



# Pharmacoeconomic evaluation of drug supply for chemotherapy in small cell lung cancer

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Academic editor: Oleg Gudyrev ♦ Received 16 March 2023 ♦ Accepted 25 May 2023 ♦ Published 01 July 2023

**Citation:** Lunyova YeA (2023) Pharmacoeconomic evaluation of drug supply for chemotherapy in small cell lung cancer. Research Results in Pharmacology 9(3): 1–9. <https://doi.org/10.18413/rrpharmacology.9.10037>

## Abstract

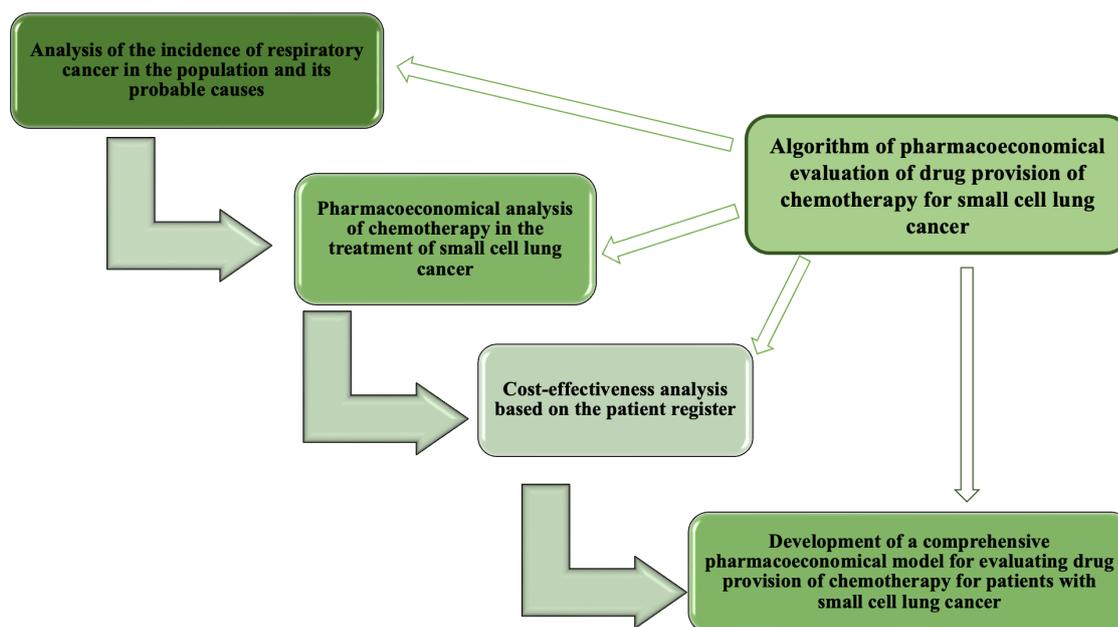
**Introduction:** In recent decades, pharmacoeconomic analysis of multiple diseases has significantly progressed; in particular, the most prevalent one is the cost-effectiveness analysis. Chemotherapy remains the leading and most effective treatment option for small cell lung cancer, which accounts for more than a quarter of all other forms of respiratory cancers.

**Materials and Methods:** An assessment of the incidence of lung cancer and its probable causes was carried out. The main methods used in the study were cost-of-treatment analysis, ABC/VEN analysis and cost-effectiveness analysis. Survival rates (number of years or months, interval and average number of years/months) and the cost of a month of life were also evaluated.

**Results and Discussion:** The results obtained on the basis of a questionnaire survey of patients with lung cancer demonstrate that smoking is the leading risk factor – 24.9% of the pro rata contribution. The author identified the most expensive drugs, costing 60-80% of the budget, that is scheme 2 ‘etoposide + carboplatin’, and the least expensive drugs, costing 5-10% of the budget, which are auxiliary drugs. According to the study results, patients managed following a chemotherapy regimen ‘etoposide + carboplatin’ have the highest survival rate at the highest cost of treatment compared to patients following a chemotherapy regimen ‘cyclophosphamide + doxorubicin + vincristine’, which is the least expensive.

**Conclusion:** Evidence-based comprehensive pharmacoeconomic model for evaluation of drug supply for chemotherapy in small cell lung cancer improves registration of history cases and allows for pharmacoeconomic cost-effectiveness analysis considering features of each patient.

## Graphical abstract:



## Keywords

small cell lung cancer, chemotherapy, cost-effectiveness, pharmacoconomics, ABC/VEN analysis, cost of the survived month

## Introduction

The urgency of pharmaco-economic studies is due to the fact that their results provide an opportunity to scientifically validate the scheme of medical interventions and use of medications, and choose the most appropriate variant of all possible options, both for the sake of a patient and to reduce costs of treatment for medical facilities (Svistunov et al. 2016; Anoshkina 2020; Petrov 2022; Yagudina and Gavrilova 2022).

In recent decades, pharmaco-economic analysis of multiple diseases has significantly progressed; it includes such methods as ‘cost analysis’, ‘cost minimization analysis’, ‘cost-effectiveness analysis’, ‘cost-utility analysis’, and ‘cost-benefit analysis’. The most prevalent is the ‘cost-effectiveness’ analysis, which determines the ratio of costs and efficiency obtained in the compared therapeutic options (Yagudina and Skulkova 2011).

Lung cancer ranks first in the structure of malignant neoplasms in Russia and globally. It is more often detected in men than in women and is characterized by the highest mortality rates among oncological diseases. The highest mortality rate is associated with the difficulties of its early detection (especially for small cell lung cancer), since it develops asymptotically for a long time, and has manifestations similar to non-oncological respiratory diseases (pneumonia, alveolitis, tuberculosis). Therefore, most patients consult oncologists when the disease has already progressed to stages III-IV (Chen 2016; Tsiouprou et al. 2019; Makimbetov and Dzhunushalieva 2019; Mukhambetzhon et al. 2020; Ulumbekova et al. 2022).

According to experts of the Department of Chemotherapy, at N.N. Blokhin National Medical Research Center of Oncology, Ministry of Health of the Russian Federation, small cell lung cancer develops quickly, is diagnosed late, and forms metastases aggressively; the disease is characterized by a severe course of treatment when symptoms appear, the survival rate of patients is relatively low. That is why, research interest in this disease is growing and will continue to grow, since every year the number of people suffering from this pathology increases (Kuzminov et al. 2019).

Chemotherapy remains the leading and most effective treatment option for small cell lung cancer, which accounts for more than a quarter of all other forms of respiratory cancers (Bagrova et al. 2013; Napreenko et al. 2020; Kuzminov et al. 2020).

Therefore, pharmaco-economic evaluation of drug supply for chemotherapy in the treatment of patients with small cell lung cancer is a critical area of research. The result of a pharmaco-economic analysis of multiple standard chemotherapy regimens for small cell lung cancer will demonstrate the level of costs and their effectiveness, and allow making decisions about the most appropriate therapeutic options.

Research literature searches give no direct references to the above subject area in the published research papers. It has been confirmed that pharmaco-economic evaluation of the chemotherapy regimens administered for small cell lung cancer treatment is an urgent task of modern medicine requiring prompt solution.

Most clinical research studies involving small cell lung cancer highlight issues to improve its diagnostics

(Früh et al. 2013; Yang et al. 2019; Dingemans et al. 2021; Kosterina and Grinberg 2019; Gimalova et al. 2020; Esakov et al. 2022; Grigoruk et al. 2022; Skurikhin et al. 2022 and others) and treatment (Bagirova et al. 2013; Gandhi et al. 2018; Tsiouprou et al. 2019; Napreenko et al. 2020; Kuzminov et al. 2020; Meijer et al. 2022).

Despite the increased number of pharmacoeconomic investigations related to lung cancer management, there are few studies on pharmacoeconomic analysis of pembrolizumab and nivolumab application in the second line of therapy for advanced non-small cell lung cancer (Avksentiev et al. 2019) and pharmacoeconomic evaluation of the effectiveness of chemotherapy for malignant neoplasms of the bronchi and lungs (Yarovoy and Shikina 2020).

Currently, interest in the problem of pharmacoeconomic evaluation of drug supply for chemotherapy in the treatment of patients with small cell lung cancer results from the increased incidence rate, severity, high degree of the disease aggressiveness, its high sensitivity to chemotherapy, and younger age of patients newly diagnosed with this pathology.

Thus, the development of a pharmacoeconomic model and methodological approaches for pharmacoeconomic evaluation of drug supply for chemotherapy in the treatment of patients with small cell lung cancer, including cost-effectiveness analysis, is a crucial area of medical research.

**The aim of study:** to validate a pharmacoeconomic model for evaluation of drug supply for chemotherapy in the treatment of patients with small cell lung cancer.

## Materials and Methods

### Study design

Evaluation of the lung cancer incidence and its probable causes included a statistical data analysis on the disease incidence in the population, an analysis of carcinogenic environmental factors based on laboratory control findings from the Center for Hygiene and Epidemiology of Voronezh Region in 2017-2022, and an investigation of the lifestyle of the patients with small cell lung cancer based on the questionnaire data (2017-2021, 410 patients diagnosed with small cell lung cancer). The experimental protocols were approved by the local Ethical Committee of Voronezh State Medical University named after N.N. Burdenko of the Ministry of Health of the Russian Federation (Minutes No. 7 of 22.10.2020).

The authors performed a pharmacoeconomic analysis of the costs for basic and auxiliary drugs included in three different chemotherapy regimens for small cell lung cancer (regimen 1: **etoposide** 100 mg/m<sup>2</sup> on days 1-3 + **cisplatin** 100 mg/m<sup>2</sup> on day 1; regimen 2: **etoposide** 100-120 mg/m<sup>2</sup> on days 1-3 + **carboplatin** AUC 4-6 on day 1; regimen 3: **cyclophosphamide** 1000 mg/m<sup>2</sup> on day 1 + **doxorubicin** 50 mg/m<sup>2</sup> on day 1 + **vincristine** 1.5 mg/m<sup>2</sup> on day 1).

Costs for auxiliary drugs, which are used to ensure means to ensure water load and to eliminate adverse reactions after chemotherapy (**ondansetron**, **metoclopramide**, **furosemide**, sodium chloride solution complex [**potassium chloride** + **calcium chloride** + **sodium chloride**], **sodium bicarbonate**), were also evaluated.

The main methods used in the study were cost-of-illness analysis, ABC/VEN analysis, and cost-effectiveness analysis.

The 'cost-of-the-disease' parameters included direct

costs: the cost of a bed-day, laboratory and diagnostic tests, and the cost of medications. Calculations were made per 1 course of chemotherapy.

ABC/VEN analysis divided the drugs into groups – A (the most expensive drugs), B (less expensive), C (the least expensive), and into three categories – V (vital), E (essential), and N (non-essential).

### Statistical analysis

For a cost-effectiveness analysis, the minimum sample size of patients was validated? and the analysis was performed based on the recommendations developed by A.N. Narkevich and V.N. Vinogradov, who generalized common approaches used to validate the sample size (the method by V.I. Paniotto, the method by K.A. Otdelnova, the method by N. Fox, the transformation of the margin of sampling error method, etc.); this provides the "enhanced accuracy of research", and is recommended for use when preparing PhD dissertations and making final conclusions. This validation demonstrated that the minimum sample size with an accepted statistical error of no more than 5% should be at least 400 patients.

To evaluate the treatment effectiveness parameters, the author analysed medical records of 638 patients who underwent chemotherapy for small cell lung cancer during 2017-2021 in Lipetsk regional oncological hospital and Voronezh regional oncological hospital, since it was impossible to provide the required minimum sample size within specified period on the basis of one hospital. The analysis included survival rates (number of years or months, interval and average number of years/ months), and the cost of a survived month of life.

## Results and Discussion

The main lines of research were:

- 1) to evaluate the lung cancer incidence and its probable causes;
- 2) to perform pharmacoeconomic analysis of therapy for small cell lung cancer;
- 3) to develop a comprehensive pharmacoeconomic model for evaluation of drug supply for chemotherapy in small cell lung cancer.

The first stage of research was carried out at the Center for Hygiene and Epidemiology in Voronezh Region.

The second and third stages of research were carried out based on the data obtained in Lipetsk regional oncological hospital and Voronezh regional oncological hospital.

The main unit for analysis in the study was the cost of drugs included in three different chemotherapy regimens for small cell lung cancer (regimen 1; regimen 2; regimen 3).

The cost of medical treatment was calculated for 11 drugs (**cisplatin**, **carboplatin**, **etoposide**, **vincristine**, **cyclophosphamide**, **doxorubicin**, **ondansetron**, **metoclopramide**, **furosemide**, sodium chloride solution complex [**potassium chloride** + **calcium chloride** + **sodium chloride**], **sodium bicarbonate**) used in the analysed chemotherapy regimens for small cell lung cancer.

Pharmacoeconomic analysis of the small cell lung cancer therapy for the analysed treatment regimens included 'cost-of-illness analysis', 'ABC/VEN analysis', and 'cost-effectiveness analysis'.

The treatment effectiveness parameters were evaluated based on the medical records of 638 patients who had undergone chemotherapy for small cell lung cancer

during 2017-2021 in Lipetsk regional oncological hospital and Voronezh regional oncological hospital.

### Respiratory cancers in the population: analysis of the incidence and probable causes

The analysed respiratory cancer incidence in the population of Voronezh and Lipetsk regions demonstrated that the annual morbidity values of trachea, bronchi, lung cancers in men range within 61.19 - 86.7 cases per 100 thousand male populations; in women this parameter was much lower and equalled 9.89–16.80 cases per 100 thousand female populations. Long-term average annual value in men was  $77.89 \pm 3.62$  cases per 100 thousand, in women –  $15.95 \pm 0.55$  cases per 100 thousand in Voronezh region; that average annual value was higher compared to Lipetsk region ( $58.23 \pm 12.9$  and  $14.14 \pm 2.5$ , respectively). However, in Voronezh region there was a downward trend in the number of cases of diseases (the 5-year rate of decrease for men was 16.60%, for women – 10.47%), while in Lipetsk region an upward trend was recorded (the 5-year growth rate in men was 5.26%, in women – 24.18%).

The analysed probable risk factors and causes of respiratory cancers demonstrated that environmental factors (concentration of carcinogens in the atmospheric air was detected using objective methods of laboratory control; a radioactive factor associated with the probable presence of radon in the air of residential premises) were not the leading ones, since the risks were at an acceptable level, and no correlations with the morbidity rates of the population were traced.

The analysed data from a questionnaire survey of the patients with lung cancer revealed that smoking was the leading risk factor and constituted 24.9% of pro rata contribution. Notably, 82.4% of patients smoked prior to being diagnosed with cancers of the trachea, bronchi, lungs (90.5% of male patients, 37.1% of female patients). Of 338 smoking patients, 14 patients smoked 1-2 cigarettes per day (4.1% of smokers), 76 patients smoked 3-5 cigarettes per day (22.4%), 128 respondents smoked 6-10 cigarettes per day (37.8%) and 121 patients smoked more than 10 cigarettes a day (35.7%).

Thus, lung cancer ranks the first in the structure of oncological morbidity of the population, the ratio of the trachea, bronchi, lung cancers based on gender (m/f) ranges within 4.53-6.52 across years. The leading cause is smoking. Lung cancer is diagnosed at stages III-IV in more than 50% of cases (in Voronezh region, cancer stage III was diagnosed in 28.8% of cases, cancer stage IV – 34.6%; in Lipetsk region, cancer stage III – 22.1%, cancer stage IV – 40, 3%), the fact requiring improved preventive diagnostic interventions of medical facilities.

### Pharmacoeconomic analysis of chemotherapy in the treatment of lung cancer

The analysed direct costs for the treatment of small cell lung cancer demonstrated that the cost for one course of chemotherapy according to regimen 1 ranged within 9521.80-11797.55 rubles, for one course of chemotherapy according to regimen 2 ranged from 8150.20 to 10947.35 rubles, and for one course of chemotherapy according to regimen 3 ranged from 5830.40 to 6929.90 rubles. The costs included the cost for a bed-day of a patient's stay at hospital – from 660 to 1650 rubles, with an average value equalling 1305 rubles; and the cost of diagnostic and laboratory tests for one course of treatment ranging from

1265 to 2105 rubles, with an average value equalling 1685 rubles.

It has been established that the cost of the basic and auxiliary drugs for one chemotherapy course depending on the treatment regimen was from 2970.60 rubles up to 5922.00 rubles: when taking the average values, it amounted to 4742.60-5286.80 rubles for regimen 1, 3892.40-4005.20 rubles for regimen 2, and 3174.90-3605.40 rubles for regimen 3. Elimination of undesirable (side) effects of basic medications cost from 80.20 to 184.90 rubles, with an average value equalling 131.00 rubles.

Evaluation of the cost structure of various chemotherapy regimens for small cell lung cancer based on ABC/VEN analysis demonstrated that the regimen 1 treatment (etoposide + carboplatin) accounted for 61.4-61.9% in the cost structure, the regimen 2 treatment (etoposide + cisplatin) – 20.7-20.8%, and the regimen 3 treatment (cyclophosphamide + doxorubicin + vincristine) – 8.9-10.2%. The cost of auxiliary drugs accounted for 7.7-8.4% in the cost structure (Table 1).

**Table 1.** Results of the ABC analysis: the share of financial costs of the provision of drugs for chemotherapy in small cell lung cancer

Groups of medications	Chemotherapy regimens	Financial costs of medications and their share of total costs	
		Abs., rubles	%
<b>Lipetsk regional oncological hospital</b>			
A	Regimen 2	382 455.20	61.4
B	Regimen 1	129 121.30	20.7
	Regimen 3	63 225.90	10.2
C	Auxiliary drugs	48 168.00	7.7
<b>Voronezh regional oncological hospital</b>			
A	Regimen 2	740 157.00	61.9
B	Regimen 1	248 460.00	20.8
	Regimen 3	107 082.00	8.9
C	Auxiliary drugs	100 884.50	8.4

VEN analysis performed at the Lipetsk regional oncological hospital demonstrated that in 2021 all drugs applied in three chemotherapy regimens for the small cell lung cancer treatment were included in category V (vital), since they were from the list of vital drugs; this accounted for 92.3% of the costs. Five auxiliary drugs constituted category E (essential), they accounted for 7.7% of the costs. There were no drugs in category N (non-essential) (Table 2).

**Table 2.** Results of the VEN analysis: the share of financial costs and % of all drugs for chemotherapy in small cell lung cancer

Groups of medications based on financial costs	Chemotherapy regimens	Financial costs of medications and their share of total costs	
		Abs., rubles.	%
<b>Lipetsk regional oncological hospital</b>			
V	Regimen 2	382 455.20	61.4
	Regimen 1	129 121.30	20.7
	Regimen 3	63 225.90	10.2
E	Auxiliary drugs	48 168.0	7.7
N	0	0	0
<b>Voronezh regional oncological hospital</b>			
V	Regimen 2	740 157.00	61.9
	Regimen 1	248 460.00	20.8
	Regimen 3	107 082.00	8.9
E	Auxiliary drugs	100 884.50	8.4
N	0	0	0

VEN-analysis performed at the Voronezh regional oncological hospital demonstrated similar results: category V (vital) included drugs applied in three chemotherapy regimens, they accounted for 91.6% of the costs; category E (essential) included 5 drugs, they accounted for 8.4% of costs; no drugs were included in category N (non-essential).

The results of the ABC/VEN-analysis performed at the Voronezh regional oncological hospital and Lipetsk regional oncological hospital demonstrated that of all drugs included in the list, 75% were vital, and 25% were essential (Table 3).

**Table 3.** Results of the ABC/VEN analysis, %

Groups of medications based on financial costs	Distribution of medications depending on the degree of need			Average
	V	E	N	
<b>Lipetsk regional oncological hospital</b>				
A	25	0	0	25
B	50	0	0	50
C	0	25	0	25
<b>Total</b>	<b>75</b>	<b>25</b>	<b>0</b>	<b>100.0</b>
<b>Voronezh regional oncological hospital</b>				
A	25	0	0	25
B	50	0	0	50
C	0	25	0	25
<b>Total</b>	<b>75</b>	<b>25</b>	<b>0</b>	<b>100.0</b>

Notably, group A (61.4% of total costs and 61.9%, respectively) included 25% of drugs from group V, 50% of drugs from group E and 0% of drugs from group N. Group B (30.9% of total costs and 29.7%, respectively) included 50% of medications from group V, and 0% of medications from groups E and N. Group C (7.7% of total costs and 8.4%, respectively) included 0% medications from group V, 25% of medications from group E, and 0% medications from group N.

Thus, parallel studies conducted at two medical facilities – the Lipetsk regional oncological hospital and Voronezh regional oncological hospital – evidenced that the structure of costs and the results of ranking for drugs

in terms of relevance had no significant differences.

The author identified the most expensive drugs, costing 60-80% of the budget: this was regimen 2 (etoposide 100-120 mg/m<sup>2</sup> on days 1-3 + carboplatin AUC 4-6 on day 1), and the least expensive ones, costing 5-10% of the budget: they were auxiliary drugs necessary to ensure the course of chemotherapy and eliminate unwanted reactions, i.e. furosemide 10 mg/mL, metoclopramide 5 mg/mL 2 mL, 5% sodium bicarbonate solution, 0.9% solution NaCl.

#### Cost-effectiveness analysis based on the patient register

Due to high variability of the survival rate (from 0.6 to 132.5 months), it was appropriate to evaluate the effectiveness of the regimens in terms of the patients' distribution by 1, 2, 3 and 4-year survival rate groups (Table 4, Fig. 1).

It was found that administration of the treatment regimen 'etoposide + carboplatin' in patients with stage I resulted in an almost 2-time higher 1-year survival rate (46.2%) than administration of the treatment regimen 'etoposide + cisplatin' (27.3%).

As reported, the percentage of patients with stage I who received 'etoposide + cisplatin' had the highest 3-year survival rate (45.5%), the percentage of patients with stage I and 3-year survival rate who received 'etoposide + carboplatin' was 15.4%.

Patients with stage III had approximately similar percentage of 2-year survival rate: this value was 34.4% in patients treated following regimen 1, 33.9% in patients treated following regimen 2 and 42.9% in patients treated according to regimen 3. Three-year survival was 8.4% for regimen 1, 11% for regimen 2, and 7.1% for regimen 3.

These values evidence that patients receiving the chemotherapy regimen 'etoposide + carboplatin' have the highest survival rate at the highest cost of treatment, compared with the regimen 'cyclophosphamide + doxorubicin + vincristine', which is the least expensive.

Thus, it was found that, at stages III and IV, it is more rational to give preference to the cyclophosphamide + doxorubicin + vincristine regimen, and at stages I and II, priority should be given to the most cost-intensive regimens.

**Table 4.** Evaluation of the 1, 2, 3 and 4-year survival rate (absolute number of patients, % of patients)

Survival rate	Therapy regimens											
	Regimen 1 etoposide + cisplatin (n=262)				Regimen 2 etoposide + carboplatin (n=285)				Regimen 3 cyclophosphamide + doxorubicin + vincristine (n=91)			
	I	II	III	IV	I	II	III	IV	I	II	III	IV
<b>Absolute number of patients</b>												
1-year	3	6	66	71	6	6	61	85	-	-	25	22
2-year	1	12	45	19	2	11	43	19	-	-	24	10
3-year	5	5	11	2	2	7	14	3	-	-	4	-
4-year	2	3	9	2	3	5	9	3	-	-	4	2
<b>Total number of patients</b>	<b>11</b>	<b>26</b>	<b>131</b>	<b>94</b>	<b>13</b>	<b>29</b>	<b>127</b>	<b>116</b>	<b>0</b>	<b>0</b>	<b>57</b>	<b>34</b>
<b>% of patients</b>												
1-year	27.3	23.1	50.4	75.5	46.2	20.7	48.0	73.3	0	0	44.6	64.7
2-year	9.1	46.2	34.4	20.2	15.4	37.9	33.9	16.4	0	0	42.9	29.4
3-year	45.5	19.2	8.4	2.1	15.4	24.1	11.0	2.6	0	0	7.1	0.0
4-year	18.2	11.5	6.9	2.1	23.1	17.2	7.1	2.6	100	0	5.4	5.9
<b>Total number of patients</b>	<b>11</b>	<b>26</b>	<b>131</b>	<b>94</b>	<b>13</b>	<b>29</b>	<b>127</b>	<b>116</b>	<b>1</b>	<b>0</b>	<b>56</b>	<b>34</b>

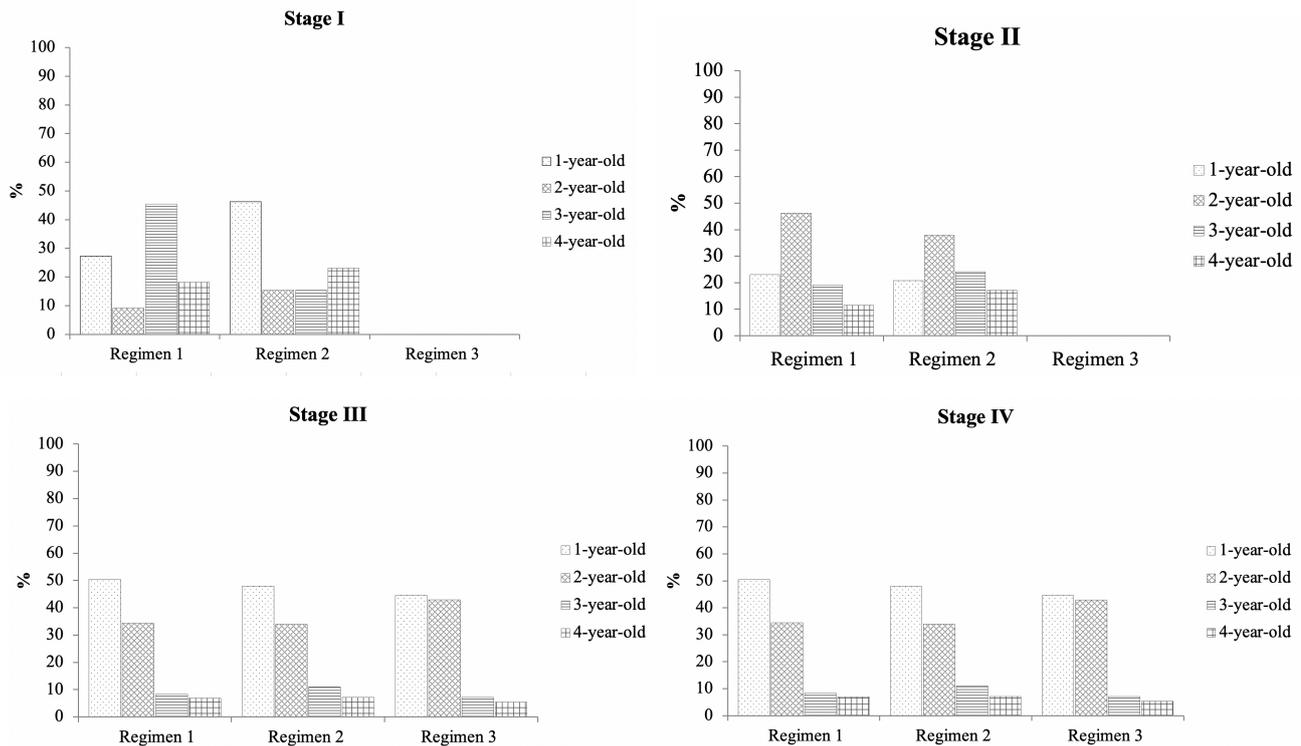


Figure 1. Survival of patients depending on the treatment regimen.

**Developed comprehensive pharmacoeconomic model for evaluation of the drug supply for chemotherapy in patients with small cell lung cancer**

A comprehensive pharmacoeconomic model is aimed to improve the registration of history cases of patients with small cell lung cancer to provide pharmacoeconomic cost-effectiveness analysis.

The registration of history cases of patients with small cell lung cancer was improved for pharmacoeconomic analysis using modern computer data processing algorithms. To implement this task, the author developed a computer program (No. 2023611048 dated January 16, 2023) to carry out a pharmacoeconomic analysis of small cell lung cancer treatment. The pharmacoeconomic analysis was performed to assess economic efficiency of

pharmacotherapy in oncological inpatients having varying severity of the disease.

The software module automatically calculates the cost of therapy for a particular patient; this fact was taken into account in the subsequent pharmacoeconomic analysis.

The program provides automatic calculation of the following required parameters: patient’s age; the number of months survived; and direct medical costs. Pharmacoeconomic analysis forms the patient sample parameters from the database; implements pharmacoeconomic analysis algorithms for a sample of patients; visualizes the analysis results in the form of a list of tables. The data that are entered about the patient, their medical history and treatment are presented in the diagram (Fig. 2).

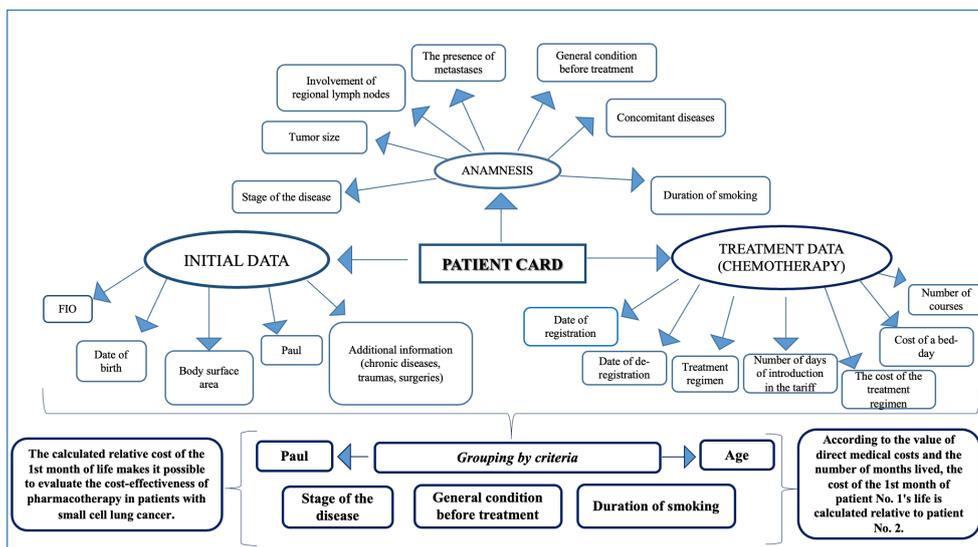


Figure 2. Total scheme of the program.

The program is designed to conduct a pharmacoeconomic analysis of chemotherapy for patients with small cell lung cancer of varying severity in oncological hospitals to assess the economic efficiency of pharmacotherapy.

The algorithm for processing and consolidating information from the search results in the database allows selecting patients that meet the specified search criteria. Patients who meet the criteria are placed in the same group and then compared, since these patients, despite the same parameters, receive different chemotherapy and, as a result, have different survival rates after received treatment. Next, patients from the sample are compared in pairs. If the next two patients in the line are administered different treatment regimens, then a pharmacoeconomic analysis is performed for this pair of patients:

- based on the value of direct medical costs and the number of months survived, the cost of the 1<sup>st</sup> month of life of patient No. 1 is calculated relative to patient No. 2;
- the calculated relative cost of the 1<sup>st</sup> month of life allows evaluating the cost-effectiveness of pharmacotherapy in patients with small cell lung cancer.

For each pair of patients, a resulting table is formed that represents the analysed findings of pairs of patients, they are displayed as a list in the "Analysis" section of the main program window.

A table is formed according to groups of patients who receive the same therapy regimen, with the criteria presented above. The average number of survival months and the average cost of treatment are calculated for this group of patients. Then, the cost-effectiveness analysis of chemotherapy for small cell lung cancer is carried out for the group of patients with the highest statistical significance.

Pharmacoeconomic analysis "costs - effectiveness" is automatically performed according to the formula:

$$CEA = (DC1 - DC2)/(Ef1 - Ef2)$$

where DC1 and DC2 (direct cost) – direct medical costs for regimen 1 and regimen 2 treatments, respectively;

Ef1 and Ef2 (effectiveness of treatment) – effectiveness of treatment for chemotherapy according to regimens 1 and 2, respectively.

The algorithm for conducting pharmacoeconomic analysis is presented in Figure. 3.

The program was tested on the basis of the Voronezh regional oncological hospital. In particular, there was a sample of patients grouped according to the principle of forming "copy-pair" groups in view of various treatment regimens and a risk factor that aggravates the course of the disease. An example of the software module implementation is processing the data of patients being at risk for the smoking factor who are in the same age group. The criteria to evaluate patients in the database included in one "copy-pair" were gender (men), age (61 years and older), stage of the disease (IIIA, IIIB), general condition before treatment (ECOG 1) and duration of smoking (11-20 years). The analysed survival rate of patients receiving different regimens evidenced that the patient who had undergone the *etoposide + carboplatin* treatment regimen lived 5 months longer than the patient who had received the *etoposide + cisplatin* regimen, and the cost of 1 month of life for this patient was 24488 rubles; thus, prolongation of life in monetary terms amounted to  $24\,488 \times 5 = 122\,440$  rubles.

The implemented program also allowed for a pharmacoeconomic analysis of patient groups, combined according to one criteria – gender (men), age (61 years and older), stage of the disease – (IV),

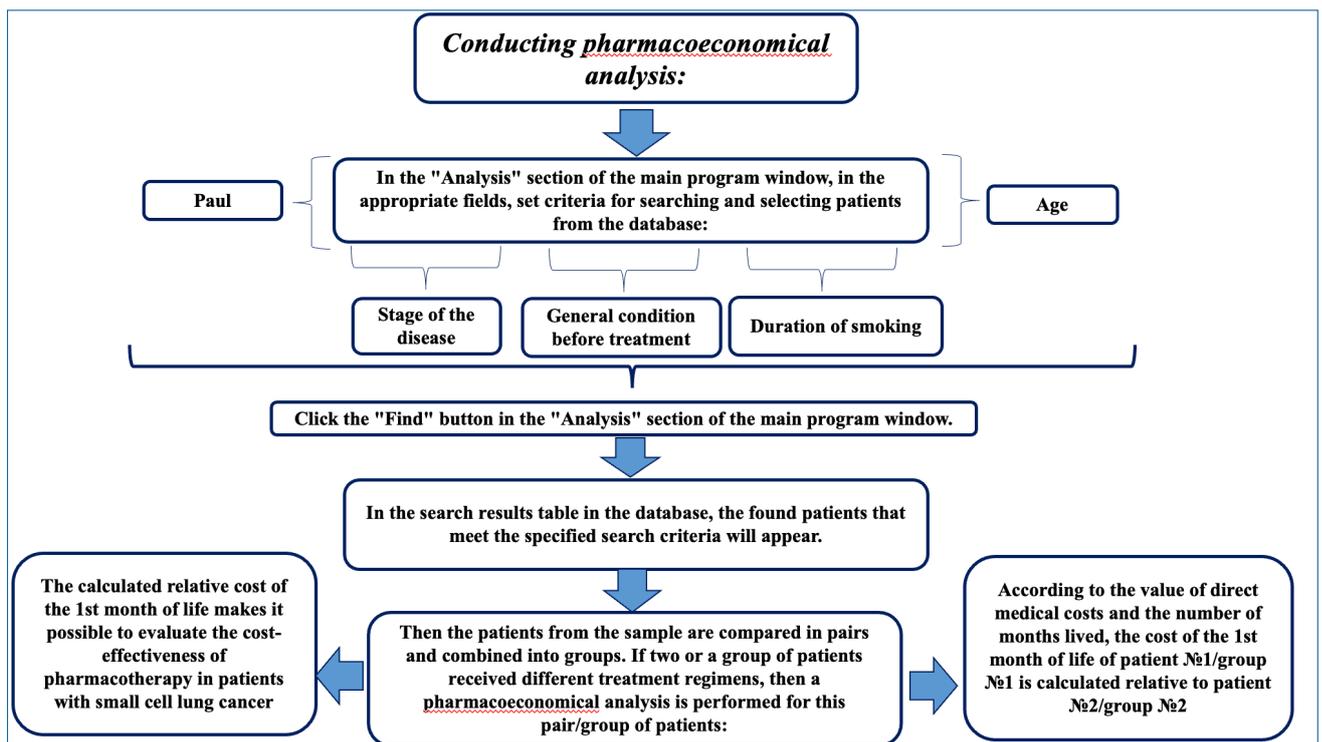


Figure 3. Conducted pharmacoeconomic analysis

general condition before treatment (ECOG 1) and duration of smoking (6–10 years). A survival rate analysis of patients treated with different regimens demonstrated that the group of patients receiving the **etoposide + carboplatin** regimen lived 7 months longer than the group of patients receiving the **etoposide + cisplatin** regimen. The cost of 1 month of life of these patients was 27 676 rubles; thus, prolongation of life in monetary terms was  $27\,676 \times 7 = 193\,732$  rubles.

The results of the study demonstrate that the use of chemotherapy with different costs have different results in terms of survival rate, and, therefore, a more expensive regimen allows extending the patient's life with a moderate cost of a survived month of life.

## Conclusion

The results obtained demonstrate that chemotherapy regimen 2 (**etoposide + carboplatin**) is more often administered at stages I and II for small cell lung cancer treatment – for 52.0% and 57.7% of patients, respectively. At stage III, the priority of use is shifted towards regimen 1 (**etoposide + cisplatin**): it accounted for 41.7%. Therapy regimen 2 also prevails at stage IV: it accounted for 47.5% of cases. Regimen 3 is not administered at stages I and II; however, it is the least expensive in terms of the economic cost. The average survival rate of a patient when administering chemotherapy regimen 2 is 14.3 months; when treated according to chemotherapy regimen 3 makes 18.1 months. Evaluated cost of a survived month of life for patients with stages III and IV evidenced that savings on the cost of a survived month of life for stage III using regimen 3 would be 22 270.3 rubles for 1 month of life, and for stage IV – 11 044.5 rubles. It has been proven that at stages III and IV it is more rational and efficient to use the **cyclophosphamide + doxorubicin + vincristine** regimen, and at stages I and II it is preferable

to administer more cost-intensive regimen 2 ‘**etoposide + carboplatin**’.

It should also be noted that the conducted pharmacoeconomic analysis revealed specificity of its use in oncology, namely, its main aim was to increase the survival rate of patients but not to minimize costs; therefore, it should be recommended for oncological hospitals to conduct this analysis in terms of increased survival rate rather than amount of costs.

Taking into account the complexity of the oncological disease, it is necessary to pay attention to the features of the course of a specific pathology, in particular, the size of the primary tumor, involvement of regional lymph nodes, and presence of distant metastases.

Thus, minimized cost of treatment cannot be the main criterion to evaluate the effectiveness of chemotherapy for small cell lung cancer.

An evidence-based comprehensive pharmacoeconomic model evaluating the drug supply for chemotherapy in patients with small cell lung cancer improves the registration of history cases and allows for a cost-effectiveness pharmacoeconomic analysis considering features of each patient. Validation of a software module that provides statistical analysis of the number of patients with a certain stage of the disease and treatment regimens they receive has shown the potential to improve the quality of medical care at the current level of drug costs. Data on expenses of medical facilities for this pathology are being updated to assess the economic costs of chemotherapy, which allows attracting more funds to medical organizations to provide quality medical care to cancer patients.

## Conflict of interest

The authors do not declare a conflict of interests.

## References

- Anoshkina EV (2020) The role of pharmacoeconomical research in optimizing the quality of drug care. Eurasian Scientific Association [Evrasiiskoe Nauchnoe Ob"edinenie] 9-3(67): 244–248. [in Russian]
- Avksentieva NA, Frolov MYu, Makarov AS (2019) Pharmacoeconomical study of the use of pembrolizumab and nivolumab in second-line therapy of advanced non-small cell lung cancer. Effective Pharmacotherapy [Effektivnaya Farmakoterapiya] 15 (24): 38–47. <https://doi.org/10.33978/2307-3586-2019-15-24-38-46> [in Russian]
- Bagrova SG, Bychkov MB, Gorbunova VA, Kuzminov AE, Naskhletashvili DR (2013) Comparative evaluation of various platinum-containing chemotherapy regimens in the treatment of advanced small cell lung cancer (experience of the Chemotherapy Department of N. N. Blokhin Russian Research Medical Center of the Russian Academy of Medical Sciences). Russian Journal of Oncology [Rossiiskii Onkologicheskii Zhurnal] 2: 4–10. [in Russian]
- Chen KN (2016) Small cell lung cancer and TNM staging. Chinese Journal of Lung Cancer 19(6): 409–412. <https://doi.org/10.3779/j.issn.1009-3419.2016.06.22> [PubMed] [PMC]
- Dingemans AC, Früh M, Ardizzoni A, Besse B, Faivre-Finn C, Hendriks LE, Lantuejoul S, Peters S, Reguart N, Rudin CM, De Ruyscher D, Van Schil PE, Vansteenkiste J, Reck M; ESMO Guidelines Committee (2021) Small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 32(7): 839–853. <https://doi.org/10.1016/j.annonc.2021.03.207> [PubMed] [PMC]
- Esakov YuS, Shriner IV, Kirpichnikova EI, Kulikova EA, Efteev LA, Tukvadze ZG, Khvedelidze GV, Galkin VN (2022) Clinical efficacy of ct-guided transthoracic needle biopsy of peripheral lung lesions. Pirogov Russian Journal of Surgery [Khirurgiya. Zurnal im. N.I. Pirogova] 5: 34–42. <https://doi.org/10.17116/hirurgia202205134> [in Russian]
- Früh M, De Ruyscher D, Popat S, Crinò L, Peters S, Felip E, ESMO Guidelines Working Group (2013) Small-cell lung cancer (SCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 6: vi99–105. <https://doi.org/10.1093/annonc/mdt178> [PubMed]
- Gandhi L, Rodríguez-Abreu D, Gadgeel S, Esteban E, Felip E, De Angelis F, Domine M, Clingan P, Hochmair MJ, Powell SF, Cheng SY, Bischoff HG, Peled N, Grossi F, Jennens RR, Reck M, Hui R, Garon EB, Boyer M, Rubio-Viqueira B, Novello S, Kurata T, Gray JE, Vida J, Wei Z, Yang J, Raftopoulos H, Pietanza MC, Garassino MC; KEYNOTE-189 Investigators (2018) Pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer. The New England Journal of Medicine 378: 2078–2092. <https://doi.org/10.1056/NEJMoa1801005> [PubMed]
- Grygoruk OG, Tsoi DA, Bazulina LM, Vihlyanov IV (2022) Small-cell lung carcinoma. Cytological diagnostics. Malignant Tumors [Zlokachestvennye Opukholi] 12(1): 36–43. <https://doi.org/10.18027/2224-5057-2022-12-1-36-43> [in Russian]
- Gimalova GF, Abdullin ZS, Khusnutdinova EK (2020) MLPA-analysis of the TP53 gene in patients with small-cell lung cancer. Medical Genetics [Meditsinskaya Genetika] 19-6(215): 83–85. <https://doi.org/10.25557/2073-7998.2020.06.83-85> [in Russian]
- Kosterina NE, Grinberg LM (2019) Cytological research methods in complex morphological diagnosis of small cell lung cancer on "small

- specimens". Ural Medical Journal [Ural'skii Meditsinskii Zhurnal] 10(178): 23–27. <https://doi.org/10.25694/URMJ.2019.10.18> [in Russian]
- Kuzminov AE, Laktionov KK, Egorova AV, Breder VV, Barbolina TD (2019) Immunotherapy for small-cell lung cancer. Medical Council [Meditsinskii Sovet] 10: 22–27. <https://doi.org/10.21518/2079-701X-2019-10-22-27> [in Russian]
  - Kuzminov AE, Borisova TN, Breder VV, Reutova EV, Barbolina TD, Laktionov KK (2020) Firsthand experience of chemoradiotherapy in patients with localized small cell lung cancer. Retrospective assessment. Medical Council [Meditsinskii Sovet] (9): 190–195. <https://doi.org/10.21518/2079-701X-2020-9-190-195> [in Russian]
  - Makimbetov EK, Dzhunushalieva GS (2015) The state of oncopediatric service and epidemiology of malignant neoplasms in the Kyrgyz Republic. Oncopediatrics [Onkopediatriya] 2(3): 292–294. [in Russian]
  - Meijer JJ, Leonetti A, Airò G, Tiseo M, Rolfo C, Giovannetti E, Vahabi M (2022). Small cell lung cancer: Novel treatments beyond immunotherapy. Seminars in Cancer Biology 86(Pt 2): 376–385. <https://doi.org/10.1016/j.semcancer.2022.05.004> [PubMed]
  - Mukhambetzhana AZh, Urazaeva ST, Urazaeva ON, Tusupkalieva KSh, Begalin TB, Amanshieva AA, Tashimova ZhK, Kumar GB, Nurmukhamedova ShM (2020) Modern ideas about epidemiology and risk factors for lung cancer. Literature review. Science and Health [Nauka i Zdravoohraneniye] 2: 27–37. <https://doi.org/10.34689/SH.2020.22.2.003> [in Russian]
  - Napreenko IV, Asimova LF, Satyreva AV (2020) Comparative evaluation of the effectiveness and toxicity of various chemotherapy regimens in the treatment of small cell lung cancer (according to the literature). Student Bulletin [Studentcheskii Byulleten'] 44-4(142): 70–73. [in Russian]
  - Petrov VI (2022) Pharmacologistics - a new paradigm in clinical pharmacology. Bulletin of the Volgograd State Medical University [Vestnik Volgogradskogo Gosudarstvennogo Meditsinskogo Universiteta] 19(2): 3–6. <https://doi.org/10.19163/1994-9480-2022-19-2-3-6> [in Russian]
  - Skurikhin EG, Pershina OV, Pakhomova AV, Ermakova NN, Zhukova MA, Goldberg VE, Simolina EI, Pan ES, Morozov SG, Kubatiev AA, Dygai AM (2022) Stem tumor cells as a potential diagnostic marker and drug target in small cell lung cancer. Questions of Oncology [Voprosy Onkologii] 68(S3): 492–493 [in Russian]
  - Skurikhin EG, Zhukova MA, Dygai AM (2022) Prospects of using programmed CD8+ T-lymphocytes in the treatment of small cell lung cancer. Genes and Cells [Gheny i Kletki] 17 (3): 212–213. <https://doi.org/10.23868/gc123521> [in Russian]
  - Svistunov AA, Yagudina RI, Abdrashitova GT, Babiy VV, Makarova EI, Pochuprina AA, Rybchenko YuV, Tolordava GA, Ugrekheldze DT (2016) Features of pharmacoeconomic analysis in various nosologies. The Sechenov Medical Journal [Sechenoskii Vestnik] 2 (24): 42–50. [in Russian]
  - Tsiouprou I, Zaharias A, Spyrtos D (2019) The role of immunotherapy in extensive stage small-cell lung cancer: A review of the literature. Canadian Respiratory Journal 2019: 6860432. <https://doi.org/10.1155/2019/6860432> [PubMed] [PMC]
  - Ulumbekova GE, Alvianskaya NV, Petrachkov IV (2022) Organization and financing of cancer care in the Russian Federation in 2018-2024. Healthcare Management: News. Views. Education Bulletin of the Higher School of Healthcare Organization and Management [Orgzdrav: Novosti, Mneniya, Obuchenie. Vestnik Vshouz] 8(1): 33–74. <https://doi.org/10.33029/2411-8621-2022-8-1-33-74> [in Russian]
  - Yagudina RI, Gavrilina NI (2022) The use of the MIN-MAX method in assessing the effectiveness of healthcare and drug provision of the population. Remedium 26(2): 139–142. <https://doi.org/10.32687/1561-5936-2022-26-2-139-142> [in Russian]
  - Yagudina RI, Skulkova RS (2011) Fundamentals of pharmacoeconomic analysis. Bulletin of the Scientific Center for the Examination of Medical Products [Vestnik Nauchnogo Tsentra Ekspertizy Meditsinskikh Izdelii] 2: 56–59. [in Russian]
  - Yang S, Zhang Z, Wang Q (2019) Emerging therapies for small cell lung cancer. Journal of Hematology and Oncology 2-12(1): 47. <https://doi.org/10.1186/s13045-019-0736-3> [PubMed] [PMC]
  - Yarovoy SK, Shikina IB (2020) Pharmacoeconomic efficiency of chemotherapy of malignant neoplasms of bronchi and lungs. Pharmacoeconomics. Modern Pharmacoeconomics and Pharmacoepidemiology [Farmakoekonomika. Sovremennaya Farmakoekonomika i Farmakoepidemiologiya] 13(1): 13–22. <https://doi.org/10.17749/2070-4909.2020.13.1.13-22> [in Russian]

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