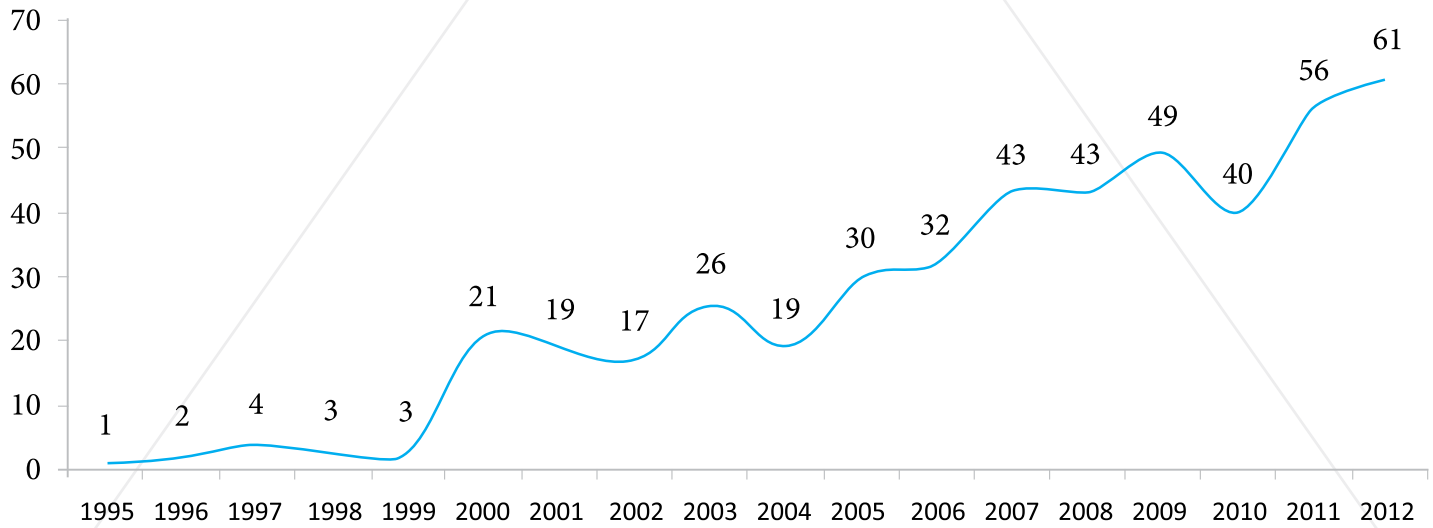

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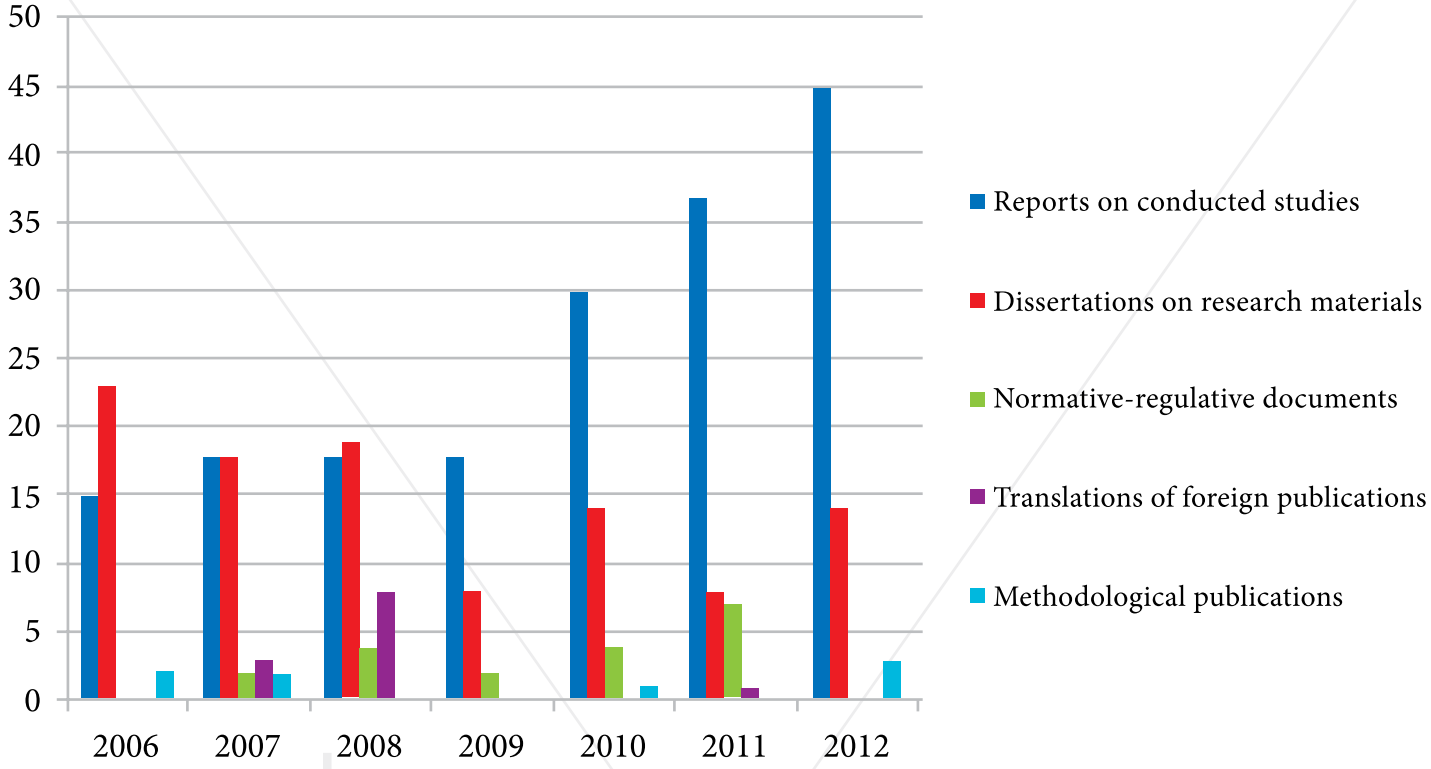
Figure 2. Structure of articles published in Russia in 2007-2012



Based on conducted analysis, it has been found, that all pharmacoeconomic publications in Russia, presented by the Central Scientific Medical Library of the First Moscow State Medical University named after I.M. Sechenov, can be conditionally divided into 5 groups:

- Reports on conducted studies;
- Dissertations;
- Normative-regulative documents;
- Translations of foreign publications;
- Methodological publications.

As illustrated on the Figure 2, all the published papers in the RF are divided into 6 groups: reports on the conducted studies, mainly published in scientific journals and article collections; dissertations containing research results; normative-legal documents; translations of foreign researches; methodological publications and dissertations; researches addressed to the development of pharmacoeconomic methodology. It has been found that the most popular type among the publications analyzed during the mentioned period are dissertations based on study materials which represent 47% of all publications; then follow reports on the implemented studies with 44%; methodological publications don't exceed 5%; dissertations dedicated to the methodology of pharmacoeconomics form 3% of all publications; normative-methodological documents and translations of foreign researches, respectively, constitute 1%. As a result, totally up to 93% of all the publications for the mentioned period are the materials reporting on the results of conducted researches. However, it's worth mentioning that the increase in quantity of pharmacoeconomic researches doesn't guarantee the symmetrical increase in their quality.

Pharmacoeconomics is the symbiosis of a range of academic disciplines such as medicine, pharmacy, economics and mathematics which in its turns implies to the use of all the scientific and technical apparatus offered by these fields to obtain more complete and verified results and to promote the best decision-making in the system of health care. Medicine and pharmacy, first of all, touch the issues of efficiency and security evaluation of the analyzed technologies, while economy and mathematics are the immediate tools for the conduct of analysis. The symbiosis of these sciences allows assessing the results obtained in the scopes of researches in terms of their accuracy and sensitivity to the changes in the input data. It should be noted that the analyzed medical technologies can integrate different aspects of the medical assistance: prevention, diagnosis and screening programs, therapy and rehabilitation of patients, and this fact as well requires a special design of the study. The peculiarities of pharmacoeconomics as a complete discipline apply to the significant differences in the complexity of the ongoing studies.

Pharmacoeconomic studies vary in terms of the methodology, patients' population and opinion, final products and other characteristics. The hierarchy of levels in the pharmacoeconomic studies is illustrated on the Figure 3.

From the point of the final product. In regards to the resultant product pharmacoeconomic studies are subdivided into three groups:

✓ Basic design calculations which can be represented, on the one hand, through the adapted foreign studies and, on the other hand, through the local national studies in the scopes of which the cost-evaluation and other methods of the pharmacoeconomic analysis are used. This type is the simplest among the pharmacoeconomic analysis products and is related to the "pharmaco-accounting" through which the cost estimation of the patients' therapy course is conducted within the alternative technologies.

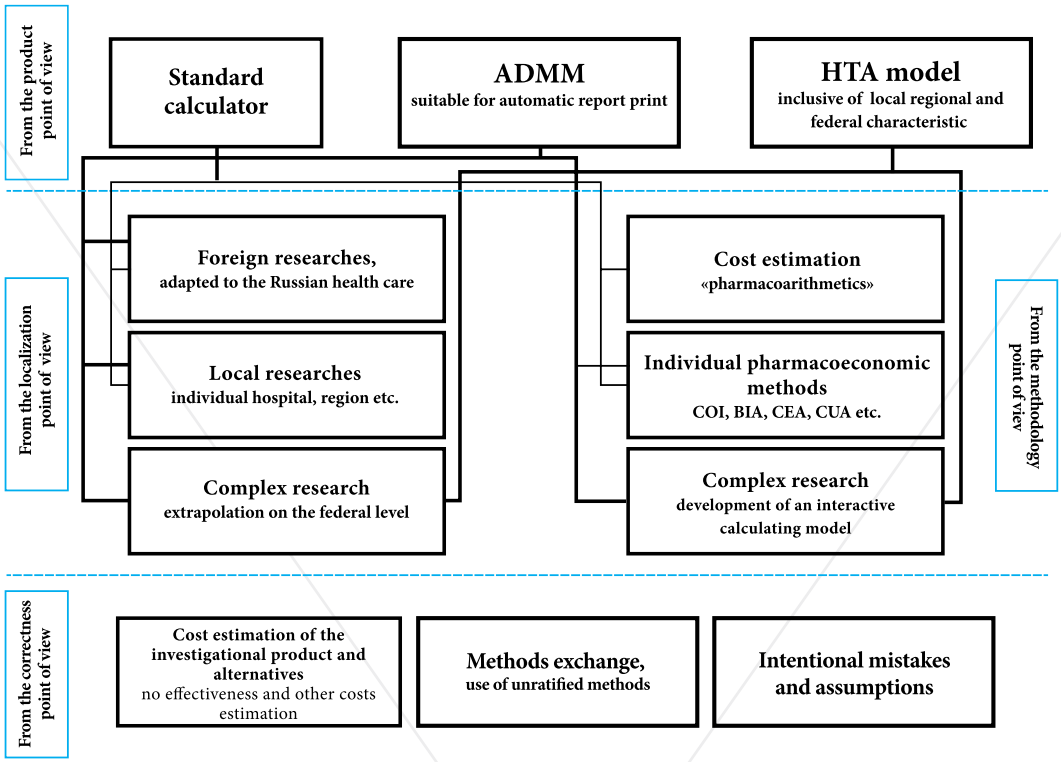
✓ Automatic decision-making models (ADMM) have the ability to print an automatically generated reports presented in the foreign and local researches, as well as in comprehensive researches allowing us to extrapolate the results to the regional or state level, as well as to use separate methods of pharmacoeconomic analysis or integrated approaches, including the design of an interactive computational model. This type of product is the most appropriate for the evaluation of health technologies on the level of individual health facilities or regions; it provides more complete data on pharmacoeconomics and considers the effectiveness/usefulness of the analyzed technologies.

✓ The health technology assessment model is the most difficult and complex product which takes into account local, regional and federal features of the epidemiology of the disease, approaches to therapy, health organizations, etc. These models are always presented by a comprehensive study, having in their composition the interactive computational model and providing data that can be extrapolated to the regions and federal level as a whole.

From the point of mathematics, statistics and general economy, the model is an instrument for the assessment and indication of aims, best options for their achievement, and also for the distribution of the existing resources among the settled aims. The technical model is the interpretation of the real situation which can be erected by the help of various means – from verbal explanation to computer programming.

Herewith, in regards to the pharmacoeconomic analysis, the model is the visualized form of the conducted analysis containing all the necessary calculations and, in

Figure 3. Levels of pharmacoeconomic studes in Russia



terms of non-static input data (for example, the cost of medical procedures and pharmacotherapy), allowing to obtain results which mirror the real situation for the exact user or organization of the health care on the known level. More often the pharmacoeconomic models are designed in Michrosoft Excel which allows using them freely on computers with Microsoft Office operating system and don't require additional programs.

The standard pharmacoeconomic model presented in the Microsoft Excel handbook contains several pages allowing the user to get acquaintance with the operations of the model and ongoing researches, to implement analysis and result in solutions. The general structure of pharmacoeconomic model is illustrated on the Figure 4.

The pages illustrating the pharmacoeconomic analysis and, particularly, the "cost-benefit" analysis allows the user to try some actual data which is not considered as static. The changing data in the pharmacoeconomic model includes:

- Cost of the medical services and pharmacotherapy;
- Multiplicity purpose of medical services and pharmacotherapy;
- Number of patients;
- Frequency of complications of the main disease, and etc.

Along with this, it should be noted that not all these details are provided in each pharmacoeconomic model and their availability depends on the baseline survey.

Figure 4. Common structure of pharmacoeconomic model

Front Page	**Research title and authors**
	Research overview (time horizon, population, data source and methods)
	Model navigation (legends)
Model Index	**Quick model navigation**
Pharmacoeconomic analysis	**Effectiveness analysis based on the clinical research data**
	Cost analysis (direct and/or indirect costs)
	Pharmacoeconomic analysis (CEA, CUA, BIA,COI etc)
Findings	**Automatic conclusion on pharmacoeconomic effectiveness / not effectivenes of the investigational product**
Sensitivity analysis	**Estimation of computational stability**
References	**Clinical researches and methodological data**

Thus, in the scopes of the pharmacoeconomic models, the data obtained through the analysis corresponds to the peculiarities highlighted by researchers, i.e. it [data] reflects the real situation for the certain health care facilities, city, region or country.

From the point of view of research/study localization: Based on the study localization viewpoint, the pharmacoeconomic studiesare divided into three groups:

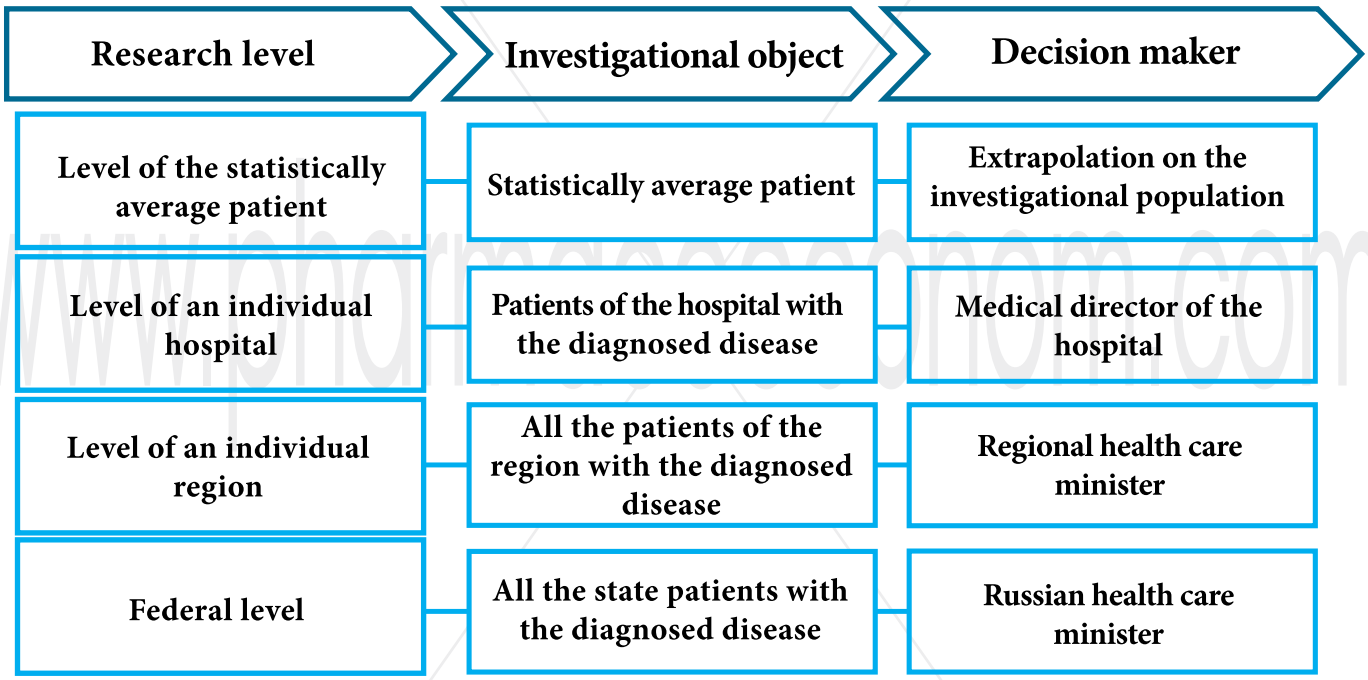
- ✓ Foreign studies adapted to the conditions of the Russian health care. This method of pharmacoeconomic study allows to get the fastest results of the analysis, but it should be noted that the transfer of results from one country into another makes them void, and the recalculation of costs and changes in their structures on the basis of the actual situation of the local health care can lead to diametrically opposite conclusions.
- ✓ Local studies carried out on the level of an individual medical center, municipality or region, mostly allowing to obtain input data on the patients' number which shows the real epidemiological situation of the considered administrative unit, and as well as taking into account the peculiarities in the approaches to the patients' therapy with various diseases based on the normative documents, disease history or expert opinions.
- ✓ Complex studies allowing to obtain analysis results adapted to the decision-making in health care on different levels: from regional to federal.

The considered population of patients is a separate aspect of localization of pharmacoeconomic studies. The levels of pharmacoeconomic analysis in regards to patients' population are illustrated on the Figure 5.

The levels of a particular region and the country as a whole, in their turn, enlarge opportunities to conduct a pharmacoeconomic analysis of the general population of patients with a specific nosology or in a certain state (prevention of infectious diseases, postsurgery rehabilitation, etc.). The accounting for indirect costs is appropriate for the analysis in a particular region or several regions across the country, as these costs directly affect the regional budget. Just on these levels of evaluation there can be a statistical analysis of epidemiological data to assess the real incidence of patients, the frequency of use of a technology and the probabilities of the outcomes of the disease; if it is impossible for such an assessment within a region or country, the epidemiological data can be taken from public sources. Along with this, the analysis on the level of a particular region or country can be sensitive to cultural, social, religious and other characteristics of patients with varying nosology, or to the application of a medical technology.

From the point of view of the methodology used. Pharmacoeconomics has extensive analysis and, at the same time, continuously developing methodological apparatus, and the classification of levels of studies in terms of methodology is the following:

- ✓ Analysis of the disease cost, as already mentioned, is not a method of pharmacoeconomic analysis in pure form: it assesses the cost of therapy by the compared technologies. This analysis does not provide sufficient data for the decision-making in the health system in terms of selection of pharmacotherapy alternatives and can only be used either to compare the cost structure of various diseases or as part of an integrated pharmacoeconomic analysis.



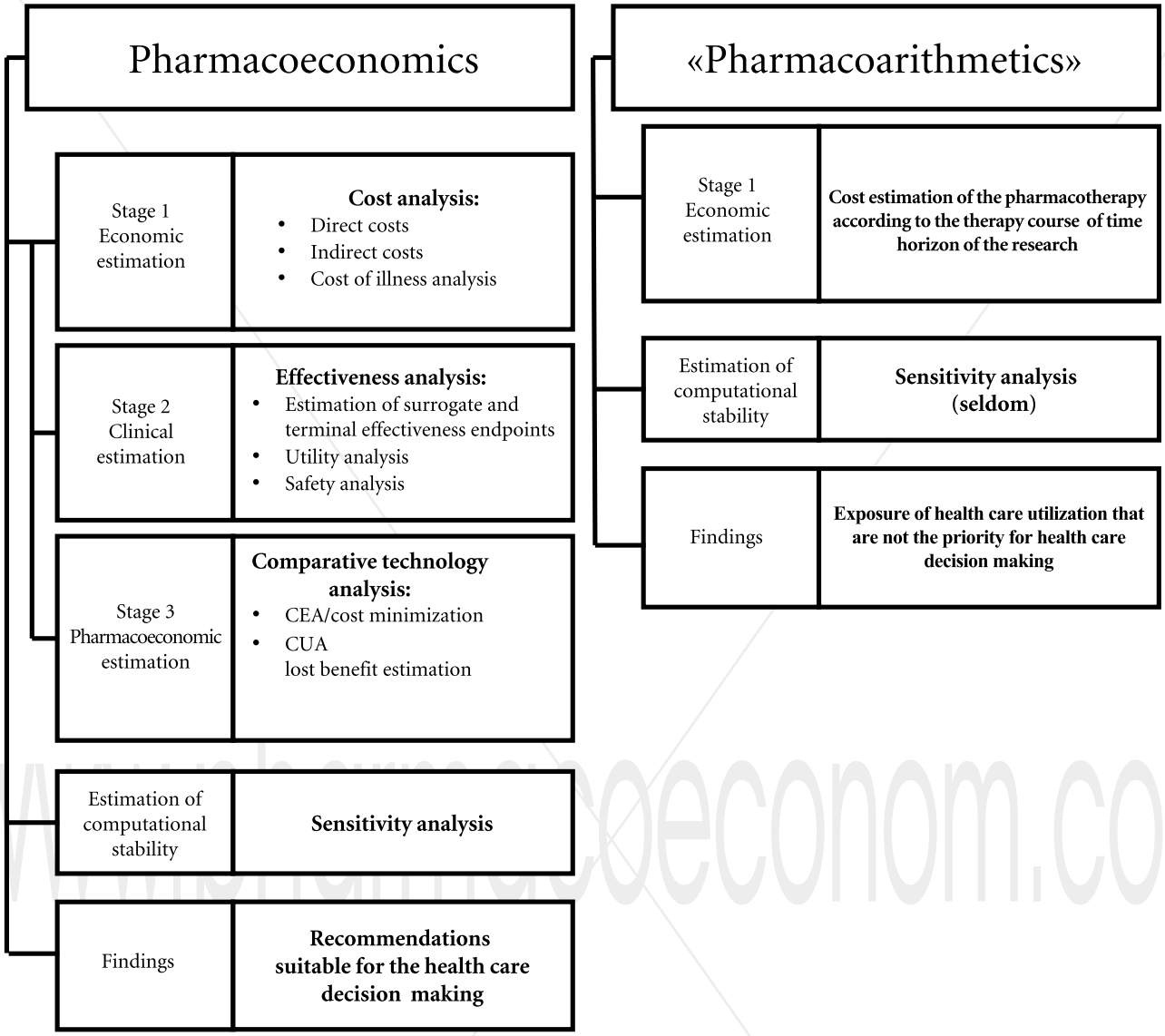
The decision making on different levels allows to carry out the analysis of the concrete medical technology in terms of determined nosology based on the example of the average patient. The analysis on this level is primarily accounted for the direct costs, the structure of which is determined on the basis of regulatory documents on management of patients with specific nosology (standards of care and recommendations) or clinical practice (survey of specialists, analysis of patients' disease histories or registers) . Also on this level the indirect costs are supposed to be considered (loss of GDP, temporary sick leave payments, etc.). The obtained data in the scopes of this pharmacoeconomic analysis in the future can be extrapolated to a larger population of patients.

The level of individual health care facility (HCF) is most commonly used for the assessment of medical technologies practiced only in the stationary phase to assist the sick, and it is not applicable in the ambulatory medical practice. Such studies grant opportunities for the analysis of specific medical technologies both for the individual patient and for a specific patients' population, expressed, for example, through the number of beds in health facilities or in its certain department, as well as through the number of surgeries using the evaluated technologies, etc. On the level of individual health care facilities the most relevant is the analysis of direct costs on direct patient care, since the indirect costs, primarily denominated by GDP losses in the region or country, are not directly taken into account when the budget of the hospital is planned.

- ✓ Separate pharmacoeconomic analysis methods, such as analysis of the "cost of illness", analysis of the "budget-impact", "cost-effectiveness", "cost-utility", etc., provide the data more acceptable for policy-makers to take into account the effectiveness/utility and security of technologies, as well as consider the peculiarities of their application and therapy of patients with various diseases in the context of the clinical conditions of a concrete region or countrywide.
- ✓ Comprehensive studies provide the most complete data and allow them to adapt to the real clinical setting with the ability to change a number of cost and clinical characteristics accounted for in the analysis, in case of health care organizers will use interactive computational model.

The current level of development in pharmacoeconomics as an applied science abroad portrays the high-level of complexity and quality of ongoing studies which are considered as benchmarks for Russian researchers. The implementation of a pharmacoeconomic study on this phase of development of the science highlights the importance of a range of obligatory phases in studies which will enable the scholars to obtain the most valid, complete solutions focused on the decision-making in the health care system (Figure 6).

Figure 6. Phases of complete pharmacoeconomic analysis.



From the viewpoint of the correctness of studies. There are some common inaccuracies made during the pharmacoeconomic evaluations. Based on this, we offer the following classification:

- ✓ Assessment of costs per treatment and alternative therapy without regard to their effectiveness, utility and security, which in their turn require additional costs and may significantly affect the results of analysis; Russian researchers often evaluate only per course prices for different pharmacological approaches and compare them with each other, which, in fact, is the above mentioned "pharmaco-accounting."
- ✓ Substitution of methods is most often observed when dealing withthe methods of analysis, such as the analysis of "cost-effectiveness" and "cost-minimization" analysis. The latter, in fact, is a special case of the analysis of "cost-effectiveness": it takes place in the absence of reliable data on the difference in the effectiveness between the treatment technologies, and implies a requirement for the "efficacy analysis", the results of which either are recorded in the further evaluation, expressed by the coefficients of efficiency of the analyzed technologies, or advance in clinical comparability of technologies to assess the relative costs in future. However, in regards to national studies based on the method of the cost minimization, weoften face the absence of the "effectiveness analysis" conducted by an author or its incorrect results refuted by the literature search process. Hereby, the analysis of "cost-minimization» in such cases provides false data, which generally has a misleading nature and reduces the credibility of the pharmacoeconomics in Russia.
- ✓ Deliberate errors and incorrect assumptions made by authors most often are related to the analysis of efficiency, choice of source data on the structure and amount of the costs, as well as to the time horizon of research and modeling results.

One of the examples with a kind of incorrect reference to the methodological analysis can be considered the analyzed paper dedicated to the pharmacoeconomic evaluation of the application of LHRH analogues in the treatment of prostate cancer [1]. This study focused on evaluating the use of agonists luteinizing hormone-releasing hormone (LHRH) in the Russian pharmaceutical market, according to their dosage and frequency of injections per cycle of therapy in the treatment of prostate cancer (PCa). The purpose of this study was to determine how the existing differences in the efficiency and frequency of the application of medicines, along with different prices for medicines of LHRH agonists affected the overall annual cost of treatment. The study included the following medicaments with regard to their form:

1. Eligard fit for 1, 3 and 6 months of receiving
2. Zoladex - 1 and 3-month form
3. Buserelin - 1-month form
4. Lyukrin Depot - 1-month form
5. Diferelin - 1-month form

As the main method of the analysis the "cost-effectiveness» was in the limelight of the authors' attention. The data considered in the analysis of cost included: frequency of injections for various forms of medicines (12 injections for 1 month formulations, 4 to 3 months injection molds and 2 to 6 months); the number of physician visits depending on the frequency of injection of the appropriate medicine; therapy of side effects by the Venlafaxine medicine; cost of medicines in the 12 months of the study horizon.

The average annual cost of medicines was consisted of the total cost of medicines for a year of treatment on the basis of IMS Health Russia, as well as of the cost of relief and side effects of injection of medicines. Also, when assessing the average

cost it was assumed that about 2.5% of patients discontinued treatment for 1 year, and hence would receive half therapeutic dose when compared with patients who would complete the treatment.

The cost of one year of therapy through the individual medicaments ranged from 57 184 rubles (Eligard, 6 months.) to 123,813 rubles (Diferelin). The cost of the medicaments' use was based on the price of the visit to a physician for injections, which was adopted by the authors, as mentioned in the article, on the basis of norms of financing approved by the RF Government on the average for 3900 rubles per visit. But it's known, that some of the open pricelists of Russian hospitals offer significantly lower costs for such procedures. Thus, according to the pricelist of the hospital of the First MSMU after I.M. Sechenov, the cost for the intramuscular or subcutaneous injection is 150 rubles. Initial visit to an urologist - 800 rubles, the subsequent - 700 rubles. According to the pricelist of the Institute of Urology, the RF Ministry of Health, the cost of intramuscular or subcutaneous injection is 100 and 150 rubles, respectively, the initial consultation at urologist ranges from 1100 to 2450 rubles, the secondary - from 850 to 1950 rubles depending on the qualifications of the specialist. In this sense,ifthe analysisof costswas formedon the basis of a comprehensive price data onthe cost of open procedures, the initial reception and injection,according to the pricelistof the hospital of the First MSMU named afterI. M.Sechenov would be 950 rubles, the subsequent - 850 rubles; according to the Institute of Urology, the Ministry of Health, the initial reception costs would be about 1900 rubles, later - about 1525 rubles; the average cost of the primary ingestion of the medicine, as well as considering a visit to doctor would be 1425 rubles, the subsequent - 1187 rubles.

So, the recount cost analysis conducted only in Moscow revealed that the estimated costs based on the individual taking of the drugs is significantly lower than the value used by researchers, which generally means lowering the annual cost of therapy (2.7 times lower than for the initial reception and 3.2 times for the followed below) (Table 1).This example illustrates the significant impact on the final results of analysis of the selected information source.

Table 1.Results of the analysis of the open pricelists of the hospital of the First MSMU after I.M.Sechenov and Institute of Urology of the Ministry of Health (Moscow)

Cost category	Pricelists	
	First MSMU after I.M.Sechenov	*Institute of Urology of the Ministry of Health*
Intramuscularinjection	150 rub.	100 rub.
Subcutaneousinjection		150 rub.
Initialvisit tourologist	800 rub.	1100 - 2450 rub.
Subsequentvisit tourologist	700 rub.	850 – 1950 rub.
TOTAL	***850 - 950 rub.***	***1525 - 1900 rub.***

As a result, the researchers concluded that the budget savings in the transition to the use of 6 –month lasting form of Eligard, would be an average of 50,552 rubles per patient for a year, i.e. the move of 1000 patients from the existing medicaments to the 6 –month lasting form of Eligard, it would exceed 50 million rubles per year, or 250 million rubles within 5 years.

However, such an assessment of the budget savings, which implies multiplication costs for the management of patients for one year over the number of years in terms of modeling for more than 2 years, is not correct in terms of the modern methodology of pharmacoeconomics. For the long-term modeling the assessing of the amount of the cost of the selected horizon studies is conducted taking into account the discounting - the conversion of future costs and effects of today's prices with the discount rate equal to 3-5% per year. Thus, if we assume that the savings per year will be about 50 million rubles, the savings for 5 years, with regard to the discount rate of 3.5 %, will be 233 101 856.28 rubles, which is 7% less than the amount presented by the authors. This methodological error, coupled with properly selected source costs of injection to patients leads to significantly inflated test results.

In the conclusion, the authors, summarized the following: «the minimum cost of using Eligard 45 mg is subsequent to the high efficiency of the therapy ...» and «a 3-month lasting form of Eligardhas a good cost/efficiency ...» However, it becomes obvious from the publication of the text that the efficacy was not considered and the conclusions formulated this way may result in confusing issues.

In 2012 a study paper was published on the comparison of clinical and economic evaluation of hormonal therapy for prostate cancer using analogues of gonadotropin releasing hormone (leuprolide, goserelin, triptotrelin) [2].In this study, on the whole, a similar analysis is conducted on the «minimization of costs» for the medicaments such as Lyukrin depot, Zoladreks and Diferelin in the form of monthly injections. In this study there's only assessed the cost of therapy by compared medicines for one patient and for 100 patients per year. Thus, this study is identical to the previously discussed, but it does not consider the cost of injection and edema of side effects, as well as it considers a narrower range of comparators and does not include the leader medicine of the previously published study. It the end of the article the authors shared a link to the above discussed publication - «Pharmacoeconomic evaluation of the application of LHRH analogues in the treatment of prostate cancer in Russia: the rationale for preferential supply» and confirmed the compliance of the results of the assessments. This, obviously, devalues the presented paper.

Another example of studies where the method of analysis of "cost minimization" was used inappropriately is the publication titled "Clinico-economic analysis on the use of pazopanib in advanced kidney cancer» [4]. The aim of this study was to analyze the use of pazopanib compared with other medicaments for targeted therapy of kidney cancer. The compared alternatives were the following medicaments: sunitinib, sorafenib, bevacizumab plus interferon alfa-2a, everolimus and temsirolimus. At the time of analysis, the clinical researches over the direct comparison of the selected medicaments were missed, which resulted in the need for indirect comparison.

In the scopes of the study there were conducted the analysis of the efficacy and safety of selected medicaments, the calculation of the expected cost for treatment of advanced kidney cancer listed by targeted medicaments and the subsequent calculation of the clinical and economic indicators.

For the assessment of the efficiency of the compared medicaments the researchers chose the method of non-direct comparison with the use of general control. For the realization of this objective the information search was designed and carried out the criterions of which were the presence of RTC (randomized control trials), participation of patients only with metastatic kidney cancer, study of clinical efficiency of medicaments. As a result of the information search process, the following studies were selected: Pazopanib - C.N. Stenbergetal (2010), sunitinib - R.J. Motzeretal (2009), bevacizumab - B. Escudieretal (2007), sorafenib - B. Escudieretal (2007), everolimus – R.J. Motzeretal (2010) and temsirolimus - G. Hudesetal (2007).

It's worth mentioning that for a range of studied medicaments the control factor in the scopes of clinical study was Placebo (pazopanib, sorafenib, everolimus), and for sunitinib, bevacizumab, sorafenib and temsirolimus as a control performed interferon alfa-2a. As mentioned by the authors of the study, it had been hard to find studies containing the comparison of placebo and interferon alfa-2a, and in regard to which interferon alfa-2a was compared with medgidroksiprogesteron, which is equal to placebo by its clinical efficacy, but different from it in regards to safety.

In the further phase of the study they excluded the medicaments of evevrolimus (due to the heterogeneity of patients included in the study) and temsirolimus (lack of data on the relative frequency of disease progression). In the further analysis pazopanib was compared with sunitinib and bevacizumab in the first-line therapy and with sorafenib in the second-line therapy.

As a result of the analysis of effectiveness, the researchers identified and presented the following data:

- The relative frequency of use for the progression of pazopanib versus sunitinib was 1.03 (95% CI 0,62-1,70).
- The relative frequency of use for the progression of pazopanib versus bevacizumab was 0.88 (95% CI 0,53-1,46).
- The relative frequency of use for the progression compared with pazopanibsorafenib was 1.23 (95% CI 0,75-2,01).

It was concluded that the statistically significant probability of time without disease progression was absent, and all the medicaments were recognized equal in the clinical efficacy. The further analysis was based on the method of the "cost minimization.»

However, the information search conducted showed that there had been data on the comparative efficacy of the medicaments of sunitinib, sorafenib and bevacizumab, as reflected in a number of published clinical studies (Figlinet. al. 2008 for sunitinib, Escudier et.al. 2009 for bevacizumab and Gollob J.A. 2007 for sorafenib). According to the data obtained from these studies, there's a significant difference in the effectiveness of the considered technologies, as expressed through the life years beforehand the progression, and through the shared years of life. Thus, the data showed that patients who had received sunitinib, had an average time to the progression of 1.35 years, and the overall survival of these patients was 2.9 years; the patients treated with IFN -α, sorafenib and bevacizumab had time to the progression of 0.72; 0.83; 1.15 years and the overall survival was 2.47; 2.74 and 2.67, respectively (Table 2).

Table 2.Results of the analysis of efficacy of targeted therapy for kidney cancer.

Medicaments	**Sunitinib**	**IFN-α**	**Bevacizumab**	**Sorafenib**
Reference	[13]	[12]	[14]	[12]
Time interval before the disease progression	1,35 years	0,72 years	0,83 years	1,15 years
Overall survival	2,9 years	2,47 years	2,74 years	2,67 years

Thus, the findings highlight the unreasonableness of the analysis of «minimizing costs», as the effectiveness of compared medicaments is not equal.

Hereby, the assessment of the health technologies in general, and pharmacoeconomics, in particular, allows us to carry out a comprehensive assessment of innovative and conventional medical technologies; these research areas are affordable and effective tool for the decision-making in the health care, regardless of the level of decision-making. The pharmacoeconomic models, considered as the visualized representation of the analysis, simplify the applicability of the study results and enable to put the results of the pharmacoeconomic analysis into practice more actively, including as well the incorrect choice (on the inappropriate level), and etc. At the same time, an incorrect choice of data on the efficacy and safety, pharmacoeconomic analysis methodology and the use of simplified models can lead to incorrect results.

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