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Yurkova Yuliia Petrovna

MEDICAL AND SOCIAL ASPECTS OF BUILDING OF A CLINICAL MODEL OF A PATIENT WITH MALIGNANT NEOPLASMS OF THE BRONCHUS AND LUNG

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Merabishvili V.M.

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INTRODUCTION

Relevance of the study

Malignant neoplasm (MN) ranks first in terms of incidence among oncological diseases worldwide. Every year, more than 19 million primary cases of MN are registered in the world, and the number of deaths from them is almost 10 million. According to the data of the International Association for Research on Cancer (IARC), the incidence of MN bronchi and lung (C33, C34) among all oncological diseases in 2022 was 12.4 % (2,480,675 patients), almost as high as the incidence of MN breast (2,296,840 patients) [103, 104, 105].

More than 90 % of MN bronchi and lung incidence is accounted for by men, although it is worth noting that the incidence among the female population is increasing in many developed countries, which is associated with an increase in the number of women who smoke. According to Wild C.P. et al. (2020) smoke exposure also contributes to both incidence and mortality caused by MN bronchi and lung. About 9.5 % of patients who died of MN bronchi and lung were passive smokers [140].

The age that accounts for the highest percentage of MN bronchi and lung diagnoses (32.4 %) according to the IARC ranges from 65 to 74 years [105].

In the structure of overall incidence among all oncological diseases in the Russian Federation (RF), MN bronchi and lung ranks third – 9.7 % in 2021 (in 2019 – 9.4 %), after MN breast – 12.1 % and MN skin – 11.8 %. The average age of patients with MN bronchi and lungs in 2021 is 66.1 years. MN of the bronchi and lung ranks first in the structure of mortality from MN in the RF – 16.8% in 2021 (2019 – 17.0%) and in the world – 18% [36, 37, 38, 105].

Based on the IARC data, it can be concluded that the prevalence of MN bronchi and lung varies widely and does not depend on the economic situation of the country in the world. About 60 % of all cases of MN bronchi and lung occur in developed countries. In economically underdeveloped countries in Asia and Africa, the incidence of MN bronchi and lung is 4–9 cases per 100 000 populations, while in the United States it is as high as 41.6 per 100,000 populations [106].

Despite the positive progress in the MN bronchi and lung treatment, which we can judge by the increase in survival and decrease in mortality due to the introduction of new effective chemotherapy, different regimens, options of radiation exposure to the tumor, this disease remains in first place among other oncological diseases in the world.

At the same time, according to Nechaev O.B., Shikina I.B. et al. (2019), despite the increase from 2005 to 2017 in the number of oncology beds by 14.3% and the number of doctors by 19.3%, medical organizations providing care in the “oncology” profile are not yet sufficiently equipped to fulfill the set goals for reducing mortality from MN [72].

There is plenty of available information on MN bronchi and lung in the world, publications on survival analysis based on clinical cases, global incidence data, articles and training materials demonstrating the use of new surgical approaches in MN bronchi and lung treatment and diagnostic capabilities, but, as a rule, there is no information on the analysis of a patient medical pathway to create a clinical model of the disease.

The data on MN bronchi and lung incidence and mortality in RF, which are published annually, are based on general information on MN, collected and summarized from statistical forms of state reporting, thanks to which it is possible to analyze by gender and age groups, but there is no possibility to analyze the medical care received by a patient at different stages of his disease, to predict the necessary resources for treating patients in accordance with the stage and morphology of the disease.

There are publications that reflect clinical and epidemiological analysis of survival in MN bronchi and lung, but as a rule, they do not contain detailed analysis and prognosis for patient.

According to Avksentyeva M.V. et al. (2018) the direct medical expenses for treatment of patients with MN bronchi and lung diagnosed in 2016 amounted to 6.83 billion rubs, of which 74 % were the costs of inpatient care (60.0 % – costs for round-the-clock inpatient facility and 14.6 % – for day inpatient facility). In 59.1 % of all hospital admissions to the round-the-clock inpatient facility, patients received drug therapy, in the day inpatient facility they accounted for 81.8 % [1].

In the study of Yarovoy S.K. and Shikina I.B. (2020) showed that the use of targeted therapy for MN of the bronchi and lung is associated with additional costs, which amount to 1,136,155.90 rub. per patient based on an average duration of therapy of 39 months [99].

In 2019 Kravchuk S.G. (2018) noted that funding of medical care for patients with MN in the RF under the compulsory health insurance (CHI) may increase by 72 % over two years [85]. At the Oncological forum "White Nights" in 2020 Stozharov V.V. (2020) noted that despite the increase in the planned volume to 11.2 billion rubs (+38.6 % year-on-year), there is a risk of a financial shortage of funds in the amount of 1.4 billion rubs [88, 89].

The construction of the entire medical pathway of a patient with MN associated with his treatment can only be carried out by tracing each patient on the basis of the database (DB) of population cancer registries (PCR), which allow to trace the fate from the time of diagnosis to death. But unfortunately, the registers lack complete information on treatment and diagnostics received by a patient during the entire time, this information is available only in medical information systems (MIS) of medical organizations (MO) where patients are served or Territorial Compulsory Health Insurance Funds (TCHIF) that pay for medical services, but they are deprived of information contained in cancer registries. Consequently, based on these two systems, it is quite possible to trace the fate of patients with MN [15, 42, 102].

The ability to predict mortality, the proportion of patients with different stages of the disease, the required medical care and its volume over time – all this would allow more accurately planning for the need of the health care system to treat patients with MN bronchi and lungs treatments, to calculate scope of necessary diagnostic and therapeutic services. However, such prediction is absolutely impossible without construction of a medical or clinical model patient that takes into account the epidemiological features and medical and social aspects of the disease [40].

Timely detection, diagnosis and treatment of patients with c in the RF is an urgent problem, which requires additional research to improve the organization of specialized medical care.

The aim of the study is to scientifically substantiate, develop and implement a clinical model of a patient with a malignant neoplasm of the bronchi and lung.

The main objectives of the research

The following tasks arise from the goal set for the researcher:

1. Conduct an analytical study to assess the dynamics of medical and social indicators of morbidity, mortality and survival in patients with malignant neoplasms of the bronchi and lungs, among difficult epidemic conditions.
2. Develop a digital database containing information about the medical care provided according to the “oncology” profile as the basis for building a clinical model of a patient with a malignant neoplasm of the bronchi and lung.
3. Based on the generated digital database, create a clinical model of a patient with a malignant neoplasm of the bronchi and lung.
4. To develop and provide during inplementation the possibility of using a clinical model of a patient with a malignant neoplasm of the bronchi and lung to make management and organizational decisions to improve the provision of medical care to oncologic patients.

Object of the research

All cases of malignant neoplasm of the bronchi and lung with the date of diagnosis from 2011 to 2020.

Subject of the research

Evaluation of medical care in the “oncology” profile received by a patient with a malignant neoplasm of the bronchi and lung in an inpatient setting.

Scientific novelty of the study

It has been established that in order to create a digital database containing information about patients with MN bronchi and lungs, as well as about the medical care provided to them in the “oncology” profile, it is necessary to combine data from various medical information systems: the Territorial Compulsory Health Insurance Funds of St. Petersburg, medical information and analytical center of St. Petersburg and the database of the population cancer registry of St. Petersburg.

For the first time, based on a digital database, a clinical model of a patient with MN bronchi and lung was built, which allows modeling the patient's medical path taking into account the stage and morphology of the tumor process [96], containing information on 9,025 patients (2011–2020 year of diagnosis) numbering 34 268 records of medical care provided to them in the field of oncology in a hospital setting.

A clinical model of a patient with a malignant neoplasm of the bronchi and lung has been developed and placed into practical use with the ability to calculate the necessary material, labor and financial resources to provide patients with medical care in the "oncology" profile in accordance with the stage and morphological type of the malignant neoplasm.

The possibility of modeling has been created taking into account changes in the proportion of stages of a malignant neoplasm.

Theoretical value of the study

The study is both clinical and population-based. Based on the generated digital database, a clinical patient model was developed and implemented in an inpatient setting for 9,025 cases of newly diagnosed disease with malignant neoplasm of the bronchi and lung for the period 2011–2020 in St. Petersburg. The model of a patient with a malignant neoplasm of the bronchi and lung also allows to evaluate and track the entire medical path of a particular patient from the beginning of the diagnosis of malignant neoplasm of the bronchi and lung to the outcome or "last contact".

Practical significance of the study

A developed and implemented clinical model of a patient in an inpatient setting based on a generated digital database, including 9,025 cases of newly diagnosed patients with malignant neoplasms of the bronchi and lungs for the period 2011–2020 in St. Petersburg, which allows for strategic forecasting of the necessary material, labor and financial resources for making management and organizational decisions in order to improve the provision of medical care to patients of the «oncology» profile.

The developed and implemented model of a patient diagnosed with MN bronchi and lung makes it possible to simulate the patient's medical path, taking into account the stage and morphology of the tumor process, and to calculate the probabilities of transition of patients with MN bronchi and lungs between different stages of treatment.

The results of the study made it possible to predict and plan the required number of medical personnel, the volume of surgical treatment; resources necessary for chemotherapy and radiation treatment to provide medical care to patients with MN bronchi and lungs. Calculation of forecast values will make it possible to redistribute health care resources in advance and plan the financial resources necessary to provide medical care to patients of the "oncology" profile.

This model can be recommended for use in other regions, taking into account their medical, demographic, territorial and other characteristics, since it allows to enter the required number of numerical values of disease cases (current or expected) by stage, followed by strategic forecasting of resource provision and adoption management and organizational decisions in order to improve the provision of medical care to patients of the oncology profile.

Implementation in practice

The results of the dissertation work have been implemented and used in the practical activities of the Federal State Budgetary Institution "National Medical Research Center of Oncology named after N. N. Petrov" of the Ministry of Health of the Russian Federation (National Medical Research Center of Oncology named after N.N. Petrov) (implementation certificate dated 24.08. 2023 No. 28).

A "Database of patients with malignant neoplasms of the bronchi and lungs, data on diagnosis and treatment" was generated and registered with the ability to enter initial or predicted data and automatically calculate the necessary resources in medical care in the "oncology" profile (certificate dated December 1, 2022 No. 2022623184) [95].

The created clinical model of the patient is used to predict and plan the volume of required treatment, as well as the financial and human costs associated with helping patients with MN of the bronchi and lungs.

It can be used in the educational process when training medical specialists in the field of healthcare organization, to model the necessary material, labor and financial resources in other regions or when carrying out organizational and methodological work.

Approbation of the work

The research materials were presented and discussed at: VII St. Petersburg International Oncology Forum “White Nights 2021” (St. Petersburg, 2021); VIII St. Petersburg International Oncology Forum “White Nights 2022” (St. Petersburg, 2022); XIII Congress of Oncologists and Radiologists of the CIS and Eurasian Countries (Kazakhstan, 2022); VI International Scientific and Practical Conference. Modern science, society and education: current issues, achievements and innovations (Penza, 2023); IX St. Petersburg International Oncology Forum “White Nights 2023” (St. Petersburg, 2023); XIV Congress of Oncologists and Radiologists of the CIS and Eurasian Countries (Dushanbe, 2024).

The basic provisions for the thesis defense

1. The incidence of malignant neoplasms of the bronchi and lung continue to occupy one of the first places among all malignant neoplasms and have one of the lowest survival rates among other malignant neoplasms.
2. The developed digital database facilitates the analysis of the medical path of a patient with a malignant neoplasm of the bronchi and lungs in hospital treatment, which allows to increase the survival rate of patients among other malignant neoplasms.
3. A clinical model of a patient with a malignant neoplasm of the bronchi and lung, containing information on 9,025 patients, made it possible to establish a clear relationship between the stage of the malignant neoplasm, the morphological type of the tumor and the presence of bad habits, as well as concomitant diseases.
4. Clinical models of the disease allow for strategic forecasting of the resource provision necessary to improve the provision of medical care to patients of the oncology profile.

Main scientific results

1. Based on literature data and a population cancer registry database, an analytical study was carried out to assess the dynamics of medical and social indicators of morbidity and mortality [61; P. 361–367], survival and age-sex indicators of malignant neoplasms of the bronchi and lung [62; P. 492–500]. The impact of the new coronavirus infection was assessed [98; P. 576–588] and the smoking factor on the incidence of malignant neoplasms of the bronchi and lungs in the population [92; P. 36–42].

2. The study was carried out by combining information contained in three databases: the territorial compulsory health insurance fund of St. Petersburg, the medical information and analytical center of St. Petersburg and the database of the population cancer registry of St. Petersburg [93; P. 52–58] using mathematical modeling (Markov model) and the help of the software product “TreeAge Pro 2011” (TreeAge Software, Inc. USA) [91; P. 37–44].

3. A digital database has been developed [95], containing information about 9,025 patients (2011 – 2020 year of diagnosis) and has 34,268 records of medical care provided to them in the “oncology” profile in a hospital setting, on the basis of which a clinical model of a patient with a malignant neoplasm was formed bronchi and lung.

4. This model is used in the practical activities of the Federal State Budgetary Institution “National Medical Research Center for Oncology named after N. N. Petrov” of the Ministry of Health of Russia [97; P. 20–29] and allows one to predict the volume of required treatment [94; P. 257–258], as well as financial and human costs [96; P. 473–474], associated with helping patients with malignant neoplasms of the bronchi and lungs.

The main results and provisions of the scientific work are presented:

1. Merabishvili, V. M. malignant neoplasm of the bronchi and lung (C33, 34). Incidence, mortality, reliability of accounting, localization and histological structure (population study) / V. M. Merabishvili, Yu. P. Yurkova, A. M. Shcherbakov, E. V. Levchenko [et al.] // Questions of oncology. – 2021. – Vol. 67. – No. 3. – P. 361–367. – DOI: 10.37469/0507-3758-2021-67-3-361-367 [In Russian] (0.66 pp.l.)

2. Merabishvili, V. M. The state of oncological care in Russia: malignant neoplasm of the bronchi and lung, patient survival (population study at the federal district level) / V. M. Merabishvili, Yu. P. Yurkova, E. V. Levchenko, A. M. Shcherbakov, N.

F. Krotov // Questions of oncology. – 2021. – No. 67 (4). – P. 492–500. – DOI: 10.37469/0507-3758-2021-67-4-492-500 [In Russian] (0.57 pp.l.)

3. Yurkova, Yu. P. Analysis of the distribution of patients diagnosed with non-small cell malignant neoplasm of the bronchi and lung (C33, 34) by the medical care they receive / Yu. P. Yurkova, V. M. Merabishvili, E. V. Levchenko // Qualitative Clinical Practice. – 2022. – No. 2. – P. 37–44. [In Russian] (0.62 pp.l.)

4. Yurkova, Yu. P. Smoking and malignant neoplasm of the bronchi and lung (clinical and epidemiological study) / Yu. P. Yurkova, V. M. Merabishvili // Formulas of pharmacy. – 2022. – Vol. 4. – No. 2. – P. 36–42. – DOI: 10.17816/phf108772 [In Russian] (0.71 pp.l.)

5. Yurkova, Yu. P. Drug therapy of malignant neoplasm of the bronchi and lung according to real clinical practice in 2020 and 2021 / Yu. P. Yurkova, E. V. Levchenko // Medicine. Sociology. Philosophy. Applied research. – 2023. – No. 2. – P. 52–58. [In Russian] (0.65 pp.l.)

6. Yurkova, Yu. P. Evaluation of antitumor drug treatment of malignant neoplasm of the bronchi and lung / Yu. P. Yurkova // Questions of oncology. – 2022. – Vol. 68. – No. 3. – P. 257–258. [In Russian] (1 pp.l.)

7. Yurkova, Yu. P. Certificate of registration of the database No. 2022623184 dated 01.12.2022 Russian Federation Database of patients with malignant neoplasm of the bronchi and lung, data on diagnosis and treatment. Yu. P. Yurkova; copyright holder Federal State Budgetary Institution "N.N. Petrov National Medical Research Center of Oncology" of the Ministry of Health of the Russian Federation / Yu. P. Yurkova, V. M. Merabishvili, E. V. Levchenko et al. // No.2022623105 application dated 21.11.2022 volume 430 648 KB. [In Russian] (0.46)

8. Yurkova, Yu. P. The need for types of inpatient treatment and budget forecasting for patients newly diagnosed with malignant neoplasm of the bronchi and lung / Yu. P. Yurkova, V. M. Merabishvili // Questions of oncology. – 2022. – Vol. 68. – No. 3. – P. 473–474. [In Russian] (0.5 pp.l.)

9. Yurkova, Yu. P. The need for types of inpatient treatment and budget forecasting for patients with malignant neoplasm of the bronchi and lung with a newly

diagnosed diagnosis / Yu. P. Yurkova, V. M. Merabishvili, E. V. Levchenko // Real clinical practice: data and evidence. – 2023. – Vol. 3. – No. 1. – P. 20–29. – DOI: 10.37489/2782-3784-myrwd-28 [In Russian] (0.7 pp.l.)

10. Yurkova, Yu. P. Epidemiology and survival of patients with malignant neoplasm of the bronchi and lung, the impact of COVID-19 (clinical and population study) / Yu. P. Yurkova, V. M. Merabishvili, E. V. Levchenko // Questions of oncology. – 2022. – Vol. 68. – No. 5. – P. 576–588. [In Russian] (0.69 pp.l.)

The main provisions of the dissertation research were reported and discussed at 6 international scientific and practical conferences.

Compliance with the declared specialty

The thesis corresponds to the passport of specialty 3.2.3 Public health, organization and sociology of health care, medical and social expertise.

Publication of study results

9 print works were published on the topic of the thesis, including 5 articles in peer-reviewed scientific journals included in the list of recommended by the Higher Attestation Commission of the Russian Federation for scientific publications, 1 certificate on the topic of the dissertation was obtained.

Structure and scope of the thesis

The 166-page thesis in Russian contains 30 tables, 28 figures and 4 appendices with calculations and questionnaires. It consists of an introduction, a literature review, choice of a model construction method, the materials used to create the model, a description of the resulting model of a patient with MN bronchi and lung, results and conclusions.

The list of literary sources includes 140 titles, including 41 in foreign languages.

CHAPTER 1. LITERATURE REVIEW

1.1 Medical and social aspects of malignant neoplasms of the bronchi and lung

It is possible to estimate the dynamics of MN bronchi and lung incidence in RF and the Northwestern Federal District of the Russian Federation (NWFD) according to the data from the directories of the P.A. Hertsen Moscow Oncology Research Center (branch of National Medical Research Radiological Center of the Ministry of Health of the Russian Federation) – "Malignant neoplasms in RF (incidence and mortality)" [36–38], "State of oncological care in Russia" [79–81], as well as from the reference books of the N.N. Petrov National Medical Research Center of Oncology [54, 57]. In the world – according to the monographs of the International Agency for Research on Cancer (IARC) – "Cancer on five continents" [103–105] and the PCR database [68].

The IARC "Cancer on five continents" project was founded in 1966 and currently includes 12 monographs [108, 134, 135].

MN bronchi and lung is part of the GLOBOCAN project [68], which assesses in more detail the incidence, mortality and prevalence of 36 types of MN in more than 150 countries and is part of the IARC work [129].

The volume of information recorded in the register, the reliability of its comparability, and the timeliness of its completion are of great importance for data comparison since the possibility of planning and implementation of cancer control measures depend on it. Therefore, there are enough works devoted to the analysis of the quality of registers in different countries of the world [58, 101, 110, 111, 117, 121, 122, 125].

1.2 Morbidity and mortality from malignant neoplasms of the bronchi and lung in the world

In 2022, according to the expert assessment of GLOBOCAN, more than 2 million primary cases of MN bronchi and lung were registered in the world (Figure 1), and the number of deaths exceeded 1.8 million (Figure 2). In many economically developed countries of the world, MN bronchi and lung ranks first in the mortality rate from MN and refers to diseases with a high mortality rate.

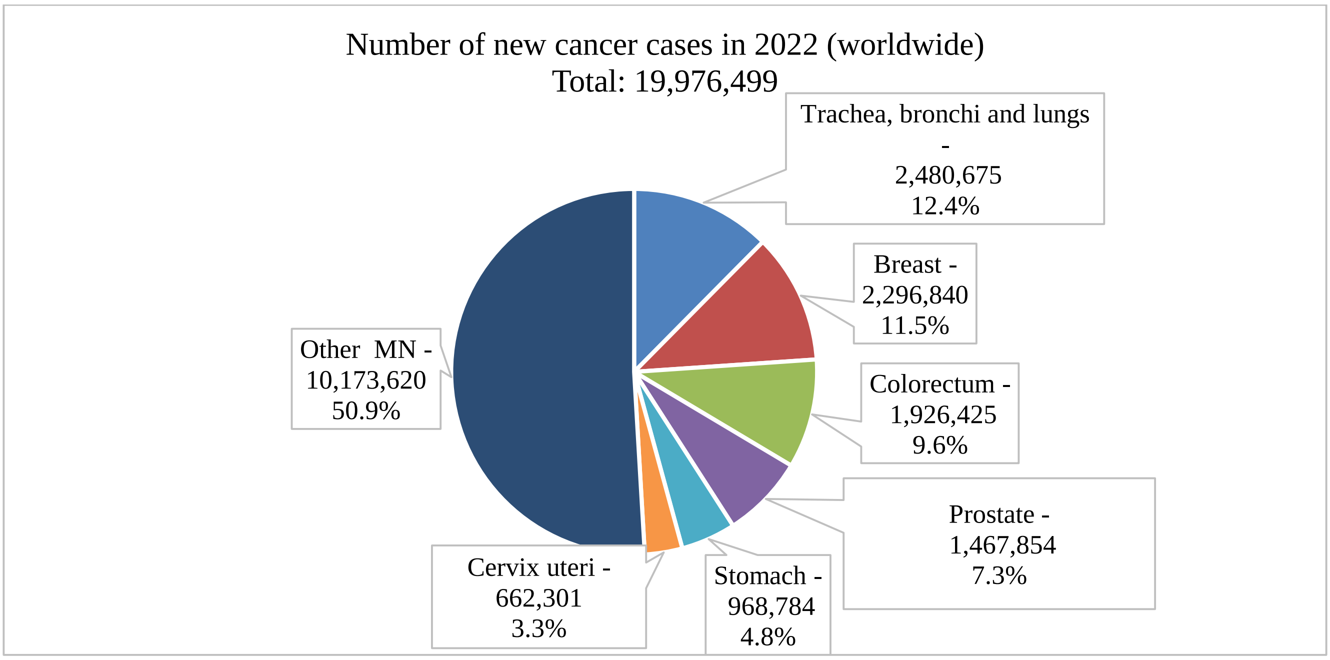


Figure 1 – Structure of malignant neoplasm incidence in the world, 2022 (number of cases), both genders [68]

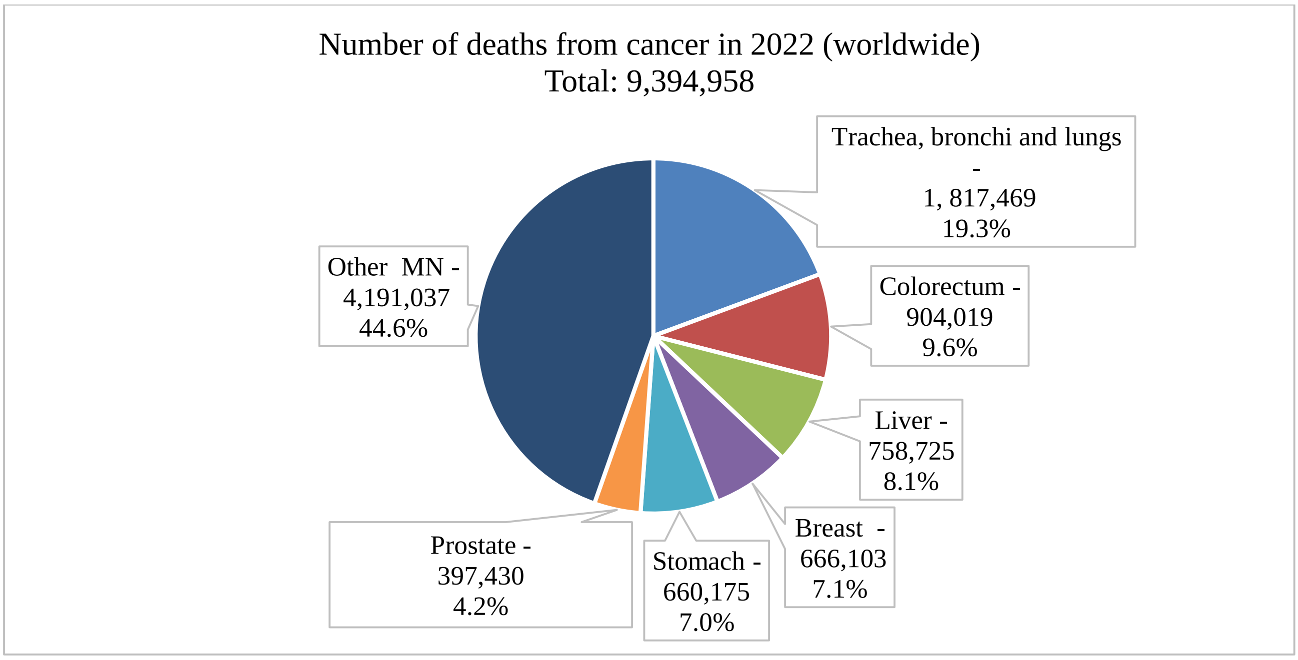


Figure 2 – Structure of malignant neoplasm mortality in the world, 2022 (number of cases), both genders [68]

In 2019, 60,113 primary cases of MN bronchi and lung were registered in RF, in 2020 – 54,375, 2021 – 56,328. The number of deaths from this cause was 50,046 in 2019, 49,158 in 2020 and 46,798 in 2021 [36, 37, 38].

Age-standardized rates are used to compare incidence in different countries around the world, which makes it possible to level out differences in the age composition of the population per indicator, the comparability of register maintenance and accounting is of great importance [59, 60, 70, 126].

According to the latest IARC data for 2017, the highest incidence of MN bronchi and lung among men was in China at 86.3 $^{0}/_{0000}$, although Turkey previously held the lead [104, 105].

The highest standardized incidence of MN bronchi and lung among women in 2013–2017 belongs to New Zealand and Canada: 75.1 $^{0}/_{0000}$ and 48.6 $^{0}/_{0000}$, respectively [68, 105].

Hungary (50.1 $^{0}/_{0000}$), Serbia (47.3 $^{0}/_{0000}$), and France (42.9 $^{0}/_{0000}$) rank first in estimated standardized MN bronchi and lung incidence rates for both genders [68, 105]. Our country, according to IARC data, which presents data on Orenburg, Murmansk, Arkhangelsk, the Republics of Komi and Karelia, Pskov, Vologda, St. Petersburg and Kaliningrad, is among the first 20 countries. Among women, the subjects of the Russian Federation represented in the IARC are characterized by a significantly lower incidence and occupy places at the end of the list. According to A.D. Caprina et al. (2022) the standardized incidence rate in the RF for both sexes in 2019 was 22.7 $^{0}/_{0000}$, in 2020 – 20.3 $^{0}/_{0000}$, and in 2021 – 20.8 $^{0}/_{0000}$, for men – 45, 4 $^{0}/_{0000}$, 40.2 $^{0}/_{0000}$ and 41.0 $^{0}/_{0000}$, respectively, for women – 7.9 $^{0}/_{0000}$, 7.3 $^{0}/_{0000}$ and 7.7 $^{0}/_{0000}$, respectively. Such a dramatic decrease in incidence in one year is largely due to the coronavirus pandemic and the decrease in the quality of primary registration of MN bronchi and lungs patients [36, 37, 38].

This suggests that in terms of total standardized incidence of MN bronchi and lung, RF ranks about 50th, and if we consider only the male population, it is in the top ten leaders in terms of incidence of MN bronchi and lung (Figure 3). RF ranks 64th among the female population (Figure 4) [20, 27, 36, 37, 105].

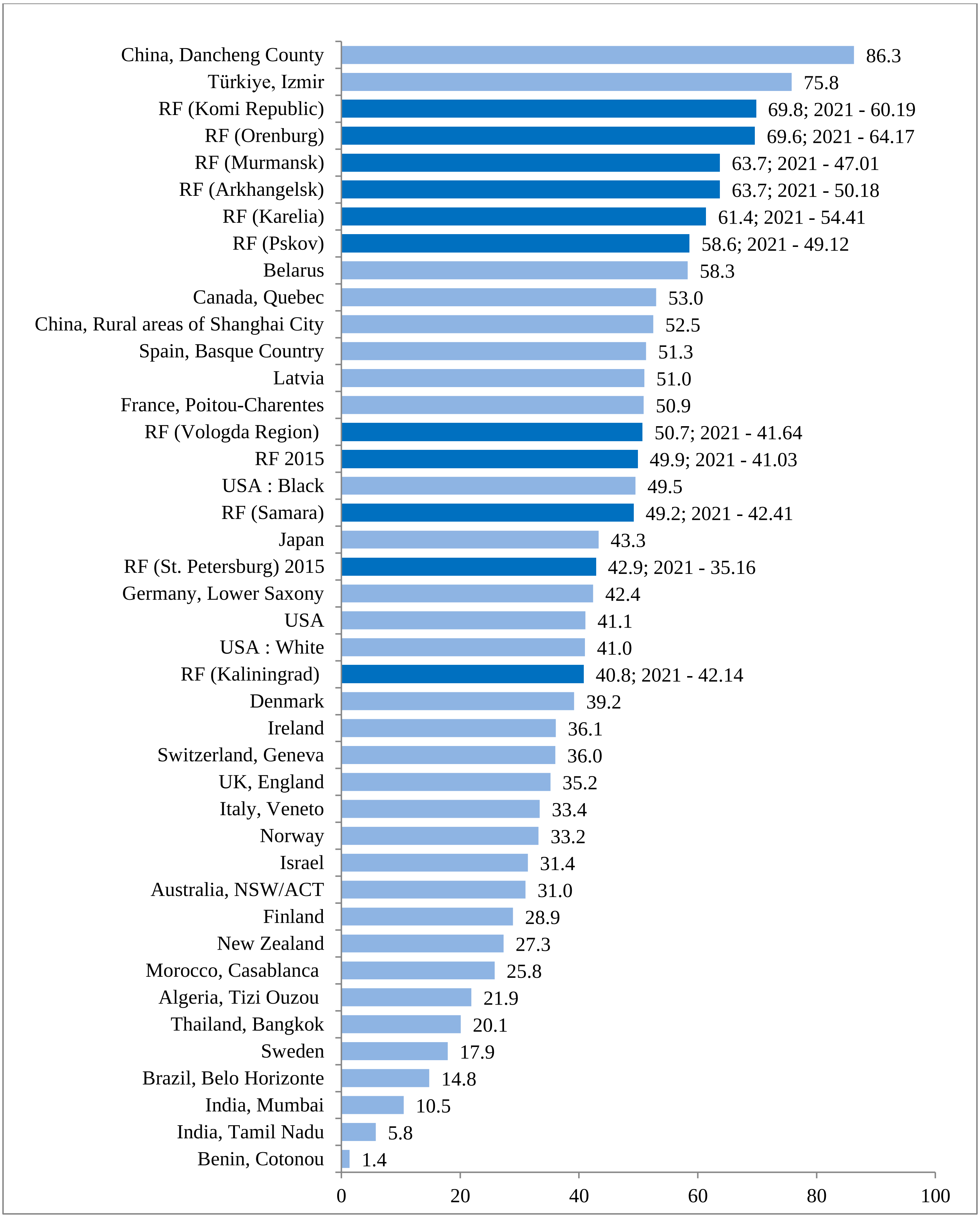


Figure 3 – Malignant neoplasm of the bronchi and lung incidence (C33, 34) in selected countries of the world. Men 2013–2017, $^{0}/_{0000}$ [27, 37, 105]

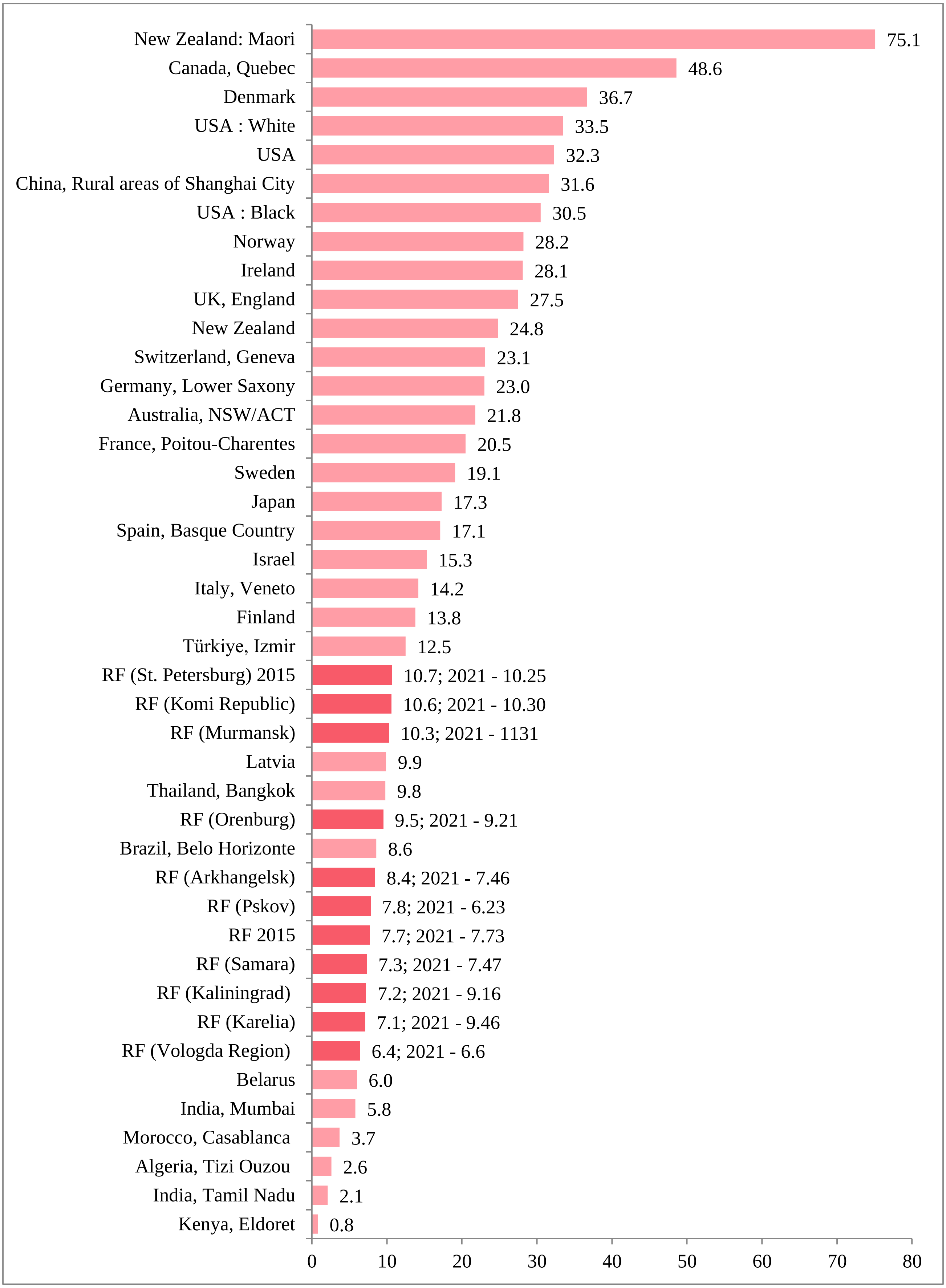


Figure 4 – Malignant neoplasm of the bronchi and lung incidence (C33, 34) in selected countries of the world. Women 2013–2017, $^{0}/_{0000}$ [27, 37, 105]

Mortality rates also vary significantly. More than 1.8 million deaths from MN bronchi and lung are reported worldwide annually, which puts it in first place among deaths from all oncological diseases – 19.0% among all MN.

It is worth noting that male mortality in countries such as the Czech Republic, the Netherlands, and Poland on standardized measures declined significantly from 1995 to 2022, from 70.05 $^{0}/_{0000}$ to 27.27 $^{0}/_{0000}$, from 61.20 $^{0}/_{0000}$ to 26.46 $^{0}/_{0000}$ and from 73.39 $^{0}/_{0000}$ to 44.65 $^{0}/_{0000}$ respectively, while in Portugal there was increase in the indicator – 27.70 $^{0}/_{0000}$ in 1995 and 30.36 $^{0}/_{0000}$ in 2022.

The first place in mortality among the male population, both in 1995 and in 2022, continues to be occupied by Turkey – 66.25 $^{0}/_{0000}$ and Hungary – 54.49 $^{0}/_{0000}$. Among the female population, the first places in the number of deaths from MN of the bronchi and lungs in 2022 belong to Hungary, the Democratic People's Republic of Korea, Denmark and the Netherlands: 28.88 $^{0}/_{0000}$, 24.99 $^{0}/_{0000}$, 23.61 $^{0}/_{0000}$ and 21.33 $^{0}/_{0000}$ respectively [68].

In the structure of mortality among all oncological diseases in RF, MN bronchi and lung has held the first place since 1985. From 2000 to 2019, the standardized MN bronchi and lung mortality rate decreased from 22.54 $^{0}/_{0000}$ to 18.43 $^{0}/_{0000}$ (both genders). The rate for the male population was 64.17 $^{0}/_{0000}$ in 2000 and 38.79 $^{0}/_{0000}$ in 2019, i.e. it has decreased by almost 40% over 20 years (Figure 5). For the female population, the decrease was just over 22%, from 7.07 $^{0}/_{0000}$ in 2000 to 5.49 $^{0}/_{0000}$ in 2019 (Figure 6) [26, 36].

Based on GLOBOCAN 2022 data, when comparing standardized mortality rates for 2022 from MN bronchi and lung in different countries of the world, the RF is among the top 20 countries in terms of the male population and the indicator is 38.11$^{0}/_{0000}$. Regarding the female population, this indicator is one of the lowest when compared with other countries (5.91$^{0}/_{0000}$).

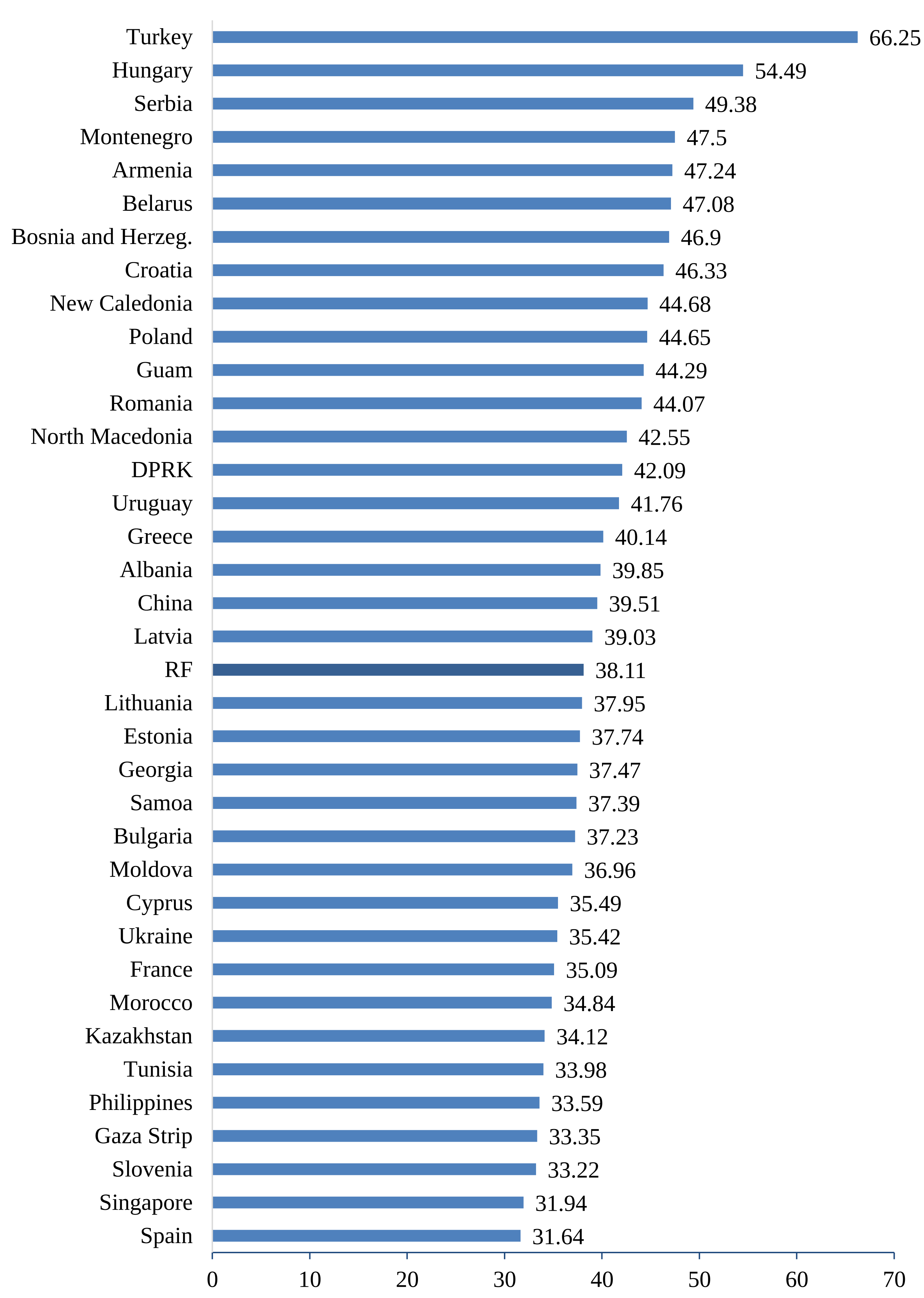


Figure 5 – Malignant neoplasm of the bronchi and lung mortality (C33, 34) in some countries of the world among men, 2022, $^{0}/_{0000}$ [68]

Figure 6 – Malignant neoplasm of the bronchi and lung mortality (C33, 34) in some countries of the world among women, 2022, $^{0}/_{0000}$ [68]

An important indicator reflecting the overall organization of detection and treatment of MN bronchi and lung is survival rate. According to the world data presented by IARC, it can be noted that from 1995 to 2016, one-year and 5-year survival rates increased from 35.8 % to 49.2 % and from 12.6 % to 21.3 %, respectively [106, 134].

In the RF, a significant increase in one-year survival rate has been observed. For example, in the Northwestern Federal District, since 2000, the 15-year survival rate has increased by 7.9 %, the 5-year survival rate during this period remained unchanged [26, 32].

The age-related incidence rates of MN bronchi and lung in the male population at working ages (35–60 years) in RF and Belarus are higher than in the United States, with Belarus being a significant leader. Men in the United States have been getting MN bronchi and lung much more frequently than in RF since the age of 70. Among the female population the incidence rates in RF and the United States are the same only under the age of 24.

In later age groups in the United States, the incidence of MN bronchi and lung in women is many times higher, which is probably due to the smoking habit. The lowest incidence rates among the female population in all age groups in Belarus [27, 57, 105].

We should also mention the decrease in the incidence of MN bronchi and lung in 2021 in all age groups in the male population, the difference among the female population is not so critical (Figure 7).

1.3 Key analytical indicators for malignant neoplasm of the bronchi and lung in the Russian Federation population

To estimate the prevalence of MN bronchi and lung at the population level, an analysis of key analytical indicators was performed. Only when assessing the dynamics of objective criteria such as incidence, survival and mortality, it is possible to evaluate the work of preventive and curative interventions aimed at combating MN bronchi and lung.

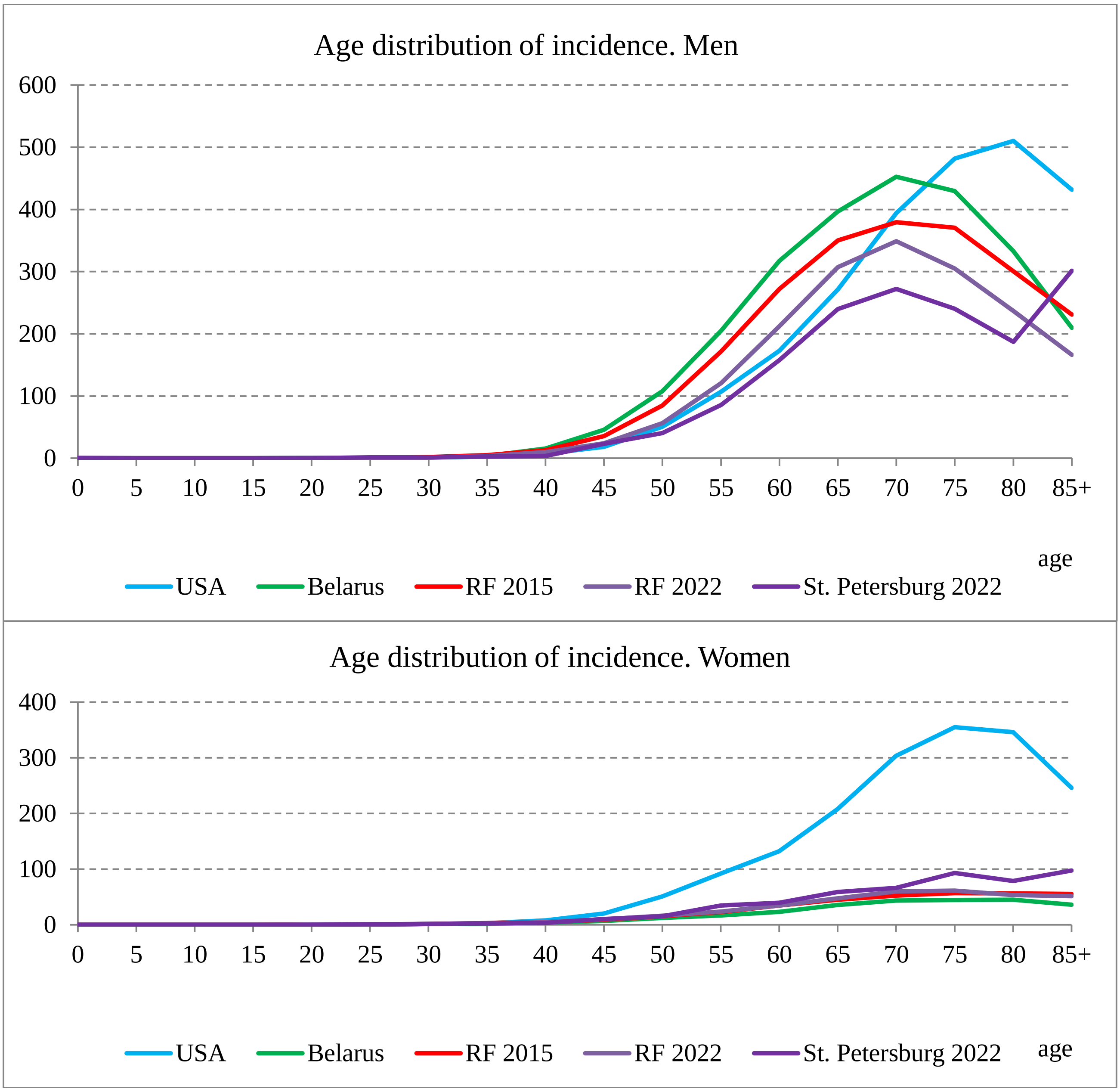


Figure 7 – Age-specific incidence rates of malignant neoplasm of the bronchi and lung in the United States, Belarus and Russian Federation, averaged to 2015 and 2022

1.3.1 Incidence and survival

There has been a steady decline in standardized MN bronchi and lung incidence over 22 years of observation in RF, with a decrease of 28.9% (2000 – 29.3 $^{0}/_{0000}$, 2021 – 20.82 $^{0}/_{0000}$). This decrease was established at the expense of the male population, since an increase in this indicator was noted among the female population (Figure 8) [57, 61].

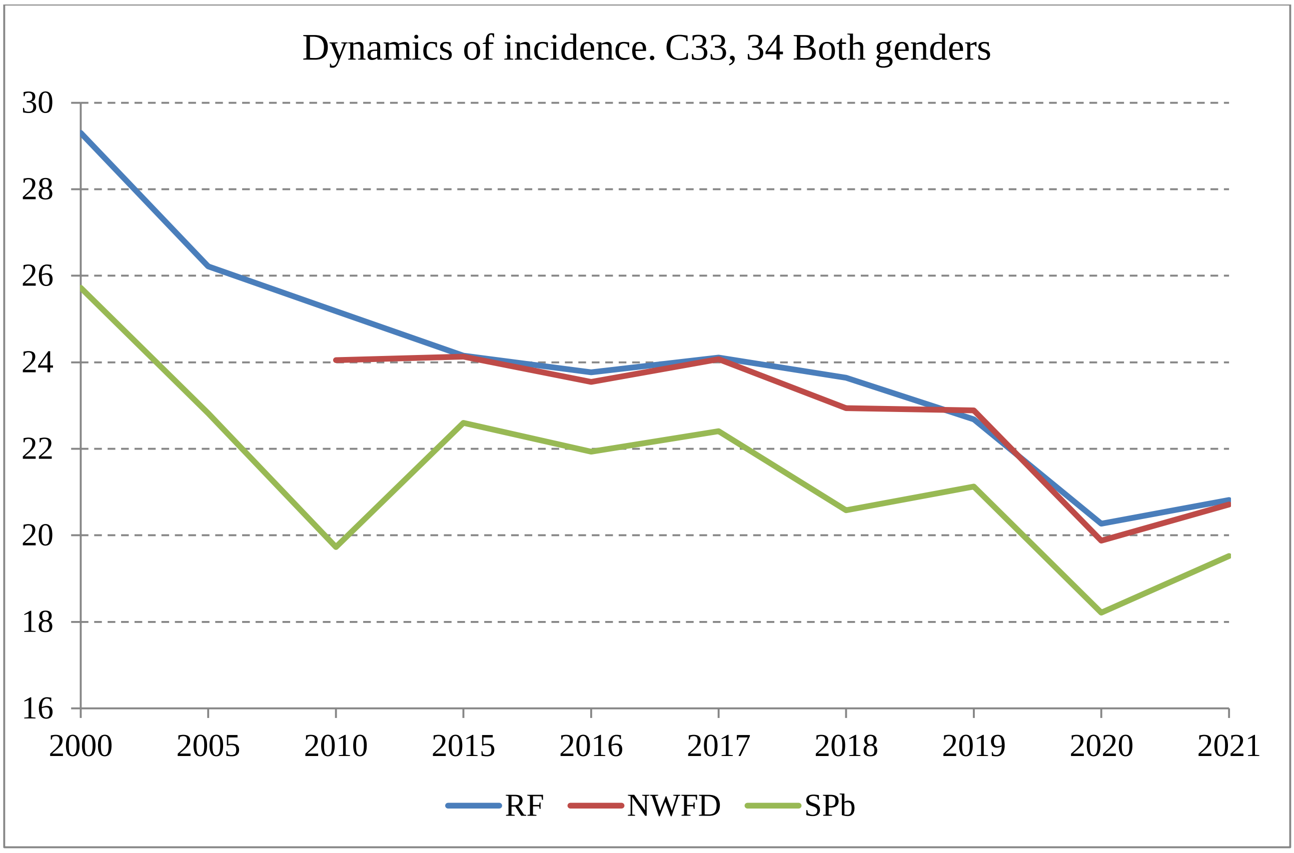


Figure 8 – Malignant neoplasm of the bronchi and lung incidence (C33,34) in Russian Federation, both genders, Northwestern Federal District and St. Petersburg 2000–2021, $^{0}/_{0000}$ (standardized rates)

The negative impact of the pandemic can be seen in a decrease in the incidence of MN bronchi and lung in 2020 and an increase in 2021, with an anticipated increase in the proportion of late stages diagnosed. Table 1 shows the "rough" incidence indicators of MN bronchi and lung in RF [45, 74, 98].

Table 1 – Malignant neoplasm of the bronchi and lung incidence (C33, C34) in Russian Federation 2000–2021, $^{0}/_{0000}$ ("rough" incidence indicators) (PCR database)

	Year of diagnosis										
	2000	2005	2008	2010	2015	2016	2017	2018	2019	2020	2021
Both genders	43.48	40.60	39.99	40.15	41.22	41.23	42.34	42.01	40.96	37.13	38.62
Men	77.89	72.75	70.83	70.70	70.97	70.7	72.06	70.93	69.01	62.22	64.29
Women	13.17	12.8	13.43	13.87	15.54	15.77	16.06	17.00	16.67	15.38	16.35

Over 20 years of observation from 1997 to 2016, the one-year survival rate of MN bronchi and lungs patients in the Northwestern Federal District of RF, according to PCR data, increased from 34.8 % to 39.2 %; the five-year survival rate was virtually unchanged. A positive trend was also noted in St. Petersburg, the median survival rate increased from 6.9 to 8.7 months (men – from 6.9 to 8 months, women – from 6.9 to 11.3 months). The one-year survival rate increased by 20.5 %, and the five-year survival rate increased by 12.9 % (Table 2) [61].

Table 2 – Median survival, one- and five-year survival rates (%) for malignant neoplasm of the bronchi and lung (C33, C34) in St. Petersburg, 1997–2016 (PCR databases)

Indicator		Year of diagnosis			
		1997–2001	2002–2006	2007–2011	2012–2016
Number of cases		8 719	8 698	7 611	8 296
Median survival		6.9 months	6.2 months	7.3 months	8.7 months
Observation period	1	35.2	33.0	37.8	42.4
	2	21.3	20.2	23.7	26.7
	3	16.5	15.6	18.5	20.2
	4	13.9	13.3	15.7	16.7
	5	12.4	11.8	13.9	14.0

The proportion of patients with MN bronchi and lungs of unspecified localization decreased from 32.0 % to 21.6 % [53–55, 59–61].

1.3.2 Mortality and reliability of records

There has been a decrease in mortality from MN bronchi and lung in RF as a whole, so for 22 years of observation it was 20.9 % ("rough" indicator: 2000 – 40.55 $^{0}/_{0000}$, 2021 – 32.08 $^{0}/_{0000}$). In St. Petersburg, the mortality decreased even more substantially over the same period, by 33.9% ("rough" indicator: 2000 – 44.18 $^{0}/_{0000}$, 2021 – 29.16 $^{0}/_{0000}$) (Figure 9).

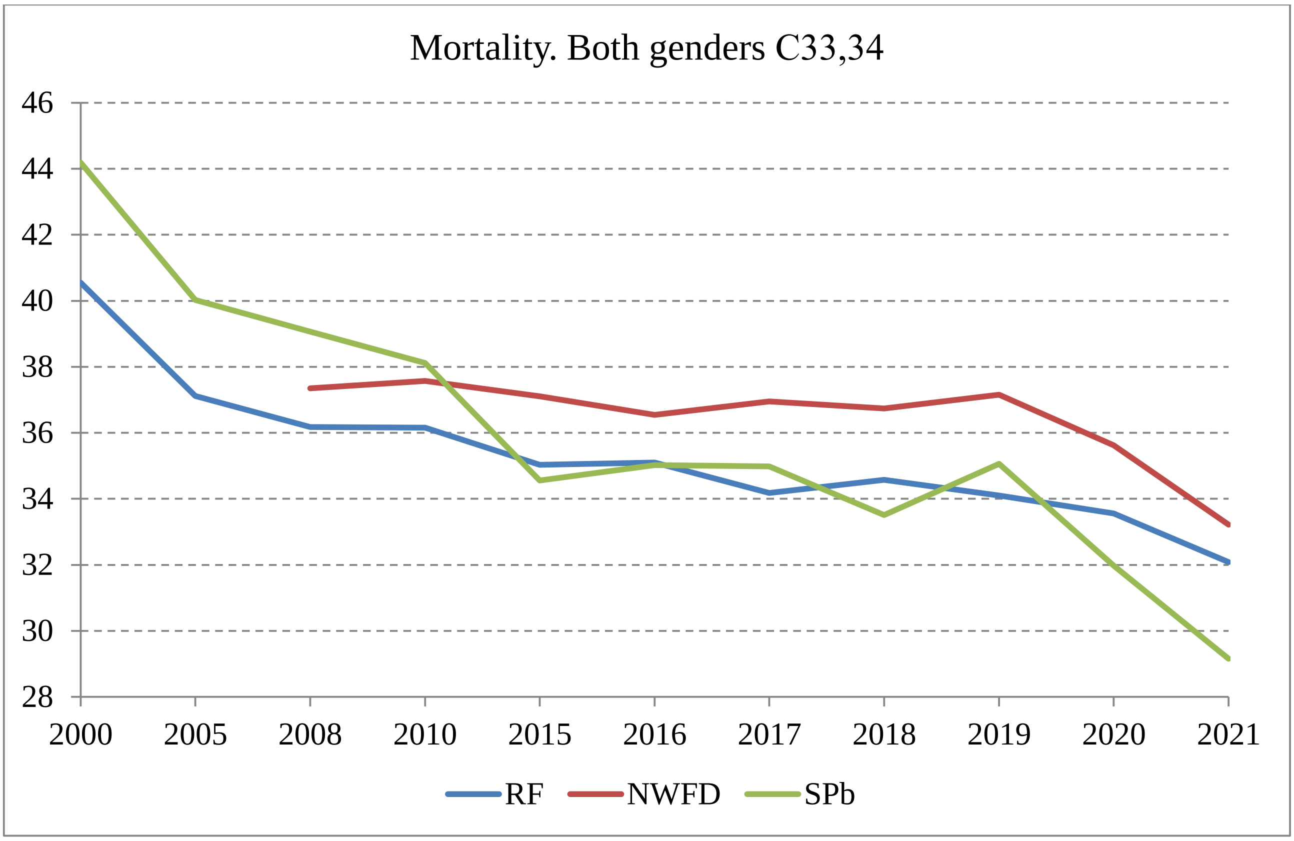


Figure 9 – Malignant neoplasm of the bronchi and lung mortality of both genders (C33, 34) in Russian Federation, Northwestern Federal District and St. Petersburg, 2000–2021 ("rough" indicators, $^{0}/_{0000}$)

The mortality rate among the male population from malignant neoplasm of the bronchi and lung in RF has significantly decreased, and the mortality rate among the female population has increased, but at a much lower pace compared to the incidence.

Such a criterion as an accounting credibility index (ACI) is used to assess the quality of patient records. The ACI is the ratio of the number of deaths to the number of newly recorded patients [53]. The value of this indicator should not exceed 1.0 or the number of deaths should not exceed the number of cases. MN of the bronchi and lung, referring to localizations of MN with a high mortality rate should have an ACI value of no more than 0.7. The dynamics of ACI values for MN of the bronchi and lung in RF as a whole, in the Northwestern Federal District and in St. Petersburg was estimated over 14 years of observation (both genders) with the use of data from the PCR database (Figure 10, Table 3).

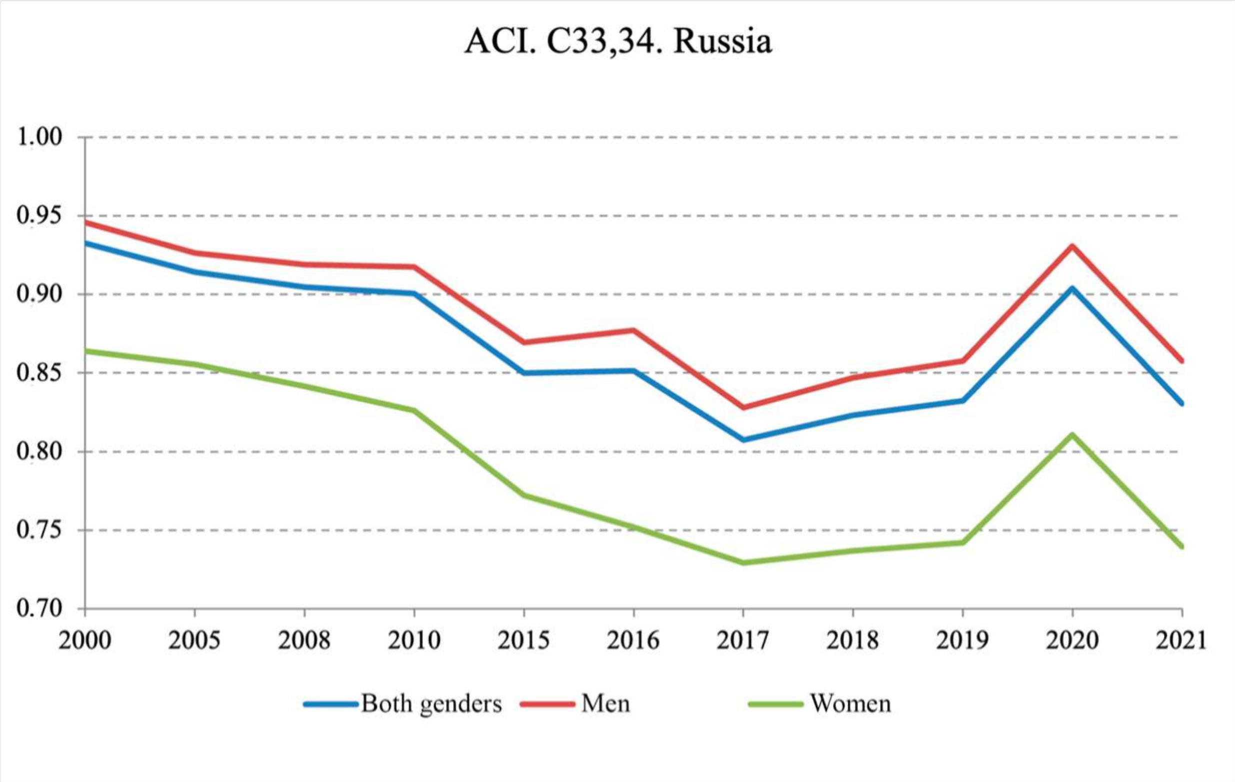


Figure 10 – Dynamics of accounting credibility index value in Russian Federation, Northwestern Federal District and St. Petersburg, 2000–2021 (both genders)

Table 3 – Dynamics of accounting credibility index change in Russian Federation for Malignant neoplasm of the bronchi and lung (C33, C34), 2000–2021

	Year of diagnosis										
	2000	2005	2008	2010	2015	2016	2017	2018	2019	2020	2021
Both genders	0.93	0.91	0.90	0.90	0.85	0.85	0.81	0.82	0.83	0.90	0.83
Men	0.95	0.93	0.92	0.92	0.87	0.88	0.83	0.85	0.86	0.93	0.86
Women	0.86	0.86	0.84	0.83	0.77	0.75	0.73	0.74	0.74	0.81	0.74

There was an increase in ACI during the beginning of COVID-19 in 2019, and a peak maximum increase in 2020 (2000 – 0.94, 2020 – 0.90, both genders). This reflects a significant underestimation of MN of the bronchi and lungs patients during the pandemic, as the number of deaths almost reached the number of first-time MN of the bronchi and lung diagnoses in 2020. In 2021, with the reduction of covid "restrictions", we see a recovery of ACI indicator to the figures of 2019 [61].

1.3.3 Age-specific indicators of incidence and distribution of patients by disease stages in St. Petersburg

From 2000 to 2021 in St. Petersburg the number of primary cases of MN of the bronchi and lung decreased from 1 623 to 1 417, or by 206 cases (by 12.7 %), among the male population and among the female population it increased from 390 to 718, or by 328 cases (by 84.1 %) [26, 36–38]. Based on the PCR data, we can present the age-specific distribution of MN of the bronchi and lungs patients by gender, taking into account the year of diagnosis in standardized indicators. Table 4 shows the age-specific incidence rates of MN of the bronchi and lung in St. Petersburg for the years 2000, 2019, 2020 and 2021.

Table 4 – Malignant neoplasm of the bronchi and lung incidence (C33, C34) in St. Petersburg, taking into account age and gender indicators in standardized rates, 2000–2021

Year of diagnosis	Age					
	0–29	30–39	40–49	50–59	60–69	70+
Men						
2000	0.48	1.66	30.59	137.51	327.28	438.17
2019	0.12	2.05	17.42	85.26	226.98	306.83
2020	0	1.61	16.28	69.15	194.59	275.04
2021	0	1.01	11.74	78.56	214.37	304.22
Women						
2000	0.25	1.7	5.32	13.97	26.09	70.31
2019	0.12	2.77	7.06	22.72	58.39	93.11
2020	0.12	1.17	7.65	26.08	47.5	73.74
2021	0	1.37	9.38	23.73	54.8	81.5

The incidence of MN of the bronchi and lung increases starting from the age 50, with an increase percentage of 389.4 % in the male age group (in 2019 40–49 years – 17.42 $^{0}/_{0000}$, 50–59 years – 85.26 $^{0}/_{0000}$) and 221.8 % in the female age group (in 2019 40–

49 years – 7.06 $^{0}/_{0000}$, 50–59 years – 22.72 $^{0}/_{0000}$). The impact of coronavirus is noticeable in all age groups, at least among the female population, which is reflected in the decrease in 2019–2020.

On the basis of the PCR database the dynamics of patient distribution by stages of the disease in St. Petersburg in 2011–2022 was studied (Table 5).

Table 5 – Malignant neoplasm of the bronchi and lung incidence (C33, C34) in St. Petersburg by stages of disease, 2011–2022 (PCR database), excluding post-mortem diagnosis

Year of diagnosis	Diagnosed with MN of the bronchi and lung (no post-mortem diagnoses)	Stage				
		I	II	III	IV	Without stage
2011	1,423	10.18 %	16.22 %	39.19 %	26.26 %	8.15 %
2012	1,452	10.53 %	15.14 %	38.40 %	27.53 %	8.40 %
2013	1,503	11.02 %	13.15 %	36.06 %	32.54 %	7.24 %
2014	1,519	13.38 %	12.13 %	31.93 %	37.31 %	5.25 %
2015	1,840	11.79 %	15.36 %	30.23 %	36.02 %	6.60 %
2016	1,865	14.80 %	15.65 %	29.70 %	34.67 %	5.18 %
2017	1,959	13.76 %	16.30 %	28.75 %	36.06 %	5.13 %
2018	1,900	17.86 %	13.76 %	26.73 %	38.18 %	3.47 %
2019	1,831	19.74 %	12.45 %	28.44 %	37.09 %	2.28 %
2020	1,461	16.61 %	12.37 %	24.68 %	43.54 %	2.80 %
2021	1,492	19.57 %	11.19 %	27.01 %	39.08 %	3.15 %
2022	1,291	23.80 %	12.95 %	23.64 %	37.05 %	2.56 %

Since 2014, the most frequent diagnosis of MN of the bronchi and lung was stage IV, while until that year stage III prevailed. The proportion of early stages of MN of the bronchi and lung in St. Petersburg (I–II) from 2011 to 2019 increased annually from 26.4 % to 32.2 %, in 2020 their proportion decreased significantly to 28.9%, this is the minimum value since 2016. In 2021, the proportion of early stages becomes equal to 2019, and in 2022 it increases significantly to 36.74 % for the first time in 12 years of observation. Diagnostic defects are possible, since MN of the bronchi and lung refers to the diseases with high mortality. The proportion of early stages can be significantly overestimated and it is possible to determine real distribution of patients by stages only on the basis of PCR database after calculation of one- and five-year survival rate of patients [57].

Additionally, based on the information in the PCR database of the St. Petersburg, the proportion of recorded post-mortem patients with MN of the bronchi and lungs by year from all newly established ones was analyzed (Table 6).

Table 6 – Proportion of recorded post-mortem patients with malignant neoplasm of the bronchi and lung (C33, C34) diagnosed after death in St. Petersburg, 2011–2022 (PCR database)

Year	Number of newly MN of the bronchi and lung diagnoses	Recorded post-mortem with a diagnosis of MN of the bronchi and lung established after death	Share of recorded post-mortem
2011	2,123	700	32.97 %
2012	2,156	704	32.65 %
2013	2,171	668	30.77 %
2014	2,168	649	29.94 %
2015	2,375	535	22.53 %
2016	2,363	498	21.07 %
2017	2,338	379	16.21 %
2018	2,379	479	20.13 %
2019	2,450	619	25.27 %
2020	2,161	700	32.39 %
2021	2,219	727	32.76 %
2022	1,971	680	34.50 %

After 2019, a significant increase in recored post-mortem patients with MN of the bronchi and lungs was detected, as evidenced by a significant increase in ACI, and reflects a significant undercount of MN of the bronchi and lungs patients during the pandemic.

1.3.4 Patients with malignant neoplasm of the bronchi and lung who received inpatient care at the National Medical Research Center of Oncology named after N.N. Petrov

The National Medical Research Center of Oncology named after N.N. Petrov annually provides inpatient care for more than 7,000 patients, more than 16,000 hospital admissions per year, of which more than 350 patients diagnosed with MN of the bronchi and lungs (about 800 hospital admissions per year). Patients diagnosed with MN of the bronchi and lungs from 2011 to 2022 account for 4.06–7.32 % of all patients treated at the institute and rank 5th in the number of hospital admissions. There are about 2 admissions per one MN of the bronchi and lung patient per year in the N.N. Petrov National Medical Research Center of Oncology. Patients are referred to the clinic from all regions of the Russian Federation and, for the most part, these are those patients who require high-tech medical care (HTMC) and specialized medical care (SMC), which cannot be provided in the subject of the place of residence (Table 7).

Table 7 – Distribution of patients diagnosed with malignant neoplasm of the bronchi and lungs by regions of the Russian Federation treated at the N.N. Petrov National Medical Research Center of Oncology, 2011–2022

Region of the Russian Federation	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Far Eastern	3	2	2	7	11	17	17	18	10	19	19	12
Volga Region	1	2	9	8	9	9	16	17	25	14	22	13
Northwestern	179	186	221	247	232	231	234	222	226	224	262	239
North Caucasian	15	18	10	24	22	27	24	27	32	28	32	36
Siberian	2	1	2	5	3	7	5	12	11	11	8	7
Urals		2	2	5	4	5	6	7	8	6	9	9
Central	8	8	12	14	22	26	33	41	27	28	32	24
South	8	10	5	16	9	15	22	19	15	20	36	22
Total	216	229	263	326	312	337	357	363	354	350	420	362

Summary of Chapter 1

Thus, MN of the bronchi and lung remains one of the global problems in the world of its leading cause of incidence and mortality. The proportion of late stages is expected to increase worldwide due to restrictive measures during the pandemic, as a result, the resources required for the treatment of patients with MN of the bronchi and lungs (burden on medical personnel, financial investments) will remain as high and will probably become even higher.

To be able to predict the volume and timing of treatment, the required material, labor and financial resources at the planning stage and making correct and informed management decisions, it is necessary to build a medical or clinical path for a patient with MN of the bronchi and lungs, taking into account epidemiological features.

CHAPTER 2. MATERIALS AND METHODS

The ongoing research aimed at creating a model of patient MN of the bronchi and lung for further use in order to predict the volume and time of treatment, the required financial costs, will allow health authorities to calculate the required volumes of resources for all of the above, as well as take into account possible changes in key analytical indicators.

The subjects of the study were all cases of MN of the bronchi and lungs (C34.0–C34.9) diagnosed from 2011 to 2020. To solve these issues, we obtained information about them from TCHIF SPb database – 49,768 unique UINs, from MIAC SPb on provided high-tech medical care in the field of “oncology”– 6,485 records and from PCR database for St. Petersburg – 44,352 people with diagnosed MN of the bronchi and lung since 2000.

The type of study is a retrospective, continuous cohort that covers the period from 2011 to 2020 (creation of a clinical model of a patient with MN of the bronchi and lung).

It should be noted that the PCR database of the Northwestern Federal District of the Russian Federation includes more than 1.5 million observations (patients with MN), taking into account the fact that the population of the Northwestern Federal District is more than 13.9 million people, which is more than the population of Belarus, Latvia and Estonia taken together.

The unit of observation is a person with MN of the bronchi and lung between 2011 and 2020.

The data were obtained by creating electronic anonymized questionnaires for each patient (Table A.1 of Appendix A).

To achieve this goal, a research program was developed, which included the following steps, described in Table 8.

Table 8 – Stages and methods of organizing a study aimed at creating a clinical model of a patient with a malignant neoplasm of the bronchi and lung

Stage	Research methods
1	2
Stage 1. Preparatory (determining the relevance, purpose and objectives of the study, planning of the study)	
Theoretical estimation analysis of key indicators: incidence, survival rate, accounting credibility index (ACI) according to the data of the national (P.A. Hertsen Moscow Oncology Research Center, PCR database of the N.N. Petrov National Medical research Center of Oncology) and foreign literature, IARC monographs	Analytical Monographic
Stage 2. Study program design	
Determination of modeling techniques, selection of the best model. Obtaining analyzed data from various databases.	
Stage 3. Organization and conduct of the study	
Creation of a database of patients with MN of the bronchi and lung, summarizing all the information in a single Access contour	Sociological Organizational
Definition of model criteria: - model states; - cycle duration; - average state value	Expert assessments Statistical
Based on the Markov mathematical model and using "TreeAge Pro 2011" software (TreeAge Software Inc., USA) calculation of the proportion of each transition between states of the model for each stage of the disease and in accordance with the morphology	Analytical
Stage 4. Creating predictive values that will allow the healthcare system to use this data for work and decision-making	
Based on the results obtained, the construction of a forecast with changes in the proportion of early stages and modeling the predicted number of hospital admissions by states of the model and the required budget	Statistical Modeling

2.1 Methodological approaches to modeling the course of diseases

The course of any chronic disease is characterized by periods of exacerbations and remissions, and the course of cancer is characterized by recurrence, progression, metastasis, which can ultimately lead to disability and fatal outcome [39]. The patient state (remission, recurrence, the presence of distant metastases) determines the amount of medical care he needs in the field of oncology. There is often a need to predict both the course of the disease itself and to assess the dynamics of the required amount of medical care in the field of oncology over time. Such prediction requires the construction of a specific model of the disease. Modeling is necessary to fill in the missing factual information and to predict the development of clinical events, without which it is impossible to conduct a full analysis [13]. The use of predictive models is necessary since they allow us to study the probability of achieving certain clinical events and endpoints [2]. The process of model construction involves several steps: development, validation, and subsequent evaluation of its value in clinical practice [133]. According to the classification proposed by Vorobyov P.A. et al. (2008) [12], the models are classified:

1) by to the presence of feedback: open, closed, combined;

2) linear and non-linear;

3) dynamic and static;

4) stochastic (probabilistic) and deterministic;

5) continuous and discrete.

The classification of prediction methods proposed by Seliverstova A.V. (2016) [78] is shown in Figure 11.

The choice of modeling methods is determined by the purpose of the study and the tasks set, so that the model is as simple as possible and at the same time most fully characterizes the course of the disease [131].

Vorobyov P.A. (2008) [14] identifies the following modeling methodologies most commonly used in healthcare:

1) decision tree method;

2) Markov model;

3) regression models;

4) longitudinal description of the disease progression based on the results of meta-analyses;

5) modeling based on neural networks.

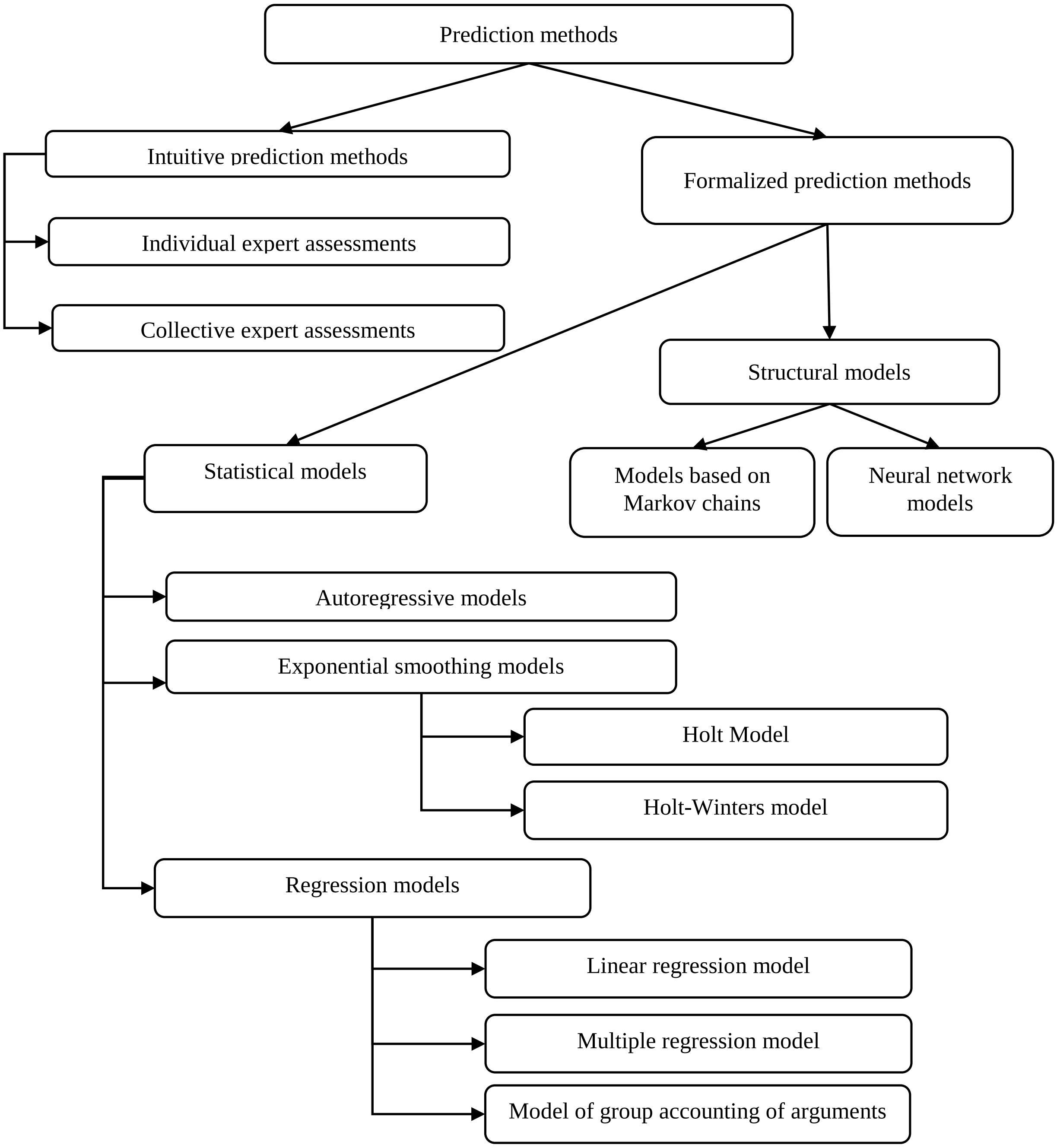


Figure 11 – Classification of prediction methods in healthcare according to Seliverstova A.V. [78]

A comparative characteristic of the modeling methods mentioned above is given in Table 9.

Table 9 – Comparative analysis of modeling methods used in healthcare

Modeling method	Methodology description	Main advantages	Limitations	Practical application
1	2	3	4	5
Decision tree method	The decision tree describes various decision sequences under the condition that each subsequent decision depends on the previous one, and is constructed according to known statistical probabilities depending on the outcome	- Graphic visibility; - Adaptation to changes in input parameters	- Can be applied when the probabilities of reaching clinical points depending on specific intermediate decisions are known, as well as quantitative indicators of the probabilistic value of making such decisions; - Not suitable for construction of models of chronic diseases	Five-year MN breast survival model [18, 114]
Markov model	The model takes into account clinical data and is based on the states a patient may be in at a given time and the probabilities of transition from one to another	- The closest description of the natural course of the disease; - Adaptation to changes in input parameters; - Construction principle of the model is similar to the nature of the course of chronic diseases	- A large array of data is needed for the construction, which is often not available in literary sources; - Complex mathematical apparatus	MN breast progression model [107, 115, 124, 138]
Regression models (including autoregressive ones)	Implemented by multiparametric regression analysis based on patient sample data	- The simplest modeling method designed to simulate the achievement of dichotomous "yes" or "no" outcomes	- The natural process of the disease is not taken into account; - The most appropriate method for selective comparison of several alternatives; - Usually requires a clinical study (experiment); - Modeling of linear processes only	There are no examples of modeling the course of diseases

Continuation of Table 9

1	2	3	4	5
Longitudinal description of the disease progression based on the results of meta-analyses	The methodology of indirect comparison by meta-analysis (D R Mould) is used	Meta-analysis versus clinical trial results allows for more objective results based on a larger patient population	More suitable for modeling the effect of treatment in a specific clinical situation or predicting clinical and/or laboratory parameters rather than the course of the disease	Model of neutropenia development in cytotoxic chemotherapy [116, 123]
Modeling based on neural networks	The mathematical apparatus of neural networks construction is used, primarily for solving classification issues	- The possibility of self-learning based on accumulated data; - The possibility of modeling non-linear processes	Models need additional verification (validation)	Most commonly used in automatic biomedical image recognition systems [100, 130]

The most commonly used methods to describe the natural course of a disease are the decision tree method and the Markov model. According to Rumyantsev A.G. et al. (2009) [73] the decision tree method is the most suitable for modeling the course of acute rather than chronic disease. Andreev D.A. et al. (2017) [2] believe that the use of the decision tree method is associated with a significant simplification and loss of accuracy of estimates and forecasts. Dzhalalov S.Ch. et al. (2015) [19] indicate a number of significant limitations of the decision tree method, which include:

– impossibility of taking into account the time factor, i.e., the method is inapplicable for solving issues when the event occurs over time;

– complexity and branching of the tree when modeling chronic diseases.

According to a number of authors, the use of the Markov model is the most suitable for modeling chronic diseases [2, 12, 19, 78]. At the same time, the main disadvantage of Markov models is the impossibility to solve prediction issues with long memory, but Sonnenberg F.A. et al. (1993) [132] note that this disadvantage is characteristic only for Markov chains, but not for Markov processes.

According to Scheller-Wolf A. (2018), the use of Markov models is most appropriate if [120]:

– the phenomenon under study (disease) is characterized by a high degree of uncertainty, which is typical for most diseases, especially chronic ones with MN;

– the disease under study can be characterized by a set of different states with the possibility of the patient being in one of them, including repeatedly;

– there is enough clinical and other data for model construction.

2.2 Selection of a method for constructing a model of a patient diagnosed with malignant neoplasm of the bronchi and lung

The following mathematical models, as the most frequently used in medical practice, were considered to implement the task of constructing a model of a patient with MN of the bronchi and lung on the basis of the available data array:

– method of mathematical modeling using multiple regression analysis;
– method of discriminant statistical modeling;
– Markov probabilistic model.

The method of mathematical modeling using multiple regression analysis and the method of discriminant statistical modeling were rejected because they do not allow to study the dynamics of the model during patient transitions to different states and repeated return to them, taking into account different probabilities of transitions to different temporal stages.

The Markov method of mathematical modeling allows to synchronize the patient states in time and consider their repeated recurrence in the course of the disease, on the basis of what this method was chosen for our work.

2.2.1 General description of the construction and principles of the model Markov

For the first time, the principles of Markov modeling were outlined by Markov A.A. in 1907, who attempted a mathematical description of stachostic (random) processes based on probability theory. Methodology, first proposed by A.A. Markov (1908) was repeatedly improved thereafter [50]. A number of terms and definitions are used in the description and construction of model Markov.

The model Markov is a Markov chain, for which we know the initial probability and the probability matrix of transitions in time (Figure 12).

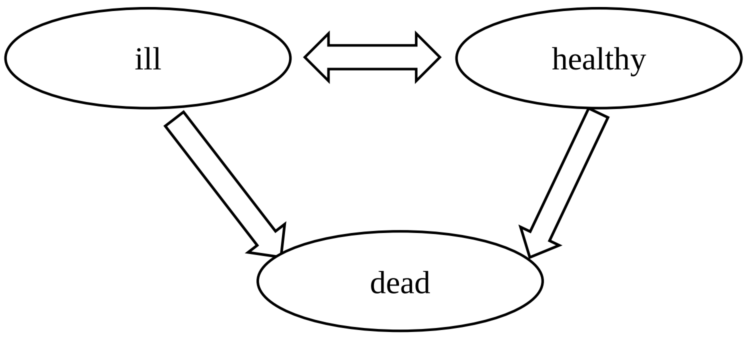


Figure 12 – Markov chain with three states

A Markov chain is a sequence of random events with a finite or countable number of outcomes, characterized by the fact that with a fixed present the future is independent of the past. The probability of transition does not depend on time and is constant [132].

A Markov process is a type of Markov model in which the transition probability is not constant and depends on time [132].

A state is a certain stage in the course of diseases that has clear clinical characteristics (for example, remission, recurrence, progression, hospital admission, etc.)

An absorbing state is a state from which further transitions are impossible (for example, death, disability, etc.). In our model, this is the "last contact with the patient" or lethal outcome.

Transition probability is the probability with which the transition from one state to another is carried out during one cycle.

A cycle is a selectable time interval within which transitions between states are impossible.

A transition diagram is a graphical representation of the model states and the possibilities of transitions between them.

Markov assumption are the probabilities of transitions in the next cycle that are determined only by the current state and do not depend on previous transitions between them.

The simulation horizon is the time during which the simulation is carried out, corresponding to the time required for all pass into the absorptive (final) states of the model.

Figure 12 shows the model Markov, which includes three states: "ill", "healthy" and "dead". At any period of time *i* the patient can be in only one of the conditions provided by the model. Arrows indicate possible transitions between conditions at time *i* + 1. Since transitions from the "dead" to other conditions are impossible, such a condition is absorptive in this model.

2.2.2 Types of Markov processes

Markov processes are divided into two types, depending on whether transition probabilities are constants or change over time, e.g., the probability of lethal outcome from any cause increases as a person ages. Given this factor, Markov chains, in which the probability of transitions between cycles remains constant, are more rational to use in construction of short-term models, and the Markov process – for long-term modeling. Since the duration of the course of oncological diseases is counted in several years or decades, when modeling them in order to reduce model error, it is most acceptable to use a Markov process, in which the probabilities of transitions between states depend, among other things, on time. However, in order to construct such a model, it is necessary to have sufficient statistical data on patients to determine the probability of each transition in the model at each separate period of time, which essentially requires tracing the disease history of each patient included in the sample used for model construction.

2.2.3 Stages of model Markov construction

Sonnenberg et al. (1993) [132] distinguish several stages in the construction of the model Markov of the disease:

1) definition of states and their description;

2) determination of possible transitions between states;

3) calculations of transition probabilities;

4) choice of the duration of one cycle.

The number of states depends on the nature of the disease itself, but at the same time it should be optimal. A small number of model states inevitably leads to significant simplification and increases the probability of inaccuracy of prediction, an unreasonably large number of states complicates the model, and makes it difficult to find data to calculate transition probabilities between states. According to Beck et al. (2016) when determining the model Markov states, the following principles should be followed:

– states should differ from each other in terms of prediction and transition probabilities;

– states should be consistent with the disease under study and have accurate clinical characteristics;

– the sequence of transitions should correspond to the natural course of the disease, i.e., from the most favorable to the least favorable.

According to Scheller-Wolf A. (2018), the number of transitions between model states and cycle length should be determined by considering the natural course of the disease as well as the available primary data that serve to construct the model [120]. In the Markov process, unlike the Markov chain, the accuracy of the model is inversely proportional to the number of calculations needed for its construction and the duration of the cycle in the model Markov. However, the software products available nowadays for calculations allow to operate with large amounts of data and perform the necessary number of calculations, so this factor is not currently considered as a limiting one.

According to Sonnenberg F.A. (1993) [132], on the basis of models Markov, including the absorptive state of "lethal outcome", it is possible to perform survival calculation and construct survival curves. In models with a patient state of "lethal outcome" it is possible to calculate the time during which the patient remains alive from the start of simulation, which corresponds to the overall survival rate. Such calculations can be carried out in the Markov model in three ways:

– simulation of individuals (microsimulation);

– patient cohort simulation;

– fundamental matrix method.

When simulating individuals (microsimulation), the passage through a set of states of each patient is simulated separately with the "pathways" of each patient being individual and determined by patient characteristics affecting transition probabilities, such as the stage of MN [19, 130]. As a result, the outcome for each simulated patient becomes known, in the case of MN it is the overall and/or progression-free survival.

2.2.4 Creating a database for analysis

At the moment there is no possibility to trace the entire medical pathway of a patient diagnosed with MN of the bronchi and lung, because the data on MN of the bronchi and lung incidence and mortality in RF, which are published annually, are based on general information on MN, collected and summarized from statistical forms of state reporting, thanks to which it is possible to analyze by gender and age groups, but there is no possibility to analyze the medical care received by a patient.

It is possible to construct the medical pathway of a patient related to his treatment by summarizing the PCR database, and data from the TCHIF and the FCHIF. Based on these data, it is possible to trace the fate of MN of the bronchi and lung patients.

2.3 Characteristics and course of sampling for constructing a clinical model of patients with malignant neoplasm of the bronchi and lung

Anonymized data on all cases of MN of the bronchi and lung and metastases of any localization (C34 and C77–C78) of residents of St. Petersburg who received medical services for the following types of medical financing were obtained from the TCHIF SPb database by request: medical care covered by CHI and high-tech medical care covered by obligatory medical insurance (HTMC from CHI) from 2011 till October 2020 – 49,768 different UIN numbers. Additionally data were obtained from the Department of High-Tech Medical Care of the St. Petersburg Medical Information and Analysis Center (HTMC MIAC SPb) for the same localizations and for the stated time period – 6,485 records. Data were extracted from the PCR database for all patients with MN of the bronchi and lung in St. Petersburg with a diagnosis established since 2000 – 44,352 patients.

An anonymized electronic questionnaire of a patient with MN of the bronchi and lung was created, where the individual code was a single policy number (Table 10, Tables A.1 and A.2 of Appendix A). Based on all the data obtained, a database was formed containing the following fields: CHI insurance policy number, date of birth, gender, date of diagnosis, start date and end date of receiving medical services, name of the medical service received, rate of this service, name of the medical institution where it was provided, type of medical service, type of financing, and the diagnosis in accordance with ICD-10 [47, 51, 52, 119, 137].

Table 10 – Questionnaire fields for each patient with a malignant neoplasm of the bronchi and lung, obtained by summarizing the data

Field	Data format	Code
CHI policy number	numeric	from 5 to 16 digits
Date of birth	date	DD.MM.YYYY
Gender	text	M-male, F-female
Date 1	date	DD.MM.YYYY start date of the service
Date 2	date	DD.MM.YYYY end date of the service
Diagnosis	text	ICD-10 (C34, C77 or C78)
Service code	text	Payment code for which the invoice is issued
Type of medical service	text	Medical service performed to the patient
Rate	monetary	Amount paid by the MO for a medical service
Name of the MO	text	Name of the MO where the service was provided
Type of medical care	text	outpatient; inpatient; day inpatient facility; out of medical organization
Type of financing	text	CHI, HTMC_CHI, HTMC

In the obtained database, based on the unique identifier (ID) of the TCHIF database and the unified number of the CHI policy (UIN), all medical services were compared with the identification code of each person, which made it possible to eliminate the loss of received medical services when changing the policy, as well as to exclude the possibility of duplication of patients.

From the data analysis, the following cases had to be excluded:

– patients identified in the PCR database diagnosed with MN of the bronchi and lung before 2011;

– patients with MN of the bronchi and lung not identified in the PCR database if they received medical services in 2011;

– medical services that do not have a CHI policy number;

– cases of receiving medical care in the “oncology” profile under the CHI policy, which did not have a unique identifier.

Initially, there were 49 768 UIN in the information on the invoices issued, when comparing them with the ID, 4,692 policies were excluded due to the lack of an identifier, the remaining policies were grouped into 39 955 patients. In turn, 2,928 of the 39,955 patients were excluded because none of the medical services submitted for payment had a diagnosis of C34. The final base included 37,027 patients who received health care services between 2011 and 2020.

For the analysis, it was decided to divide the remaining patients into two groups. The first group included patients automatically identified in the PCR database diagnosed with MN of the bronchi and lung no earlier than 2011, and the second group included all patients with MN of the bronchi and lung identified manually based on a set of attributes who did not receive medical services before 2012, which will allow full tracing of the medical services they received.

A significant proportion of untreated and unidentified patients is explained by the indication in the invoices for the MN of the bronchi and lung diagnosis in connection with its suspicion in the patient and further verification of another disease or metastases of another MN (Figure 13).

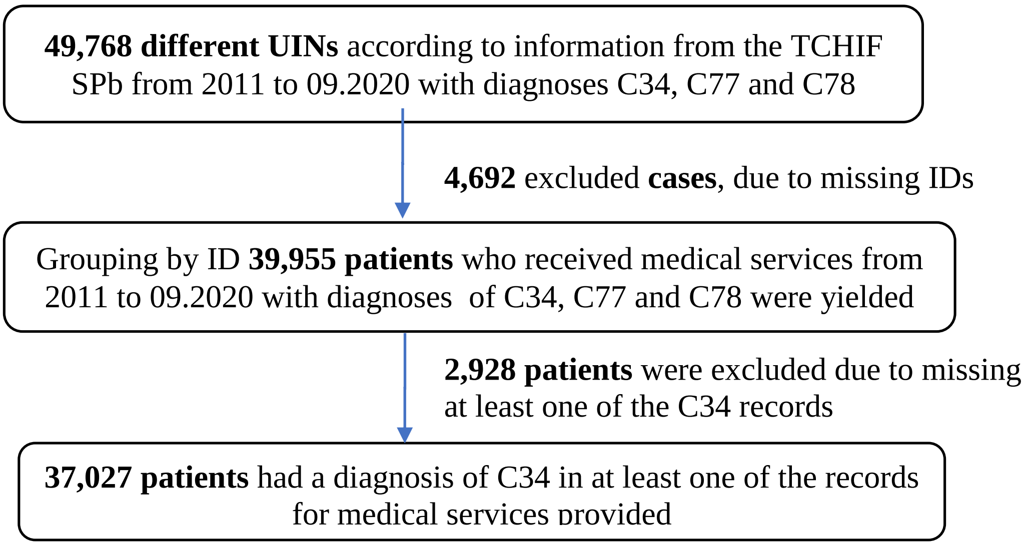


Figure 13 – Data sampling scheme for analysis and constructing a medical model of a patient diagnosed with malignant neoplasm of the bronchi and lung

The data received from TCHIF SPb, MIAC SPb, and PCR on all patients diagnosed with MN of the bronchi and lung and receiving medical services at public expense from 2011 to 2020 were structured by various identifiers in Access 2017. In addition to the anonymized data collated into an overall summary table for all cases of medical care received under different types of financing in patients diagnosed with MN of the bronchi and lung in St. Petersburg, additional codifiers were generated:

– to summarize the medical care provided into groups and further form a model of a patient diagnosed with MN of the bronchi and lung;

– all possible morphological types of MN of the bronchi and lung are divided into two groups: small cell MN of the bronchi and lung and non-small cell MN of the bronchi and lung.

2.4 Characteristics and progress of the patient search in the population cancer registry database

The search for patients in the PCR database was carried out in two stages, the first (automatic) based on a unique code and the second (manual) based on a full check of the patient data.

For automatic identification of a patient in the PCR database, it was necessary to form a unique patient code, which can only be formed on the basis of the last name and patronymic, date of birth and gender, this unique code is individual.

At the first stage of identification, a current list of 1,126,182 insured persons was received from the unified information system of the territorial fund for compulsory health insurance (UIS.CHI.HTMI.CHI) to issue invoices for payment, which contained all the necessary data to create a unique code and additional valid CHI policy number. Based on this list, Novel, the developer of the PCR program, generated the necessary code for each of the 1,126,182.

All patients included in the registry and diagnosed with MN of the bronchi and lung after 2000 were extracted from the PCR program and matched by unique code with the list from the unified information system (UIS) program. When comparing the data with the PCR database, 4,592 patients were found. 1,961 patients were not found in the formed database of medical services as having received medical care in the field of oncology from 2011 to 2020, so they were not included in the sample to construct the model. 292 patients had a diagnosis date earlier than 2011, they were also excluded from the model. The remaining 2,339 patients were included in the clinical model; the following fields were additionally filled in for these patients who could be matched and found in the PCR database: unique patient code, date of lethal outcome, TNM stage (version 7) and tumor morphological code. Of the 2,339 patients identified in the PCR database and included in the model, 1 293 had a date of lethal outcome, 2,182 had morphology, and 2,012 had an identified stage [47, 51, 52, 119, 137].

The second stage of the search for patients in the PCR database consisted of creating a field for the remaining 32,435 patients that included gender, date of birth, and the year of his first referral. Based on this data, codes from the PCR were assigned to the patient identification number from the TCHIF of these patients on the basis of a complete coincidence. An additional check was also carried out:

– by the MO assigned to the PCR and the MO in which the person received services;

– by the MO listed in the PCR as having established the diagnosis and the presence of this MO in the patient services;

– the date of lethal outcome from the PCR was compared with the dates of medical services received by the patient, it could not be earlier than the last date of the medical service provided.

All of this allowed 9,256 more patients to be identified in the PCR, of whom 55 had a date of diagnosis prior to 2011, and they were excluded from the model construction. Of the remaining 9,201 patients, 1,054 had only counseling or diagnostic services; the remaining 8,147 received treatment and were included in the model (Figure 14).

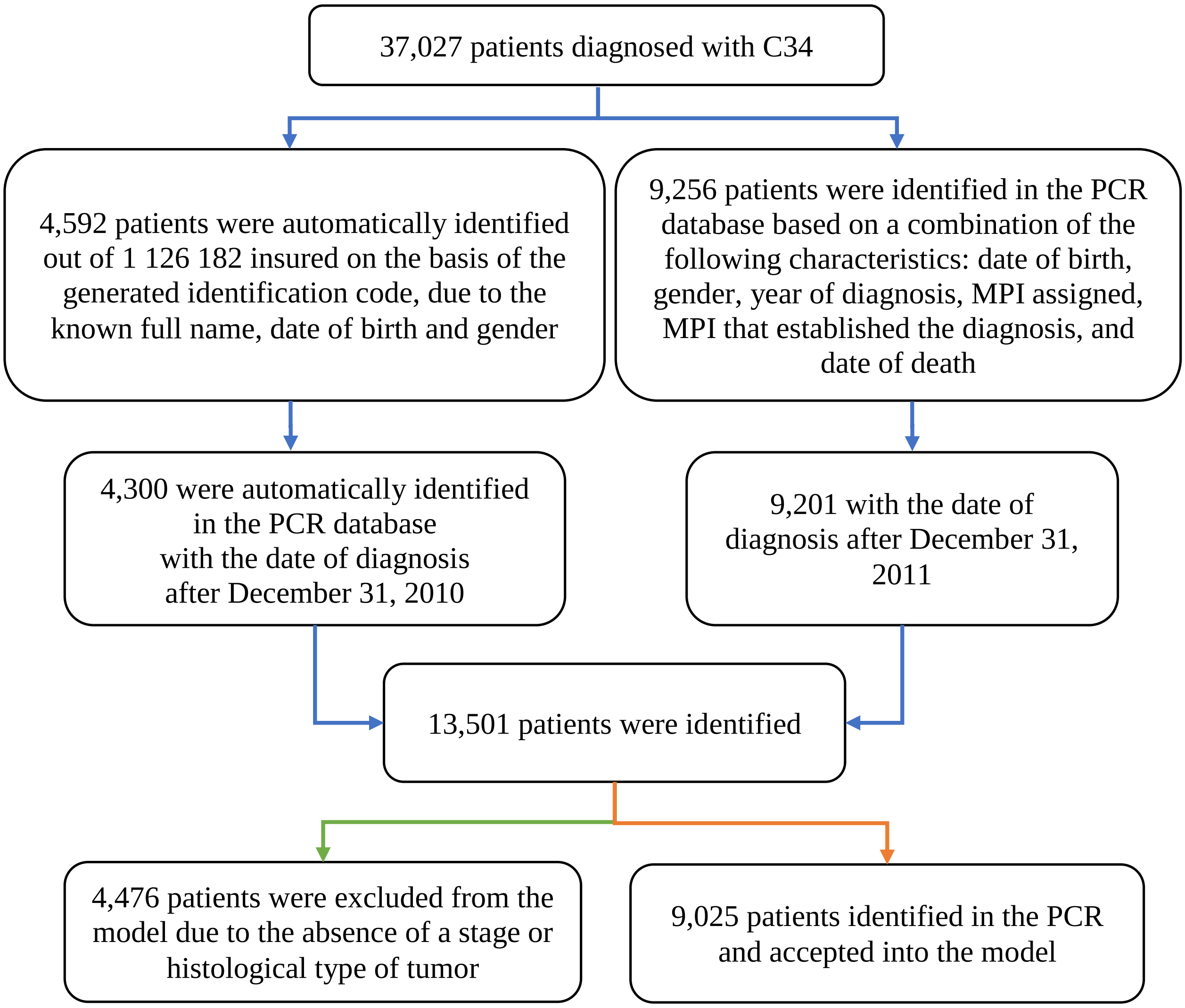


Figure 14 – Identification scheme of patients diagnosed with malignant neoplasm of the bronchi and lung in the population cancer registry database

Of the group of patients not identified in the PCR, 4,846 patients were treated according to the data of TCHIF SPb and MIAC SPb and could be included in the clinical model of MN of the bronchi and lung, but only 3,015 patients on invoices for payment managed to obtain data on morphology and stage of disease, so 1,831 patients were excluded from the model.

The following fields were additionally filled in for all patients identified in the PCR database: unique patient code, date of lethal outcome, TNM stage (version 7), and tumor morphologic code (Table 11).

Table 11 – Encoding of additional fields for patients found in the population cancer registry

Field	Format	View
Unique code	text-numeric	15 characters
Date of diagnosis	date	DD.MM.YYYY
Date of lethal outcome	date	DD.MM.YYYY
Morphological code	numeric	ICD-O-3 code
Clinical stage according to TNM7	numeric	1=stage 1, 2=stage 2, 3=stage 3, 4=stage 4, 0=unknown

2.5 Summary data on patients with malignant neoplasm of the bronchi and lung identified and unidentified in the population cancer registry

According to the stage and morphology of the disease, 15 groups of patients were obtained (Table 12). Patients who lacked staging or information on the histological type of the tumor were excluded from the analysis. The remaining 8 groups were analyzed separately and a model Markov was constructed for each.

Patients with no stage or morphology were excluded from the model. The total number of patients included in the model was 9,025, for which there were 34,268 inpatient care in the field of oncology records from 2011 to 2020.

Table 12 – Distribution of malignant neoplasm of the bronchi and lung patients in the database

Morphology	No stage	Stage I	Stage II	Stage III	Stage IV	Total number of patients according to morphology
Non-small cell LC	164	1,659	1,329	2,708	2,142	8,002
Small cell LC	25	41	107	538	501	1,212
No histology	2,270	37	238	536	1,206	4,287
Total number of patients by stage	2,459	1,737	1,674	3,782	3,849	13,501

2.6 Construction of a clinical model of a patient with malignant neoplasm of the bronchi and lung

Initial data on probabilities of transitions between model states were loaded into TreeAge Pro 2011 (TreeAge Software Inc., USA). This software was used to calculate the dynamics of the number of patients in various states of the model.

Based on the totality of the data, a model of a patient diagnosed with MN of the bronchi and lung was created, and all possible transitions between the stages the patient is at were identified. Subsequently, the probabilities of transition between states every 7 days were calculated.

2.6.1 Preparation of data for the construction of the model Markov

While working with the data, patients who received medical care before 2011 were excluded from the model, if the patient search was done manually, the assumption was made that if the person did not apply for medical care in the field of oncology in 2011, the diagnosis of MN of the bronchi and lung was not made before 2012, and therefore in the model we will be able to reflect all his states. The duration of the transition period from one state was assumed to be 7 days for the possibility of detailed tracing of the patient pathway. Initially, it was assumed that if a patient was not at any stage of inpatient care, he was at the outpatient stage.

To construct this model, the following states were proposed, at which the patient can be:

1. Outpatient state – outpatient medical services, including diagnostic, laboratory and consultative services received on an outpatient basis, as well as services that have been provided by emergency medical care.
2. Conditions of inpatient treatment:
   1) surgical treatment for the purpose of diagnosis (diagnostic surgery);
   2) surgical treatment for the purpose of basic surgical treatment (basic surgery);
   3) surgical treatment associated with complications (surgery of complications);
   4) symptomatic or palliative surgical treatment;
   5) chemotherapeutic treatment in inpatient facility;
   6) radiation treatment;
   7) therapeutic symptomatic treatment in inpatient facility associated with previous treatment or the course of the underlying disease (symptomatic treatment).

Two states were identified additionally in the model, which were the endpoints of the model:

1) "last contact";
2) lethal outcome of a patient.

The outpatient stage in the model was considered only as an intermediate stage of the patient's stay when leaving treatment, so it was not divided for the model, and consultative services of specialists, laboratory and diagnostic tests were considered as one stage.

All medical care in the field of oncology, provided within the inpatient facility was excluded from the model, resuscitation medical services were not evaluated separately, since they are part of one of the stages listed above.

The smallest date between the date of diagnosis in the PCR or the earliest date of medical service was taken as the date of diagnosis. In patients with a fixed date of death, the last stage in the model was "lethal outcome". If there is no date of lethal outcome, the last stage of the model was the "last contact" (Table 13).

Table 13 – Distribution of patients with malignant neoplasm of the bronchi and lung according to the last stages of transition in the model Markov of "last contact" or year of lethal outcome

YD	LC	Year of lethal outcome										Total
		2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	
2011	153	653	330	98	63	23	19	18	16	6	5	1,384
2012	146		664	359	120	39	25	23	12	12	5	1,405
2013	174			675	362	113	64	26	26	17	5	1,462
2014	238				666	357	104	63	25	26	11	1,490
2015	258					661	389	141	59	34	3	1,545
2016	366						651	349	127	53	13	1,559
2017	396							663	385	131	35	1,610
2018	556								552	360	62	1,530
2019	674									463	146	1,283
2020	136										97	233
Total	3 097	653	994	1,132	1,211	1,193	1,252	1,283	1,202	1,102	382	13,501

Note: YD[1] – year of diagnosis; LC[2] – "last contact"

All patients included in the model were divided into 10 groups according to the established stage of the oncological process or lack thereof and tumor morphology.

2.6.2 Description of the conditions of the clinical model of a patient with a malignant neoplasm of the bronchi and lung

The planned clinical model of a patient with MN of the bronchi and lung had 8 options of the states of care received in the “oncology” profile and 2 options of the model endpoints. The earliest date of medical service or date of MN of the bronchi and lung diagnosis from the PCR database was taken as the date of diagnosis.

If the patient did not receive inpatient care in the first cycle of the model, the initial state for such a patient was at the outpatient stage. If the diagnosis was established when providing medical care received in the “oncology” profile to a patient in inpatient facility and involves the performance of some kind of intervention, then the initial state for such a patient was a state corresponding to the type of medical care received in the “oncology” profile provided to him and provided by one of the 7 states of inpatient treatment.

The date of the "last contact" was the last date in the patient history of seeking medical care, after which there was no information in the database about any medical services provided, and no reliable information about the date of the patient's lethal outcome was also found [61].

For 10,404 patients out of 13,501, the last stage of transition according to the model Markov model was lethal outcome, which is 77.06 %. For the remaining 3,097 patients, the last stage was the "last contact", the date of which was determined on the basis of data received from the TCHIF, and is the date of the patient's last referral for medical help received in the “oncology” profile.

Based on the 10 selected states, when constructing the model Markov, the number of transitions between them equals 80, by which the probability of a patient being in each stage was calculated every 7 days (Figure 15).

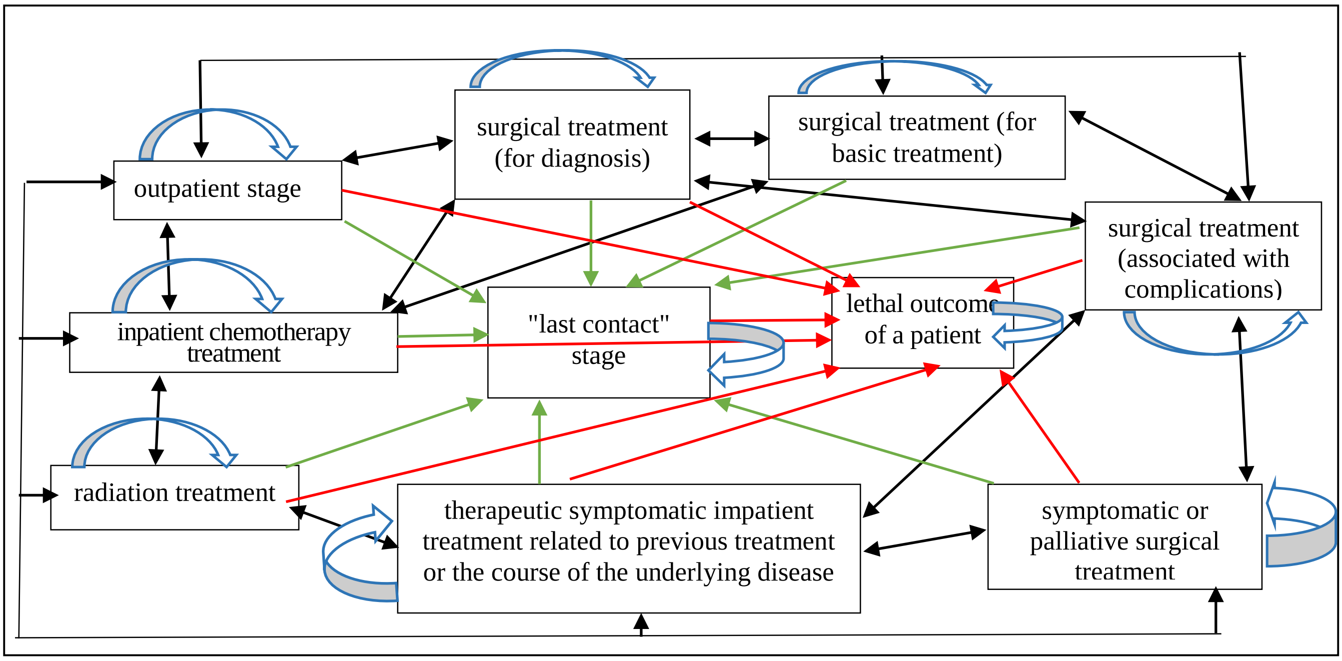


Figure 15 – Conditions of the clinical model of a patient with a malignant neoplasm of the bronchi and lung with possible transitions between them

2.6.3 Cycle duration selection model Markov

One of the important parameters in constructing a Markov model is the duration of one cycle, i.e., the period of time during which a patient can remain in only one state. The minimum cycle duration (1 day) ensured maximum accuracy of assessment since it is extremely rare for patients to receive several different types of care in 1 day. At the same time, short cycle durations are computationally intensive.

The cycle duration of 1 month is most commonly used in mathematical models, this is due to the fact that most of them are based on clinical research data, not clinical practice data. Analysis of the available data shows that a cycle duration of 1 month in our case is unreasonably long, because 39.5 % of all patients included in the model, had two or more states at the inpatient stage.

Thus, for the construction of the model, we chose a cycle duration equal to 1 week (7 days), while the assumption was the impossibility of the patient's transition to another state within 7 days. This interval seems optimal given the average length of hospital admission of 7–8 days according to the database obtained. For the inpatient stage associated with surgical treatment for major surgical treatment, the median length of hospital admission was 16 days, and for chemotherapy treatment, the median length was 5–6 days.

According to the MIS data of N.N. Petrov National Medical Research Center of Oncology, the average duration of hospital admission patients with MN of the bronchi and lungs from 2011 to 2021 was 10.5 days (7,270 hospital admissions). More detailed information on the change in the average duration of hospital admission by year is presented in Table 14.

Table 14 – Change in the duration of hospital admission of patients diagnosed with malignant neoplasm of the bronchi and lungs from 2011 to 2021 in N.N. Petrov National Medical Research Center of Oncology

Type of treatment performed	Duration of hospital admission in days by year											Average length of hospital admission from 2011 to 2021
	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	
Surgical treatment	26.8	26.5	24.9	20.1	17.1	11.9	11.8	11.8	12.2	7.9	8.6	14.6
Chemotherapeutic treatment	7.9	7.9	9.3	5.0	5.0	4.7	4.2	3.6	2.7	1.9	1.9	4.9
All hospital admissions patients	16.5	17.2	17.1	12.0	9.3	8.6	8.1	8.4	9.1	6.7	8.1	10.5

Thus, in view of the chosen cycle duration in the model equal to 1 week, the error of estimates in the model is also ±1 week.

2.6.4 Distribution of the moment of malignant neoplasm of the bronchi and lung diagnosis by model conditions

To analyze the sequence of care in the field of oncology received by a patient, it is necessary to identify the starting point, i.e., the condition of the model at which each patient in the database was diagnosed with MN of the bronchi and lung. The moment of diagnosis, i.e., the starting point in all patients, was taken in the model as week zero. For each of the conditions and in accordance with morphology, the percentage of distribution of MN of the bronchi and lung patients in week zero was calculated, which reflects under what circumstances the diagnosis was made, e.g., at the outpatient state or during hospital admission [97].

Tables 15 and 16 show the conditions of medical services highlighted in the model in numerical and percentage distribution, in which the first time a patient's medical services billed included a diagnosis of MN of the bronchi and lung for each stage of disease and in accordance with morphology [98].

Table 15 – Distribution of patients with malignant non-small cell neoplasm of the bronchi and lungs by stage of malignant neoplasm in the conditions included in the analysis at the time of diagnosis

	First contact group	Stage I	Stage II	Stage III	Stage IV
absolute numbers	1 Outpatient state	1 199	997	2 068	1 662
	2 Surgical treatment for the purpose of diagnosis	44	33	91	82
	3 Surgical treatment for the purpose of basic surgical treatment	231	112	107	35
	4 Surgical treatment associated with complications	7	4	10	14
	5 Symptomatic or palliative surgical treatment	0	0	2	4
	6 Chemotherapeutic treatment in inpatient facility	76	61	115	67
	7 Radiation treatment	0	0	0	0
	8 Therapeutic symptomatic treatment in inpatient facility associated with previous treatment or the course of the underlying disease	102	122	315	278
	9 "Last contact"	0	0	0	0
	10 Lethal outcome of a patient	0	0	0	0
	Total, person	1 659	1 329	2 708	2 142
%	1 Outpatient stage	72.27	75.02	76.37	77.59
	2 Surgical treatment for the purpose of diagnosis	2.65	2.48	3.36	3.83
	3 Surgical treatment for the purpose of basic surgical treatment	13.92	8.43	3.95	1.63
	4 Surgical treatment associated with complications	0.42	0.30	0.37	0.65
	5 Symptomatic or palliative surgical treatment	0	0	0.07	0.19
	6 Chemotherapeutic treatment in inpatient facility	4.58	4.59	4.25	3.13
	7 Radiation treatment	0	0	0	0
	8 Therapeutic symptomatic treatment in inpatient facility associated with previous treatment or the course of the underlying disease	6.15	9.18	11.63	12.98
	9 "Last contact"	0	0	0	0
	10 Lethal outcome of a patient	0	0	0	0

Table 16 – Distribution of patients with malignant small cell neoplasm of the bronchi and lungs by stage of malignant neoplasm in the conditions included in the analysis at the time of diagnosis

	First contact group	Stage I	Stage II	Stage III	Stage IV
absolute numbers	1 Outpatient state	24	88	399	397
	2 Surgical treatment for the purpose of diagnosis	2	2	20	18
	3 Surgical treatment for the purpose of basic surgical treatment	8	3	6	3
	4 Surgical treatment associated with complications	0	0	1	3
	5 Symptomatic or palliative surgical treatment	0	0	0	0
	6 Chemotherapeutic treatment in inpatient facility	4	6	20	14
	7 Radiation treatment	0	0	0	0
	8 Therapeutic symptomatic treatment in inpatient facility associated with previous treatment or the course of the underlying disease	3	8	92	66
	9 "Last contact"	0	0	0	0
	10 Lethal outcome of a patient	0	0	0	0
	Total, person	41	107	538	501
%	1 Outpatient stage	58.54	82.24	74.16	79.24
	2 Surgical treatment for the purpose of diagnosis	4.88	1.87	3.72	3.59
	3 Surgical treatment for the purpose of basic surgical treatment	19.51	2.80	1.12	0.60
	4 Surgical treatment associated with complications	0	0	0.19	0.60
	5 Symptomatic or palliative surgical treatment	0	0	0	0
	6 Chemotherapeutic treatment in inpatient facility	9.76	5.61	3.72	2.79
	7 Radiation treatment	0	0	0	0
	8 Therapeutic symptomatic treatment in inpatient facility associated with previous treatment or the course of the underlying disease	7.32	7.48	17.10	13.17
	9 "Last contact"	0	0	0	0
	10 Lethal outcome of a patient	0	0	0	0

2.6.5 Transformation of initial data for inclusion in the model Markov

The initial data is information about the performance of a specific intervention or treatment on a patient, including the date of the event. For each patient, the initial start date of the simulation was the date of diagnosis. The number of cycles passed from the moment of diagnosis to the moment of the patient transition to one of the model states (corresponding to the provision of medical care in the field of oncology to the patient) was calculated by the formula (1):

$$C = \frac{D_{оказ} - D_{уст}}{7}, \quad (1)$$

where C – cycle of the model in which the patient was provided with medical care in the field of oncology;

$D_{оказ}$ – date of medical care;

$D_{уст}$ – date of diagnosis.

When the duration of inpatient care was more than 1 cycle (1 week), formula (1) was used to determine the cycle in which the beginning and end of the inpatient care period occurred, and the entire period between these two dates was considered to be the period of care, i.e., the patient's stay in this model state.

2.6.6 Calculation of transition probabilities between model states

The probability of the patient's transition from the initial state to another was calculated by the formula (2):

$$p = \frac{n}{N}, \quad (2)$$

where p – probability of the patient's transition from the initial state to another in the model;

n – number of patients who have switched to a different state;

N – number of patients who were in the initial state in each cycle.

The sum of the probabilities of all transitions from the initial state is 100%.

The patient's probability of remaining in the initial state (no transition to another state) in the subsequent cycle was calculated by the formula (3):

$$p_{ост} = 100\ \% - \sum p_i\ , \tag{3}$$

where $p_{ост}$ – probability of the patient remaining in the initial state of the Markov cycle;

p_i – probability of transition from the initial state to other states of the Markov cycle.

Thus, given the transition probabilities in the model, the number of patients in each individual state at a given point in time (cycle) was calculated by the formula (4):

$$N_i = N_{i-1} - N_{выход} + N_{вход}\ , \tag{4}$$

where N_i – number of patients in the model state in cycle i;

N_{i-1} – number of patients in the model state in the previous cycle (i–1);

$N_{выход}$ – number of patients who have moved from the current state to other;

$N_{вход}$ – number of patients coming from other states.

2.6.7 Model non-homogeneity

The analysis of the available data shows that for 1 cycle (7 days), some patients go from the initial state to another and back. However, the calculated probability of such a transition is time-dependent, in other words, the probability of transition, for example, from "outpatient state" to "surgical treatment for the purpose of basic surgical treatment" will vary depending on the cycle in which the transition is carried out model Markov, i.e., it depends on the time elapsed from the moment of diagnosis. The greatest probability of surgical intervention is observed in the first two months from the time of diagnosis, followed by a progressive decrease.

To account for the difference in transition probabilities described in the model, when constructing the probability tables, transition probability percentages were calculated for each cycle separately based on the number of patients who received different types of treatment.

Thus, the model we have constructed is non-homogeneous.

The probabilities of transitions between model states were calculated separately for each stage of MN, separately for patients with a small cell MN of the bronchi and lung and non-small cell malignant neoplasm of the bronchi and lung of histological type, because the percentage of transitions between treatment options differs significantly depending on the parameters mentioned above (Table A.3 of Appendix A) [19, 91].

Since the number of patients in the Markov model always remains constant, all patients should be in any of the cycle states. In each new cycle, the percentage of transition from each state to the new one is calculated. For clarity, transitions from one state (outpatient state) to others (Figure 16) and transition from all states to one state (lethal outcome) (Figure 17) in a group of patients with stage III MN of the bronchi and lung at week 90 of observation are presented.

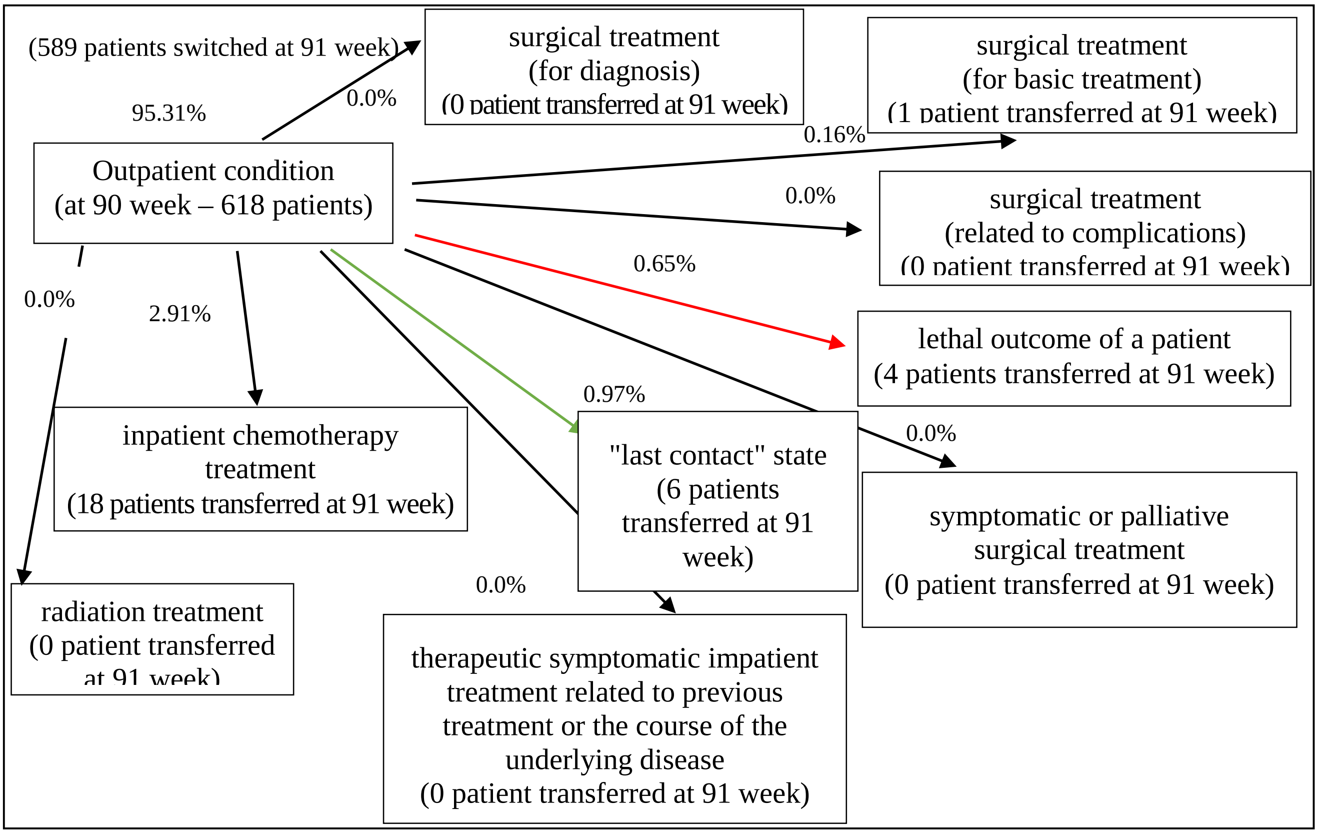


Figure 16 – Percentage of transitions of patients with stage III malignant non-small cell neoplasm of the bronchi and lungs at week 90 from outpatient to other (transition from week 90 to 91), group of 2,708 patients

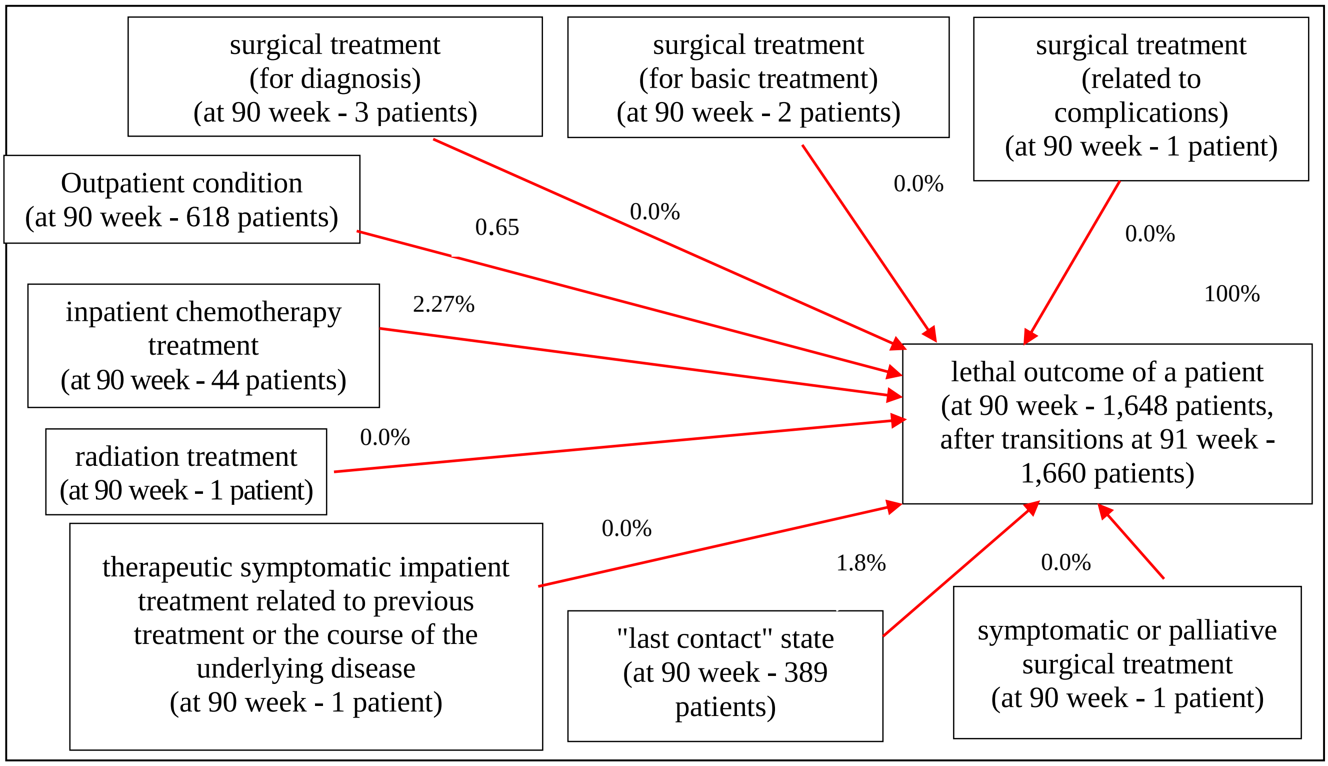


Figure 17 – Percentage of transition of patients with stage III malignant non-small cell neoplasm of the bronchi and lungs at week 90 to patient lethal outcome (transition from week 90 to 91), group of 2,708 patients

2.7 Methodology for calculating the needs for medical care in the "oncology" profile to patients with malignant neoplasm of the bronchi and lung

To create a clinical model of a patient with MN of the bronchi and lung based on the model Markov and using TreeAge Pro 2011 software (TreeAge Software Inc., USA), the proportion of patients in different states of the model according to stage and morphology every 7 days of the cycle was calculated.

Based on these data it became possible to calculate the predicted needs of providing medical care on the "oncology" profile in to patients at the outpatient and inpatients states. When predicting the further, taking into account changes in tariffs for medical care on the "oncology" profile and incidence, these calculations should contribute to making the right management decisions in the health care system.

2.7.1 Methodology for predicting the need for diagnosis and treatment of outpatient conditions

Despite the fact that the outpatient state in the model was considered only as an intermediate stage, for the possibility of closer and real prediction we calculated the necessary costs of this stage on the basis of the order of the Ministry of Health of the Russian Federation No.347n dated April 13, 2021 "On the approval of standards of medical care for adults with malignant neoplasm of bronchi and lung".

To account for medical care in the “oncology” profile in outpatient conditions, two stages of calculation were allocated based on the created model. The initial data for modeling the outpatient state are presented in tables A.4 and A.5:

1. Diagnosis and treatment. The total number of patients newly diagnosed with MN of the bronchi and lung was taken into account.
2. Dispensary observation. Calculation from the second year of observation of MN of the bronchi and lung patients, taking into account the decrease in the number of lethal outcomes in the previous year.

By the product of the average indicator of the frequency of medical service provision and the average indicator of the multiplicity of service application for specialist consultations, laboratory, instrumental and molecular-genetic methods of research in outpatient settings by the number of first-time MN of the bronchi and lung diagnoses in the simulated year, the total number of services in the first year of diagnosis for each medical service of each section was obtained according to formula (5):

$$F = Q_i \cdot V_i \cdot N \;, \qquad (5)$$

where F – total number of services in the first year of diagnosis for each medical service in each section;

Q_i – the average indicator of the frequency of medical service provision;

V_i – the average indicator of the frequency of use of medical services;

N – number of patients newly diagnosed with MN of the bronchi and lung in the predicted year.

To take into account the necessary financing of medical care provided to patients with MN of the bronchi and lungs on an outpatient basis, we took the tariffs of the TCHIF SPb database for 2022. Based on the product of the predicted amount of each medical service for the whole group of patients and the CHI tariff for their payment, the amount necessary for payment for outpatient services for MN of the bronchi and lungs patients in the first year from the moment of diagnosis was obtained according to formula (6):

$$Z_{амб.леч.} = C_{амб.} \cdot F \,, \tag{6}$$

where $Z_{амб.леч.}$ – cost of medical services provided on an outpatient basis in the first year of treatment for each medical service, rubs;

$C_{амб.}$ – tariff of the TCHIF SPb in 2022 for medical services provided on an outpatient basis, rubs;

F – total number of services in the first year of diagnosis for each medical service in each section.

To calculate outpatient costs for the second and subsequent years, we also took into account the averaged rates of frequency of provision and multiplicity of use for dispensary observation of patients diagnosed with MN of the bronchi and lungs. The number of patients for calculation decreased annually in accordance with the resulting model Markov by the number of those who died and fell into the "last contact" group for each previous year.

2.7.2 Methodology for forecasting the demand for stationary states of a model

In order to be able to predict the costs of medical care in the “oncology” profile to patients with MN of the bronchi and lung on the basis of the obtained model, we calculated in accordance with the conditions identified in the model and the cost of its provision, in different groups of patients according to the stage of the disease and tumor morphology [25, 67].

The following documents were used to determine the cost for the stationary conditions highlighted in the model: Resolution of the Government of the Russian

Federation No. 2505 dated December 28, 2021 "Program of state guarantees of free medical care to citizens for 2022 and for the planned period of 2023 and 2024" and Methodological recommendations on methods of payment for medical care at the cost of compulsory medical insurance, approved by the Ministry of Health of the Russian Federation and the Federal Compulsory Medical Insurance Fund No.11-7/I/2-1619, 00-10-26-2-06/750 dated February 2, 2022.

The use of tariffs in 2019 was not reasonable, since there is a constant increase in the average cost of hospital admission, which was announced by Tsareva O.V. at the Oncological forum "White Nights" in 2020 [89].

The calculation was carried out in the following sequence and based on the following formulas:

The number of patients in each inpatient treatment condition was calculated by the formula (7):

$$I = \frac{M \cdot P}{(X - D)}, \quad (7)$$

where I – number of patients in the model who received medical care in the “oncology” profile;

M – number of hospital admissions of each state per year according to the data of the 2011–2020 database.;

P – number of patients MN of the bronchi and lung in each state, depending on the stage and morphology, according to 2019 data;

X – number of patients in each year, depending on the stage and morphology, according to the 2011-2020 database;

D – number of patients who died in the previous year, depending on the stage and morphology, according to the 2011–2020 database.

The average cost of hospital admission for each type of inpatient care allocated in the model was calculated by the formula (8):

$$\text{C} = T \cdot E, \quad (8)$$

where *C* – the average cost of medical care per hospital admission (for each state of medical care separately), rubs;

T – tariff of 2022 established by the Federal Compulsory Health Insurance Fund (FCHIF) for the payment, rubs;

E – share of this service by type of financing in 2019.

The average costs of inpatient care for each type were calculated according to the formula (9):

$$Z_{вид.леч.} = C \cdot I\ , \qquad (9)$$

where *Z* – the average costs for 1 year of treatment, rubs;

C – the average cost of medical care per hospital admission (for each condition of medical care separately), rubs;

I – number of patients in the model who received medical care in the “oncology” profile.

The result of the calculation is the calculation of the average value of the number of hospital admissions with for model conditions of treatment and the cost of patient treatment.

2.7.3 Initial values for a clinical model of a patient with a malignant neoplasm of the bronchi and lung for modeling taking into account screening

Analyzing data on the incidence of MN of the bronchi and lungs in St. Petersburg based on data published annually by the P.A. Hertsen Moscow Oncology Research Center in the monographs "Malignant neoplasms in Russia (incidence and mortality)" and "The state of oncological care in Russia", we identified a persistent decrease in morbidity. Thus, in 2019 to 2,236 cases of newly diagnosed diagnoses were identified (1,717 without recorded post-mortem), in 2020 – 1,958 (1,523 without recorded post-mortem), and in 2021 – 2,135 cases (1,534 without recorded post-mortem), which is not due to a real decrease in the number of cases, but to insufficient screening of the population and restrictions associated with COVID-19 [36, 37, 38, 79, 80, 81]. To construct a clinical model of a patient with MN of the bronchi and lung using the Markov model, the number of cases first identified in 2019 was taken; it is assumed that after restrictions are lifted and clinical examination returns, the number of newly diagnosed cases across all MN will not only return to the "pre-Covid period", but will also increase significantly with the growth of later stages [45, 74, 98].

The distribution by stages was obtained from the collection "The state of oncologic care for the Russian population" for 2019 [79], which is similar to the PCR data, the distribution by stage without post-mortem detection (1,717 patients) was taken into account: I – 19.20 %, II – 14.10 %, III – 29.90 %, IV – 33.40 % and without state indication – 3.40 %. The distribution by morphology of MN of the bronchi and lung patients was obtained from the PCR database of SPb, the proportion of small cell MN of the bronchi and lung amounted to 8.2 % (2015–2018). All newly patients with MN of the bronchi and lung were divided into 2 groups: of small cell MN of the bronchi and lung and patients with non-small cell MN of the bronchi and lung, each of which included 5 subgroups – according to the stage of the disease or its absence.

To model inpatient state, we calculated the ratio of hospital admissions of each treatment option to the number of MN of the bronchi and lung patients for each stage and morphology. This calculation was performed for each year from the time of diagnosis for three years. Each subsequent year after the first was calculated by excluding the number of lethal outcomes in the previous period.

In order to predict the budget for all inpatient conditions of care, a source of funding was identified (Table 17).

Table 17 – Distribution of hospital admissions by funding sources (2011–2020)

Inpatient care conditions according to the model	Funding sources			
	CHI	HTMC I[1]	HTMC II[2]	Number of hospital admissions
1	2	3	4	5
1 Surgical treatment for the purpose of diagnosis	1,748			1,748
2 Surgical treatment for the purpose of carrying out basic treatment	697	722	1,493	2,912

Continuation of table 17

1	2	3	4	5
3 Surgical treatment associated with complications	469			469
4 Symptomatic or palliative surgical treatment	116	103	36	255
5 Chemotherapeutic inpatient care	22,653	22	15	22,690
6 Radiation treatment	790	123	417	1,330
7 Therapeutic symptomatic treatment in inpatient facility	3,749			3,749
Number of hospital admissions	30,222	970	1,961	33,153

Note: [1] HTMC I – high-tech medical care paid for from compulsory health insurance funds; [2] HTMC II – high-tech medical care paid for from the federal budget funds

Since in view of the fact that funding for various options of inpatient care is revised annually, so, for example, from 2011 to 2013, there was no such source of funding as HTMC included in the basic CHI program, and in 2020 a large volume of radiotherapy was transferred from HTMC not included in the CHI to HTMC included in the CHI. The calculate the share of each source of funding was based on 2019 (Table 18).

Table 18 – Share of hospital admissions by funding sources in 2019

Inpatient care conditions according to the model	Funding sources		
	CHI	HTMC I[1]	HTMC II[2]
1 Surgical treatment for the purpose of diagnosis	100 %	-	-
2 Surgical treatment for the purpose of carrying out basic treatment	12 %	36 %	52 %
3 Surgical treatment associated with complications	100 %	-	-
4 Symptomatic or palliative surgical treatment	19 %	56 %	25 %
5 Chemotherapeutic inpatient care	100 %	-	-
6 Radiation treatment	63 %	30 %	7 %
7 Therapeutic symptomatic treatment in inpatient facility	100 %	-	-

Note: [1] HTMC I – high-tech medical care paid for from compulsory health insurance funds; [2] HTMC II – high-tech medical care paid for from the federal budget funds

For chemotherapeutic treatment, based on the data of the TCHIF SPb for 2020–2021, the percentage of its use in MN of the bronchi and lung patients was calculated for each scheme and compared with the tariffs of the Federal Compulsory Medical Insurance Fund (FCHIF) of 2022 [92].

Inpatient care accounts for 74 % in the financial structure of direct medical costs [1]. The cost of inpatient care was calculated based on the clinical guidelines for bronchial and pulmonary MN in 2021 and hospital admission rates approved by FCHIF for 2022 according to the states of the proposed model. The average cost of treatment for each selected condition was obtained, taking into account the share of the source of funding, and for chemotherapy treatment, the utilization percentage for each treatment regimen was additionally applied (Table 19) [93]. The initial data on surgical treatment options, drug regimens, etc. are presented in Tables A.6–A.8, taking into account % of their use and tariffs.

Table 19 – Average cost of each condition of inpatient care according to FCHIF tariffs in 2022 (rubs per 1 hospital admission)

Inpatient care conditions according to the model	For patients with non-small cell MN of the bronchi and lungs	For patients with small cell MN of the bronchi and lungs
1 Surgical treatment for the purpose of diagnosis	30,818.43	30,818.43
2 Surgical treatment for the purpose of carrying out basic treatment	197,694.23	197,694.23
3 Surgical treatment associated with complications	86,556.58	86,556.58
4 Symptomatic or palliative surgical treatment	148,229.18	148,229.18
5 Chemotherapeutic inpatient care:		
Stage I–II	228,524.32	122,983.55
Stage III–IV	190,575.47	
6 Radiation treatment	136,866.04	136,866.04
7 Therapeutic symptomatic treatment in inpatient facility	24,327.45	24,327.45

Based on the 2021 bronchial and lung MN clinical guidelines, the average case rate of drug treatment for patients with non-small cell MN of the bronchi and lungs and for patients with small cell MN of the bronchi and lungs was calculated. For patients with non-small cell MN of the bronchi and lungs stage III–IV, the average cost of treatment accounted for the proportion of neo-adjuvant chemotherapy. In prediction based on the proposed states for patients with non-small cell MN of the bronchi and lungs and for small cell MN of the bronchi and lungs, the proportion of each group of hospital admission for each stage of disease over three years was calculated [4, 86, 87].

As a result of the distribution of newly diagnosed patients (1,717 patients) with malignant neoplasm of the bronchi and lungs in 2019 into groups in accordance with the stage and morphology provided in the study, 1,568 patients with non-small cell MN of the bronchi and lungs, stage I – 301 patients, stage II – 221 patients, stage III – 469, stage IV – 524 and no stage indicated – 53; 149 patients with small cell MN of the bronchi and lungs, of which: stage I – 29 patients, stage II – 21, stage III – 45, stage IV – 50 and no stage indicated – 4 [96].

The number of patients in each group was multiplied by the result of the ratio in the control group and the average cost, as a result, the predicted number of hospital admissions of each condition and their cost were obtained.

2.7.4 Initial values for modeling the necessary resources when distributed by disease stages for 2019 and increasing the proportion of early stages of malignant neoplasms of the bronchi and lung

Currently, much attention is paid to MN of the bronchi and lung screening, a large number of different studies for early screening are proposed: low-dose spiral computed tomography of the lungs, cytologic or immunocytologic examination of sputum, the method of gas chromatography and mass spectroscopy to assess the composition of exhaled air is also considered, endoscopic studies (fluorescence bronchoscopy, spectroscopy) are separately emphasized [3, 4, 11, 118, 139].

Another method of MN of the bronchi and lung screening, tested in the N.N. Petrov

National Medical Research Center of Oncology, is based on the assessment of the characteristics of cell nuclei from sputum for the presence of tumor-associated changes. All this is aimed at detecting MN of the bronchi and lung at earlier stages. The increase in the number of patients diagnosed at stages I–II, as a consequence of increased survival rate, will require the healthcare system to change the current volume of medical care provided in the “oncology” profile, calculate the required additional funding and necessary medical resources [49].

The clinical model of a patient with MN of the bronchi and lung allows to forecast the number of patients in different states, depending on the stage of diagnosis and morphological type of the tumor, i.e., it allows to predict the volume of medical care provided in the “oncology” profile and terms of its provision, which they will need in the future.

Thanks to the clinical model, it is possible to predict different scenarios, both an increase in the proportion of patients with early stages of MN of the bronchi and lung and an increase in the absolute number of patients, for example, with the introduction of the screening programs described above.

On the basis of the developed model, a forecast of the dynamics of changes in the volume and timing of medical care provided in the “oncology” profile for MN of the bronchi and lung patients in St. Petersburg was constructed when stages I–II increase from the current 29.8 % in 2019 in the NWFD to the predicted 58 % at primary CT screening, as calculated by Diederich et al. in a 2002 study [109].

At the same time, two possible scenarios were considered:

– maintaining the current proportion of patients with stages I and II;

– change in the proportion of patients diagnosed with MN of the bronchi and lung at stages I and II in an upward direction.

The modeling horizon was 3 years, based on the program of state guarantees of free medical care provided in the “oncology” profile for citizens, which is annually approved for the relevant period.

The results of the prediction are presented in the form of differences in the volume and timing of medical care provided in the “oncology” profile for patients diagnosed with MN of the bronchi and lung.

Summary of Chapter 2

Based on the analysis of various models, we chose the method of mathematical modeling, the Markov model, which allows us to synchronize the patient's conditions over time and take into account their repeated repetition during the course of the disease. The general sample of patients that was included in the clinical model was 9,025 patients with diagnoses established from 2011 to 2020 follow-up. They were divided into 8 groups according to the established stage of the oncological process and tumor morphology. Based on the 10 selected states of the model Markov, there are eight states in which the patient can be before moving to the desired points and two states that are the desired points of the model – "last contact", "lethal outcome of a patient". The number of transitions between them is 80 with a cycle duration of 7 days. The date of diagnosis for all was taken as week zero, and from this the probability of transitions in each cycle until death or "last contact" was calculated. Based on these data, it became possible to calculate the necessary financial support to pay for medical services predicted to provide medical care in the "oncology" profile to patients in primary health care and specialized, including high-tech, medical care. These calculations should facilitate the adoption of correct management decisions in the healthcare system when planning the necessary material, labor and financial resources when providing medical care to patients in the "oncology" profile.

CHAPTER 3. DEGREE OF RELIABILITY OF THE STUDY RESULTS

The clinical model of a patient with MN of the bronchi and lung based on the generated Markov model obtained from the "TreeAge Pro 2011" software (TreeAge Software Inc., USA) created for use for prognostic purposes to make system management decisions in healthcare, we assessed the reliability of the analyzed data. For this purpose, we compared the volume of data included in the model and the volume of patients by year in St. Petersburg, and additionally compared survival curves, as well as the distribution of patients by gender and age in our database of patients included in the model and data from the PCR SPb.

3.1 Evaluation of the analyzed data included in the model by the volume of the analyzed sample

Since a comparative assessment of the total sample was not possible, we compared the data used to construct the model with the annual incidence data provided by the P.A. Hertsen Moscow Oncology Research Center. According to the date of MN of the bronchi and lung diagnosis, the data included in the Markov model were quantitatively compared with the number of MN of the bronchi and lung patients in St. Petersburg in the corresponding years recorded by the P.A. Hertsen Moscow Oncology Research Center [28–36] (Table 20).

Based on the assessment, we can say that annually, from 2011 to 2019, we have analyzed more than 70 % of patients newly diagnosed with MN of the bronchi and lungs because the number of P.A. Hertsen Moscow Oncology Research Center takes into account MN of the bronchi and lung patients recorded post-mortem, in our database there are no such patients, as all of them received treatment. No sample comparison was performed in our study; representativeness is confirmed by the general population, which makes up more than 72.1 % of all MN of the bronchi and lung patients during the same period.

Table 20 – Comparison of data on malignant neoplasm of the bronchi and lung incidence for St. Petersburg, 2011–2019 (P.A. Hertsen Moscow Oncology Research Center and obtained database for modeling)

Year of diagnosis	MN of the bronchi and lung incidence in St. Petersburg (data from P.A. Hertsen Moscow Oncology Research Center), including recorded post-mortem	Number of patients identified by year of diagnosis
2011	1,788	1,384
2012	1,800	1,405
2013	1,826	1,462
2014	1,888	1,490
2015	2,217	1,545
2016	2,181	1,559
2017	2,285	1,610
2018	2,172	1,530
2019	2,236	1,283

3.2 Survival – comparison of data included in the clinical model and information from a population-based cancer registry

Based on the survival curve, when comparing the data included in the study clinical model patient with MN of the bronchi and lung and historical information from the PCR, it is also possible to assess the comparability of the sample with real survival data.

The generated model allows to construct a survival curve according to the stage and morphology of the disease [7]. To validate the model, we compared the survival curves of MN of the bronchi and lung patients by disease stages with the data provided by Merabishvili V.M. et al. (2015) [56, 63], for the period 2002–2006.

To be able to construct a survival curve for 5 years of follow-up for patients included in the model, we selected those diagnosed from 2011 to 2015 inclusive, because for patients diagnosed in 2016 and later, we cannot track the entire five-year survival period.

Minimal deviations were identified, which may be due to an overestimation of the proportion of early stages in the register compared to the data obtained in the model, which also confirms the high representativeness of the sample in the model (Figure 18).

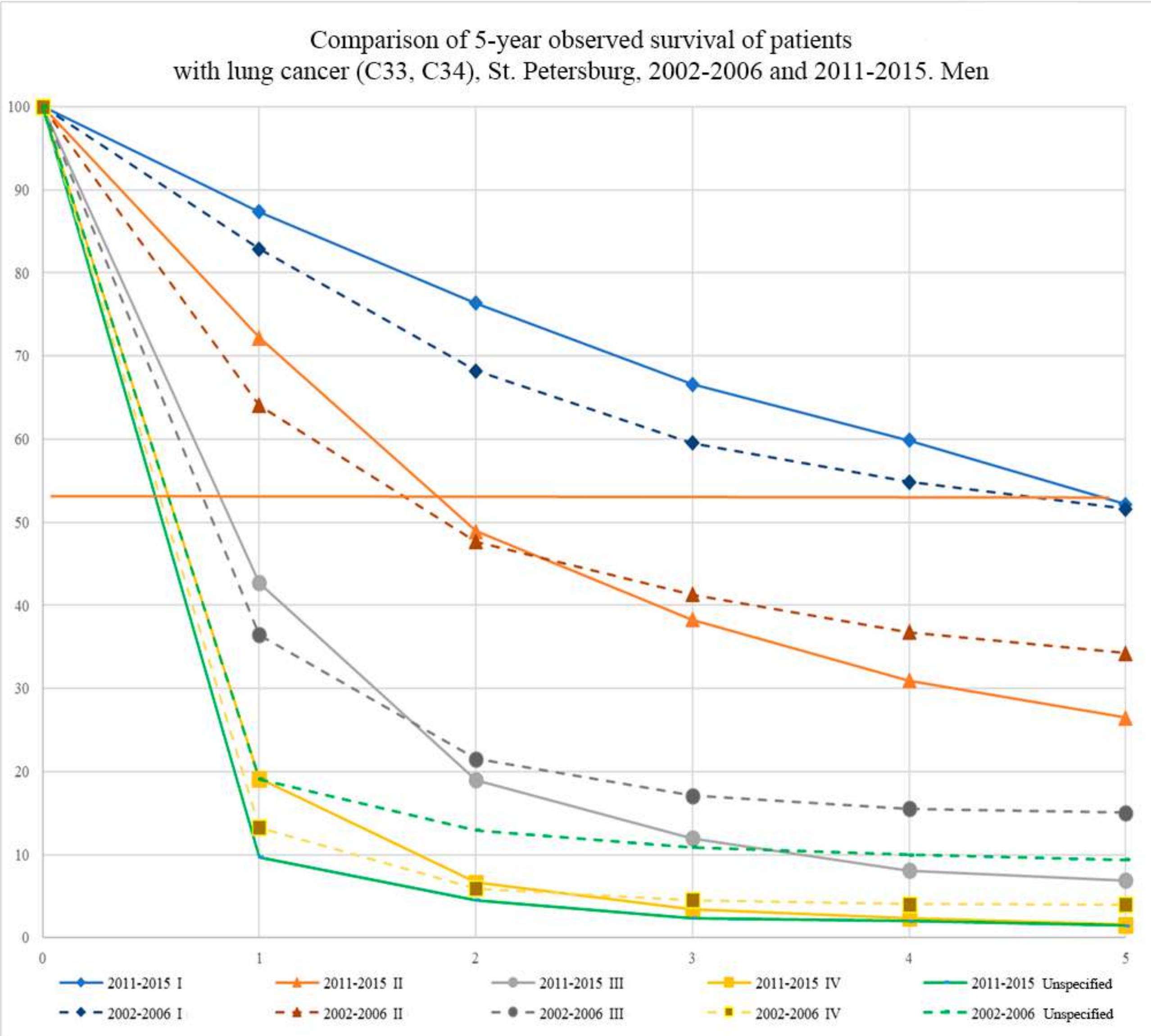


Figure 18 – Data on the five-year survival of men with malignant neoplasm of the bronchi and lung, patient comparison of two groups in 2002–2006 and 2011–2015

3.3 Demographic characteristics of malignant neoplasm of the bronchi and lung patients in the model

Descriptive statistics methods were used to assess whether the distribution of the ages of the patients included in the model Markov conformed to a normal distribution (Figure 19).

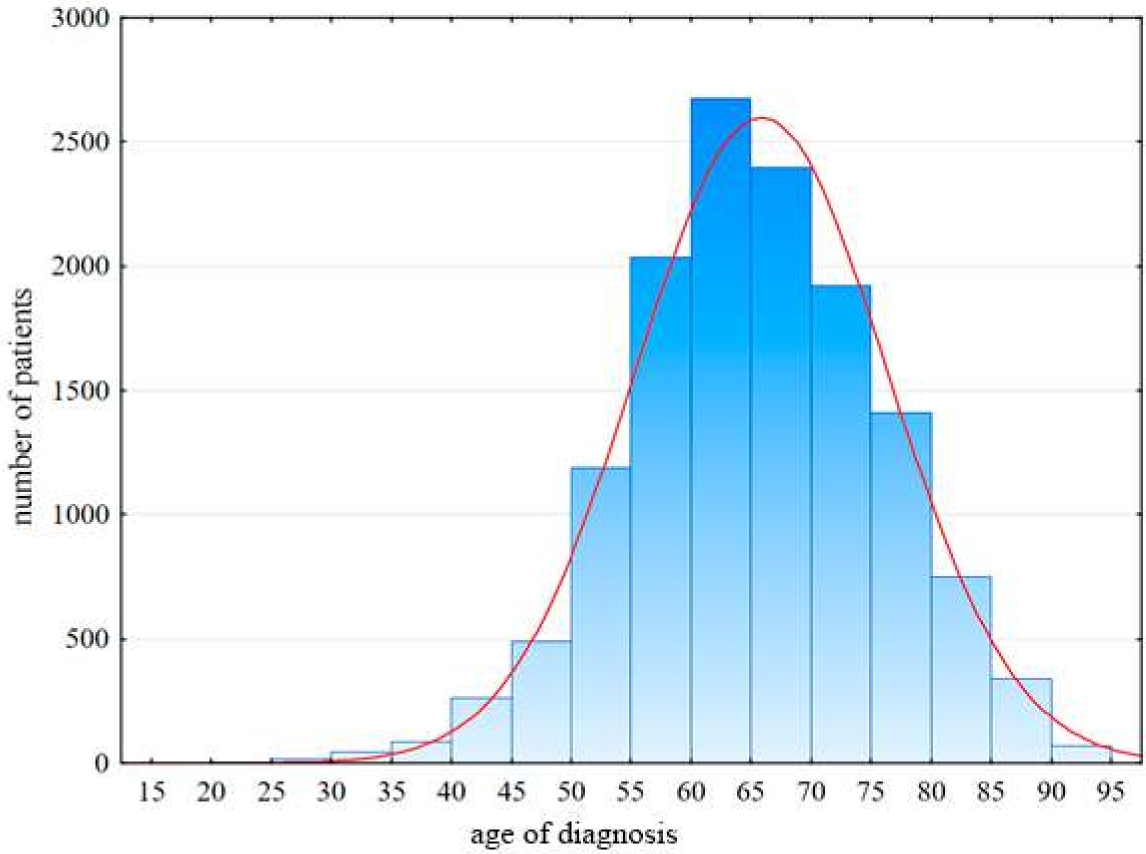


Figure 19 – Distribution of malignant neoplasm of the bronchi and lung patients by age of diagnosis identified for model Markov construction

As it can be seen from the data presented in Figure 19, the age distribution of the patients included in the model is normal.

The main parameters of the distribution of the age of diagnosis are summarized in Table 21. As it can be seen from the data presented in the table above, the parameters of the age distribution of the patients included in the model follow a normal distribution.

Table 21 – Distribution parameters of the age of diagnosis in the sample of malignant neoplasm of the bronchi and lung patients identified for Markov model construction

Parameter	Value	Parameter	Value
Number of observations	13,501	Standard deviation	10.5
Average	65.85	Asymmetry	-0.12
Median	66.00	Excess	0.08
Mode	63.00		

To assess the degree of representativeness of the sample, we compared the average age of diagnosis in patients included in the model and patients from the PCR SPb with MN of the bronchi and lung diagnosed from 2011 to 2019 by the method of variance analysis, separately in a group of men and women (Figure 20).

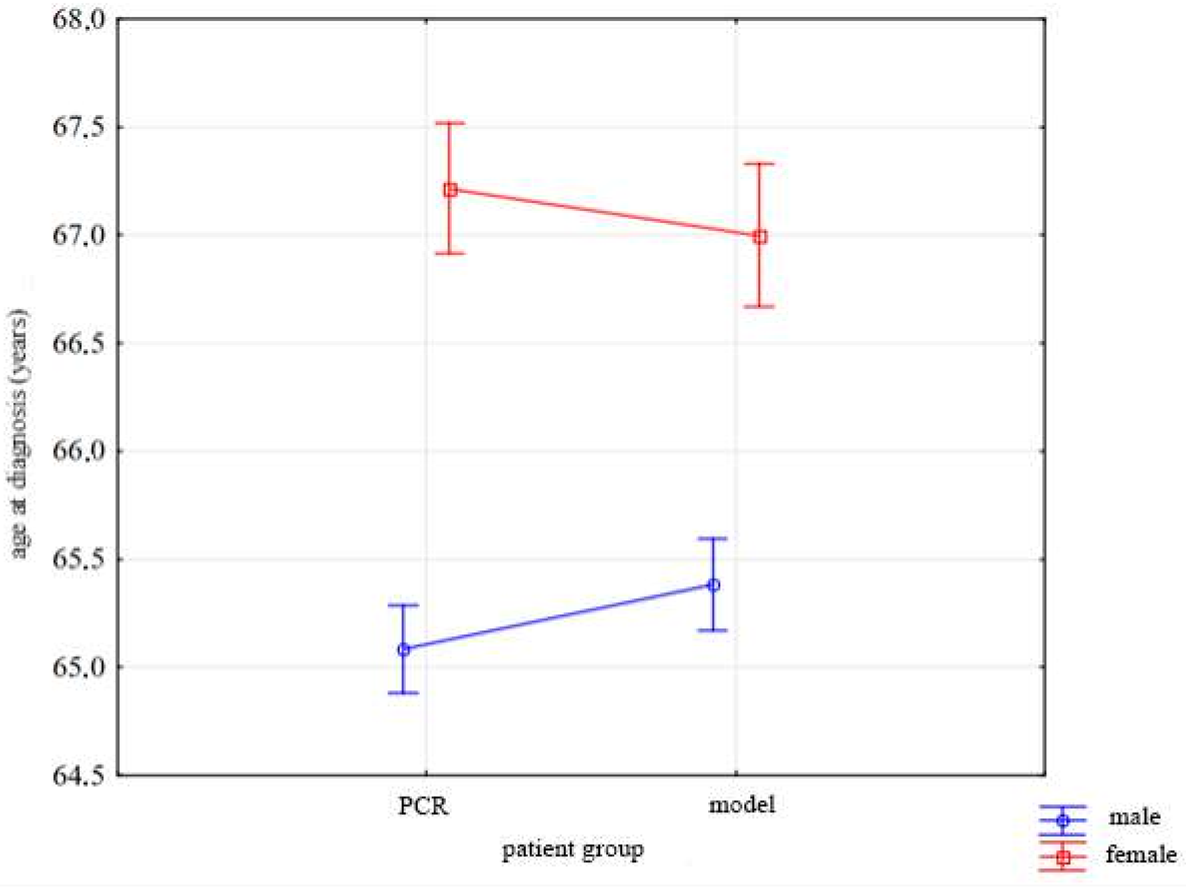


Figure 20 – Comparison of the average age of diagnosis by gender in the sample identified for the Markov model and patients registered in the population cancer registry SPb (without those recorded post-mortem), 2011–2019

The difference in the average age of diagnosis when comparing the group of patients included in the model and from the PCR SPb was not statistically significantly different, both in the male subgroup (average age 65.38 years 95 % credibility interval (CI): 65.17–65.59) and 65.08 years (95 % CI: 64.88–65.29), respectively; $p > 0.05$) and in the subgroup of women (average age 66.99 years (95 % CI: 66.67–67.33) and 67.21 years (95 % CI: 66.91–67.52), respectively; $p > 0.05$), which indicates the representativeness of the sample by the average age of MN of the bronchi and lung diagnosis.

Differences in gender distribution between the group of patients included in the model and the patients recorded in the PCR SPb database were assessed by calculating the odds ratio in a four-field table analysis (Table 22).

Table 22 – Comparative gender distribution of malignant neoplasm of the bronchi and lung patients included in the model and from the PCR SPb database

Parameter	PCR SPb database	Model	Total
Men	10,479	9,443	19,992
% by line	51.98 %	48.02 %	100 %
Women	4,718	4,058	8,776
% by line	54.07 %	45.93 %	100 %
Total	15,197	13,501	28,698

The odds ratio when comparing the groups of patients included in the model and from the PCR SPb database is 1.05 (95 % CI: 0.99–1.10), indicating that the groups do not differ according to the Chi-square with Yate's correction criterion (3.24; $p = 0.07$).

Thus, the analysis shows that the parameters of distribution by age of diagnosis of MN of the bronchi and lung in the group of patients included in the model Markov correspond to the normal distribution of the average age of diagnosis and distribution by gender in the group of patients included in the model statistically reliably does not differ from the patients recorded in the PCR SPb database.

Summary of Chapter 3

The creation of a clinical model of a patient with MN of the bronchi and lung was carried out on a group of patients living in St. Petersburg. There was no comparison with another group. To confirm the representativeness of the sample, a quantitative comparison was made of all cases with a newly diagnosed MN of the bronchi and lung in St. Petersburg.

The general population of the sample for constructing the model was 72.1 % of all newly diagnosed MN of the bronchi and lung in St. Petersburg from 2011 to 2019 (13,268 patients). Additionally, the five-year survival curves for 2002–2006 and the data in the model for 2011–2015 were compared, because it is impossible to track 5-year survival in patients included in the model with diagnoses established in 2016 and later. With this comparison, we identified minimal deviations, which may be due to an overestimation of the proportion of early stages in the registry compared to the data obtained in the model.

The average age of patients with MN of the bronchi and lungs among men and women identified to build a clinical model of the patient and from the database of the PCR SPb are similar.

The distribution by age of diagnosis of bronchial and lung MN in the group of model patients corresponds to the normal distribution of the average age of diagnosis.

The gender distribution in the group of patients included in the model is statistically significant and does not differ from the patients included in the database of the PCR SPb, which indicates the representativeness of the sample for modeling.

CHAPTER 4. MALIGNANT NEOPLASM OF THE BRONCHI AND LUNG RISK FACTORS

The conducted research on the study of risk factors in patients diagnosed with MN of the bronchi and lung allowed us to analyze the smoking factor at the inpatient level of the N.N. Petrov National Medical Research Center of Oncology, and the COVID-19 epidemic factor at the population level. Unfortunately, accounting of risk factors in the created model is impossible at the moment, since there is no registration of them. But in the future for more reliable modeling results on the severity of the course of MN of the bronchi and lung in patients with risk factors and predicting the burden on healthcare, this should be taken into account in cancer registries or UIS.

4.1 Smoking and malignant neoplasm of the bronchi and lung comparative data based on the National Medical research Center of Oncology named after N.N. Petrov

One of the most common exogenous factors of carcinogenesis is tobacco smoke. When tobacco and paper smolder, tobacco smoke containing more than 8,700 identified chemicals is released into the human body [8]. It provokes more than a third of all MN. Both active and passive smoking are considered dangerous, and even when a smoker quits the habit, he or she has a higher risk of getting sick. Due to its damaging effect on DNA and large percentage of smokers, it becomes one of the factors ranked first in the process of oncogenesis, especially MN of the bronchi and lung [6, 21, 113].

In 2016, RF entered the top five countries with the highest incidence and mortality associated with tobacco smoking (TS), and our country's tobacco market is the fourth largest in the world in terms of consumption [136].

Since 2014, the country has launched such national projects as "Demography", "Let's quit", paying great attention to the fight against smoking and the formation of a healthy lifestyle [17, 83, 90]. Health centers and communities in various social networks are being opened, where a citizen can get advice on quitting a bad habit [9, 41].

Thanks to the anti-smoking program conducted in RF, the number of tobacco companies in the RF is decreasing annually, so in 2009 the share of smokers in RF was 39.5 %, in 2013, when the campaign on the design of cigarette packs with inscriptions about the dangers of smoking and photos was just launched, the share of smokers was 41 %, in 2016 – 30.9 %, in 2018 – 28.3 %, in 2020 – 21.5 %, and in 2021 – 20.3 % [23, 69].

The All-Russian Center for the Study of Public Opinion (VTsIOM) notes that over the past 9 years the proportion of people who quit smoking is constantly growing from 10 % in 2013 to 17 % in 2022. The ratio of smokers by gender in 2022 was as follows: men made up 47 %, and women – 21 % and more than 67% of Russians do not have this habit. Whereas in 2009, the majority of smokers were people aged 18 to 44 years (48–50 % of all TS), now they are people aged 25 to 59 years (38–42 % of all TS) [48, 76, 77].

According to Rosstat, in 2020 the sale of tobacco products in RF decreased by 153.9 billion cigarettes/papyros compared to 2011 [24, 48].

Undoubtedly, this is a positive dynamic, as tobacco smoke remains one of the most dangerous exogenous factors that provoke the development of cancer, but for comparison in the USA the share of smokers is about 18 % [10]. Tobacco-dependent people have an increased risk of stroke and cardiovascular diseases, additionally increasing the toxic load on the body as a whole, which leads to a more severe course of acute and chronic diseases and increases the financial costs for treatment [6, 21, 46].

Smoking is most commonly designated as the main cause that triggers the development of MN of the bronchi and lung and MN oral mucosa [21, 46, 136].

On the basis of data on patients treated in the National Medical Research Center of Oncology named after N.N. Petrov, the number of smokers out of the total number of treated patients was analyzed (Table 23) [92].

Smoking patients with MN of the bronchi and lungs (1,275) of all smoking patients (9,201) accounted for 13.85%, and took 1st place despite the fact that patients diagnosed with MN of the bronchi and lungs among others took 4th place and amounted to 5.2%.

Table 23 – Distribution of patients treated in the National Medical Research Center of Oncology named after N.N. Petrov from 2013 to 2021, by nosology

Malignant neoplasms	ICD–10	Number of patients	Number of smokers										% of smokers
			2013	2014	2015	2016	2017	2018	2019	2020	2021	Total	
Trachea and lung	C33, C34	2,496	110	129	81	122	125	198	186	153	171	1275	**51.08** %
MN Breast	C50	8,328	74	93	75	101	93	116	77	113	99	841	10.10 %
Prostate gland	C61	2,847	25	47	45	49	44	52	78	86	98	524	18.41 %
Cervix	C53	2,144	47	56	73	47	55	35	37	33	42	425	19.82 %
Bladder	C67	1,119	23	25	36	25	60	51	59	43	65	387	34.58 %
Gaster	C16	1,805	29	36	37	59	47	57	68	56	52	441	24.43 %
Kidneys	C64	1,544	23	27	29	35	36	38	39	40	69	336	21.76 %
Esophagus	C15	641	26	48	35	38	37	43	43	40	31	341	**53.20** %
Skin	C44	1,737	14	21	34	39	36	23	31	31	40	269	15.49 %
Melanoma	C43	1,952	18	30	39	35	32	27	36	37	46	300	15.37 %
Rectum	C20	1,505	15	30	22	23	39	50	55	41	40	315	20.93 %
Uterus	C54	2,625	19	22	33	27	27	29	23	34	17	231	8.80 %
Larynx	C32	309	21	23	26	20	34	20	25	24	13	206	**66.67** %
Colon	C18	1,605	8	21	26	30	27	28	48	21	34	243	15.14 %
Soft tissue	C49	887	24	23	18	17	22	21	22	20	24	191	21.53 %
Ovaries	C56	1,676	15	21	20	17	27	19	26	18	12	175	10.44 %
	other	14,136	310	402	407	215	251	265	209	256	386	2,701	19.10%
Total		47,356	801	1,054	1,036	899	992	1,072	1,062	1,046	1,239	9,201	19.43%

Of the total number of patients receiving inpatient treatment during the specified period, records of smoking were found in 9,201, which is 19.43% and corresponds to the average share of smokers in the RF; smoking questionnaires were filled out for them (Appendix B).

During the period from 2013 to 2021, there has been an increase in the number of smokers diagnosed with MN of the bronchi and lung.

The correlation analysis method showed that for patients diagnosed with MN of the bronchi and lung, there was a statistically significant correlation between the year of diagnosis and the number of smokers ($r = 0.72$; $p = 0.028$), and the regression analysis method showed that the number of smoking patients statistically significantly increased from 2013 to 2021 ($b = 0.72$; $p = 0.029$), which was not observed for other localizations ($r = 0.59$; $p = 0.095$) (Figure 21).

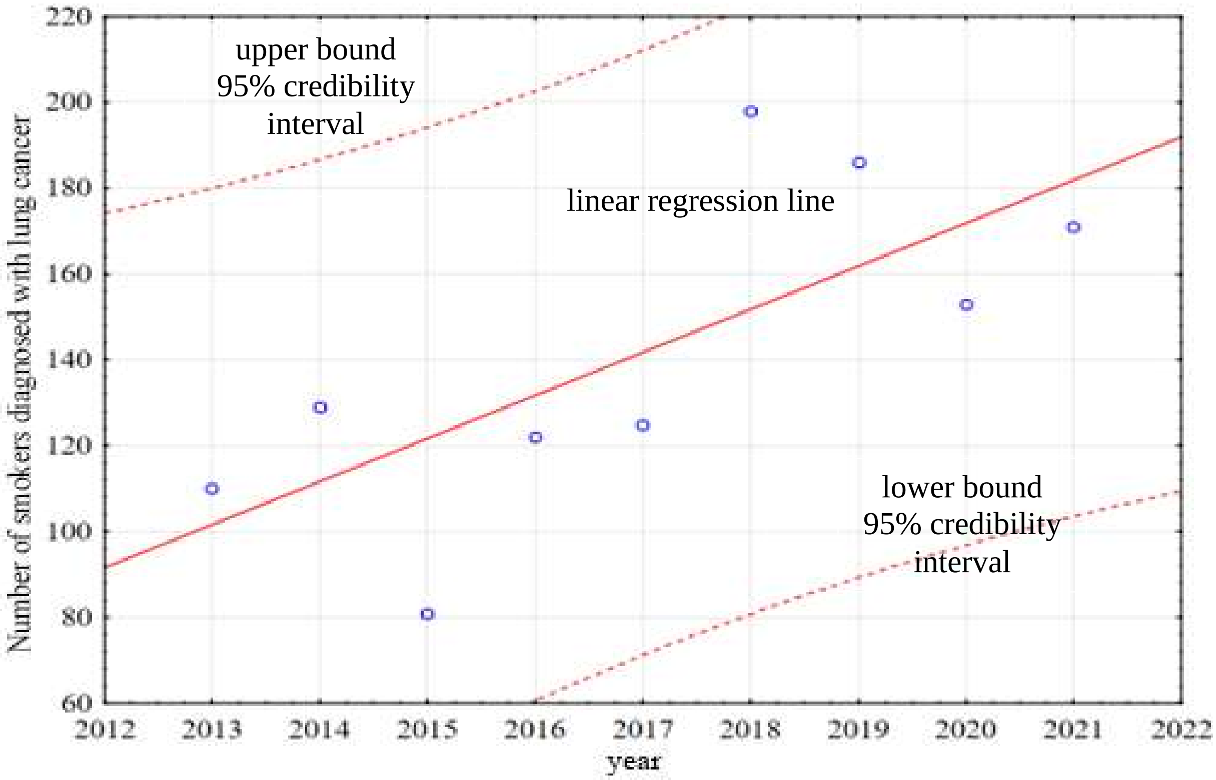


Figure 21 – Results of regression analysis of patients with malignant neoplasm of the bronchi and lung from 2013 to 2021 at the National Medical Research Center of Oncology named after N.N. Petrov

As can be seen from the information presented in Figure 21, the result of the regression analysis is a straight line reflecting an increase in the number of smokers in the period from 2013 to 2021, on average by 10 people each year. Almost all points fall within the range between the lower and upper limits of the 95 % CI for the linear regression equation, indicating a strong positive correlation ($r = 0.72$; $p = 0.028$). Thus, the obtained equation of the dependence of the number of smokers on the year allows us to build a forecast about the number of smokers in the future.

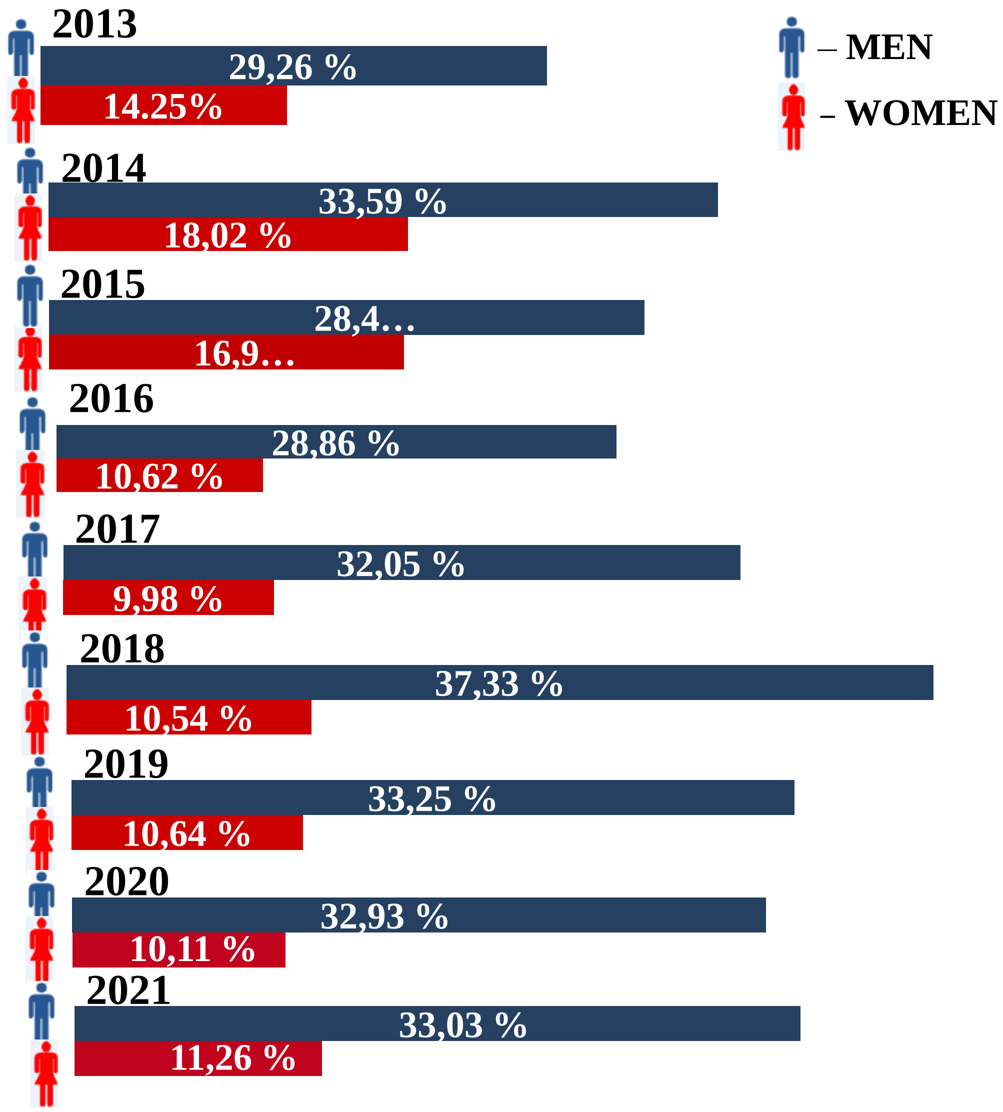
The total number of male smokers was 5,469, which is 47.59 % of the male study group, for women the number of smokers was 3,732 – 14.0 %. The proportion of male smokers from the total male group increased from 41.37 % to 49.39 % over 9 years of observation, the proportion of female smokers decreased from 16.57 % to 12.69 %. The distribution of smoking and non-smoking patients by year is presented in Table 24.

Assessment of the dynamics of the proportion of smokers to the total number of hospital admissions has significant fluctuations and ranges from 16.98 % in 2016 (minimum number of smokers) to 23.35 % in 2014 (maximum number of smokers), i.e., before the adoption of the Federal Law No.15 "On the protection of citizens' health from exposure to environmental tobacco smoke and the consequences of tobacco consumption".

Despite the fact that according to the data published on the website of the Ministry of Health of the Russian Federation the prevalence of smoking is constantly decreasing, we did not identify this trend in our study. The proportion of smokers out of all patients with MN treated at the National Medical Research Center of Oncology named after N.N. Petrov for 9 years of observation remained generally unchanged (Figure 22).

Table 24 – Distribution of patients treated in the National Medical Research Center of Oncology named after N.N. Petrov from 2013 to 2021, by gender and smoking groups (smoker/non-smoker)

Indicator	First year of hospital admission									Total number
	2013	2014	2015	2016	2017	2018	2019	2020	2021	
Number of smokers	801	1,054	1,036	899	992	1,072	1,062	1,046	1,239	9,201
- of them men	412	519	485	533	624	713	704	684	795	5,469
- of them women	389	535	551	366	368	359	358	362	444	3,732
Number of non-smokers	3,343	3,460	3,918	4,394	4,652	4,245	4,420	4,611	5,112	38,155
- of them men	996	1,026	1,219	1,314	1,323	1,197	1,413	1,393	1,612	11,493
- of them women	2,347	2,434	2,699	3,080	3,329	3,048	3,007	3,218	3,500	26,662
Number of patients	4,144	4,514	4,954	5,293	5,644	5,317	5,482	5,657	6,351	47,356
% of smokers to the total number of patients	19.33 %	23.35 %	20.91 %	16.98 %	17.58 %	20.16 %	19.37 %	18.49 %	19.51 %	19.43 %



2013 – 19.35 % of all patients with cancer at the N.N. Petrov National Medical Research Center of Oncology	**2021 – 19.51 %** of all patients with cancer at the N.N. Petrov National Medical Research Center of Oncology

Figure 22 – Percentage distribution of tobacco-smoking patients from the total number of MN patients by gender and year of first hospital admission in 2013–2021 in National Medical Research Center of Oncology named after N.N. Petrov

The method of covariance analysis (ANCOVA) was used to estimate the dynamics of the number of smoking patients in the regression model taking into account the year of diagnosis and gender. The obtained model is characterized by a high degree of predictivity (determination coefficient $r^2 = 0.92$, $p < 0.01$).

There was an increase in the number of smokers with MN between 2013 and 2021 ($p = 0.01$), driven by an increase in male smokers ($p < 0.01$) (Figure 23).

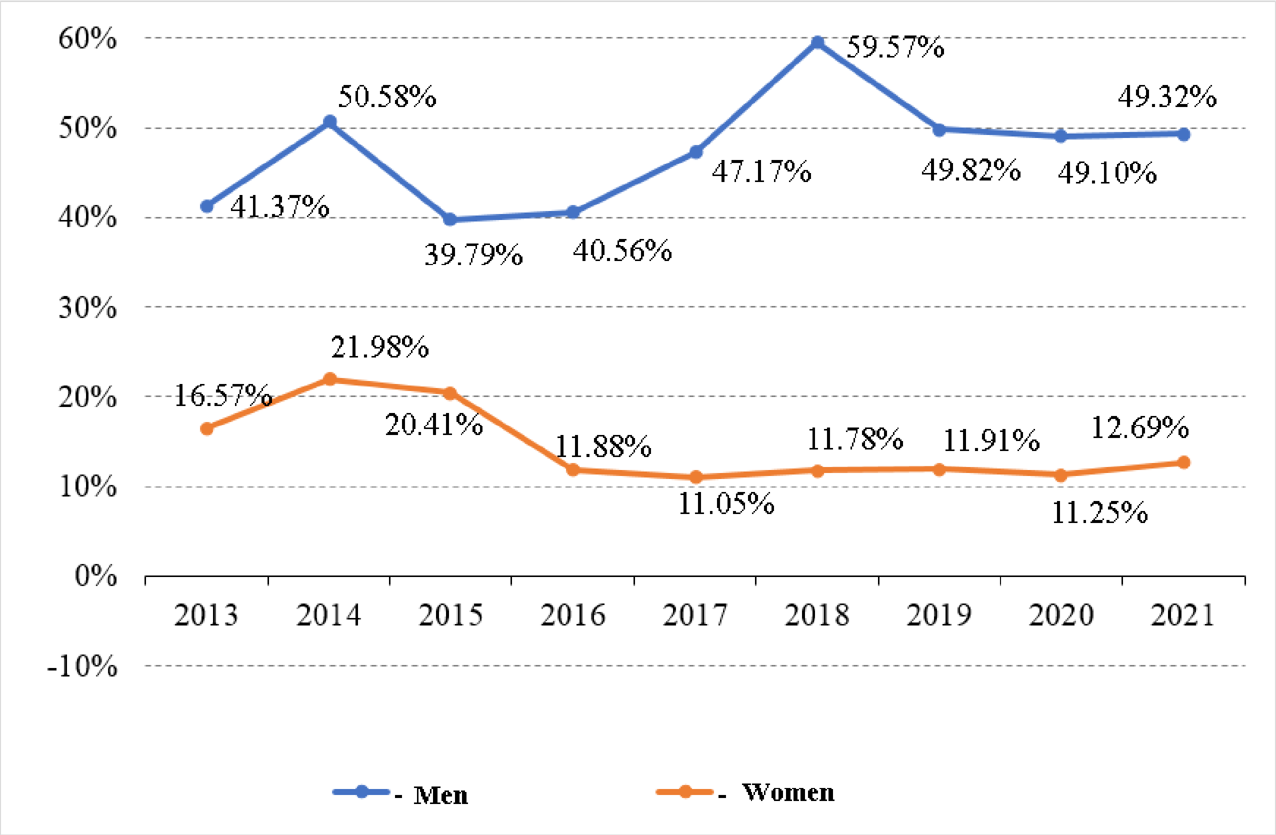


Figure 23 – Proportion of smokers by gender and first year of treatment at the National Medical Research Center of Oncology named after N.N. Petrov

When analyzing the TS structure of MN of the bronchi and lung patients from 2013 to 2021, the proportion of males among all smoking MN of the bronchi and lung patients ranged from 90 % to 81 %.

Against the background of a general increase in the number of smokers among MN of the bronchi and lung patients, the incidence of female TS during the analyzed period increased from 17 % in 2013 to 24 % in 2021, the maximum value was found in 2018 – 31 %. The share of male TS also increased from 54 % to 66 % (Table 25).

Publications have noted the relationship between the number of cigarettes smoked per day and the smoking experience with a proportional increase in the risk of developing MN [112].

Table 25 – Frequency of TS distribution of malignant neoplasm of the bronchi and lung patients, in the first year of hospital admission and gender in the National Medical research Center of Oncology named after N.N. Petrov from 2013 to 2021

ICD-10	% of smokers from the entire group of patients with MN of the bronchi and lungs	Gender	Change in the frequency of TS patients by gender									
			2013	2014	2015	2016	2017	2018	2019	2020	2021	Frequency of smoking patients
C33, C34	51.08 %	Men	54 %	60 %	37 %	50 %	57 %	77 %	66 %	68 %	66 %	60 %
		Women	17 %	23 %	10 %	11 %	7 %	31 %	25 %	22 %	24 %	20 %

When assessing the distribution of patient smokers by smoking history, it was found that more than 80% of patients across all nosologies were patients with a smoking history of 10 or more years, with the proportion of patients with a smoking history of more than 10 years not changing significantly between 2013 and 2021. If in 2013 it was 85.0 %, then in 2021 it was 87.3 % (p = 0.24 according to the Chi-square criterion) of all smoking patients with MN.

Based on the analysis of questionnaires, it was found that more than 51 % of patients with MN of the bronchi and lung in N.N. Petrov National Medical Research Center of Oncology are smokers. The proportion of smokers in other nosologies is significantly lower, except for laryngeal (C32) and esophageal (C15) MN, which is associated with maximum contact with a cigarette (cigarette smoldering temperature is 300–420 °C) [71]. We also observed an increase in the frequency of smoking in female and male patients diagnosed with MN.

4.2 Impact of the new coronavirus infection pandemic on malignant neoplasm of the bronchi and lung incidence in the population

A group of US scientists found that some of the patients who underwent the new coronavirus infection (COVID-19) and receive outpatient rehabilitation and recovery treatment need more detailed and individualized treatment than patients diagnosed with MN after antitumor therapy who did not undergo COVID-19 [128].

Thanks to the PCR NWFD, we also have the opportunity to analyze data on new coronavirus infection cases diagnosed with MN. Due to the fact that COVID-19 patients have a major impact on the lungs and only patients diagnosed with MN of the bronchi and lung were selected for the group we analyzed, it seems that these should be some of the most severe cases [43].

Questionnaires were formed for 1 120 patients who had suffered COVID-19 (Appendix B) [98].

Of the patients recorded, 389 were women and 731 were men. Of the patients treated in inpatient settings of the N.N. Petrov National Medical Research Center of

Oncology in 2020 and 2021, the total number of MN patients with COVID-19 amounted to 108 patients, of which only 7 were diagnosed with MN of the bronchi and lung (they were also found in the PCR). If we consider the number of COVID-19 patients by stage of MN, then: Stage I – 23.48 %, Stage II – 13.75 %, Stage III – 20.72 %, Stage IV – 14.11 % and no stage – 27.95 %. In 257 COVID-19 patients, the diagnosis of MN of the bronchi and lung was established post-mortem because the date of MN of the bronchi and lung diagnosis was later than the date of lethal outcome.

44.82 % COVID-19 patients with MN of the bronchi and lung were treated on an outpatient basis, 35.8 % received inpatient treatment, and in 19.3 % we were unable to obtain information about the treatment provided.

To analyze the course of COVID-19, 5 options were identified: in 46.61 % – satisfactory, in 7.5 % – moderately severe, 11.25 % – severe, 9.02 % – extremely severe, in 25.63 % information on the severity of the disease course could not be obtained (287 patients). It should be noted that of the group of patients in whom COVID-19 was not determined (287 patients) 245 patients died, i.e. 85.37 % from causes defined as pneumonia, acute infections and other respiratory diseases, from which it can be assumed that the course of COVID-19 in them was extremely severe, and therefore the proportion of such patients from the whole analyzed group was 30.9 %. The total number of lethal outcomes from the causes listed previously was 654 (58.39 %), of which more than 72.63 % died between 0 and 21 days from the time of diagnosis of COVID-19. In the distribution of COVID-19 lethal outcomes by stage of MN, 17.43 % were patients with stage I–II disease in almost equal proportions, 20.18 % – III, 16.21 % – IV and in 46.18 % of those who died the stage was not determined. Of the group of those who died without stage of MN, 73.18 % died within 15 days of the establishment of COVID-19, which may indicate initial massive lung lesions.

The mortality of MN of the bronchi and lung patients from COVID-19 was 58.39 %, which indicates a more severe course of this disease in MN of the bronchi and lung patients, since according to different data the mortality in 2020 from COVID-19 ranged from 4.6 % to 9.2 % [44, 82].

Based on the reference books of the P.A. Hertsen Moscow Oncology Research Center, N.N. Petrov National Medical Research Center of Oncology, the dynamics of MN of the bronchi and lung incidence (both genders) in RF was analyzed and the absolute number of registered MN of the bronchi and lung patients, standardized and "rough" incidence indicators were compared. A sharp drop in these numbers was revealed in 2020, from 60 113 patients (22.68 $^{0}/_{0000}$ – standardized indicator; 40.96 $^{0}/_{0000}$ – "rough" indicator) in 2019, to 54 375 patients (20.27 $^{0}/_{0000}$ – standardized indicator; 37.13 $^{0}/_{0000}$ – "rough" indicator) in 2020. A similar negative trend has been observed in almost all regions of the RF. In St. Petersburg, 2 236 patients were diagnosed with MN of the bronchi and lung for the first time (both genders) in 2019 (standardized indicator – 21.13 $^{0}/_{0000}$; "rough" indicator – 41.48 $^{0}/_{0000}$), and in 2020 – 1 958 patients (standardized indicator – 18.21 $^{0}/_{0000}$; "rough" indicator – 36.32 $^{0}/_{0000}$) (Figure 24, Table 26).

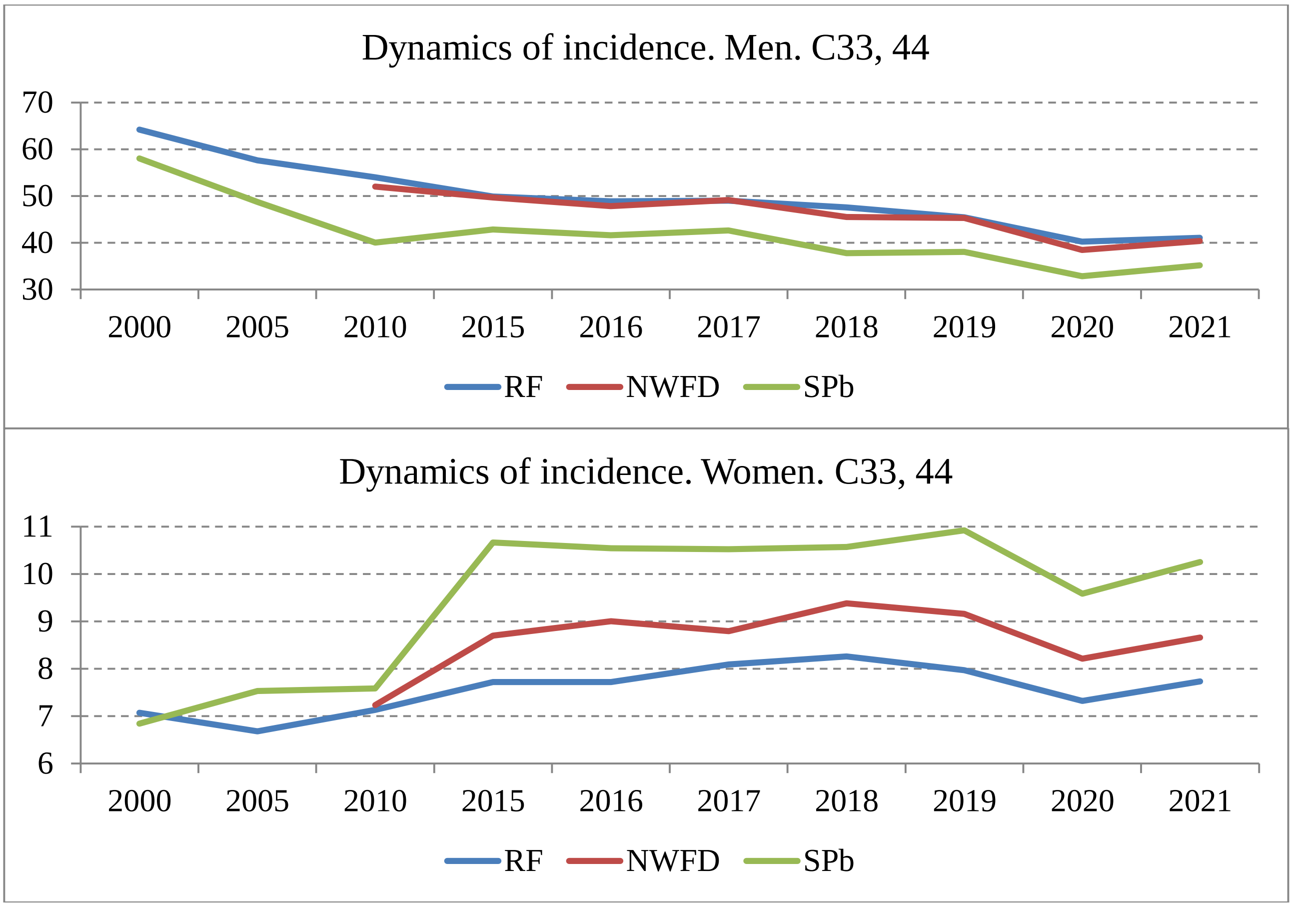


Figure 24 – Incidence of malignant neoplasm of the bronchi and lung in male and female population (C33, C34) in Russian Federation, NWFD and St. Petersburg, 2000–2021 (standardized indicators, $^{0}/_{0000}$)

Table 26 – Dynamics of malignant neoplasm of the bronchi and lung incidence in Russian Federation by gender

Gender	Indicator	Year					
		2000	2010	2015	2019	2020	2021
Men	Absolute number patients	52,961	46,407	48,139	47,005	42,303	43,555
	"Rough" indicator, $^{0}/_{0000}$	77.89	70.7	70.97	69.01	62.22	64.29
	Standardized indicator, $^{0}/_{0000}$	64.17	53.97	49.88	45.42	40.22	41.03
Women	Absolute number patients	10,164	10,578	12,212	13,108	12,072	12,773
	"Rough" indicator, $^{0}/_{0000}$	13.17	13.87	15.54	16.67	15.38	16.35
	Standardized indicator, $^{0}/_{0000}$	7.7	7.13	7.72	7.97	7.32	7.73

This cannot indicate that the incidence of MN of the bronchi and lung has become less, it is more likely that the incidence has remained the same, but due to the restrictive measures associated with COVID-19 there has been a decrease in detection and patients lost in 2020 and 2021, as evidenced by the slight increase in incidence in 2021.

We are likely to see these losses in 2023–2025, as echoes of the pandemic, some of the patients will be recorded as post-mortem and others will be diagnosed at later stages of the disease [22].

The fact that the pandemic has negatively affected the incidence of MN is also reported by the chief oncologist of the Ministry of Health of the Russian Federation Kaprin A.D. (2022), in his opinion; we should expect an increase in the later stages at which they will be identified [74].

In 2021, the number of detected cases begins to return to the indicators that were in the "pre-epidemic period", but an increase in the proportion of late stages and an increase in mortality is expected [45, 74].

Summary of Chapter 4

At this point in our study, it is not possible to account for risk factors or concomitant diseases in patients diagnosed with MN of the bronchi and lung that contribute to its development or worsen its course. These data are not recorded in any of the accounting systems.

We analyzed the smoking factor on the basis of questionnaires of patients diagnosed with MN of the bronchi and lung, undergoing treatment in N.N. Petrov National Medical Research Center of Oncology from 2013 to 2021 – 47,356 patients. It was found that more than 50 % of patients with MN of the bronchi and lung in N.N. Petrov National Medical Research Center of Oncology are smokers. The proportion of smokers in other nosologies is significantly lower, except for laryngeal (C32) and esophageal (C15) MN, which is associated with maximum contact with a cigarette (cigarette smoldering temperature is 300–420 °C). Despite the government's anti-tobacco reform and Rosstat reports of an annual decrease in the number of smokers, we observed an increase in the frequency of female and male smokers in patients diagnosed with MN of the bronchi and lung [92].

COVID-19 as a disease, presumably, aggravates the course of MN of the bronchi and lung, due to the fact that the patients have the main impact on the lungs. The data recorded in the PCR NWFD database on patients with a new coronavirus infection with a diagnosis of MN of the bronchi and lung were analyzed. 1,120 questionnaires were formed for patients who had suffered COVID-19 (Table A.5 of Appendix A) [98]. The mortality of MN of the bronchi and lung patients from COVID-19 was 58.39 %, which indicates a more severe course of this disease, since according to different data the mortality in 2020 from COVID-19 ranged from 4.6 % to 9.2 % [44, 82]. It is worth noting that based on the analysis of the dynamics of MN of the bronchi and lung incidence in RF and its revealed sharp drop in 2020, from 60,113 patients ("rough" indicator – 40.96 $^{0}/_{0000}$) in 2019, to 54,375 patients ("rough" indicator – 37.13 $^{0}/_{0000}$) in 2020, we should prepare for the growth of late stages and an increase in the number of lethal outcomes from MN of the bronchi and lung [45, 74].

CHAPTER 5. MODEL RESULTS

Based on the obtained MN of the bronchi and lung patient clinical model constructed with the Markov model based on the TreeAge Pro 2011 software product (TreeAge Software Inc., USA), it was possible to automatically predict the necessary material, labor and financial resources for medical care in the "oncology" profile. In turn, this helps to identify the right approaches in decision-making to combat this significant disease. At the moment, the costs of treating oncological diseases are constantly growing, as O.V. Tsareva (2020) reported at the oncological forum "White Nights" in 2020 [88]. To a greater extent, this is due to the use of expensive chemotherapy, the model, in turn, allows us to predict both the costs and the distribution of the burden on oncologists and the redistribution in terms of chemotherapeutic and surgical treatment (Table 27).

Table 27 – Monitoring of the volume and cost of medical care for patients with oncologic diseases in for round-the-clock inpatient facility and for day inpatient facility by insurance territories (as of June 1, 2020) [88]

Subject of the Russian Federation	Used for 5 months of 2019, thousand rubs	Used for 5 months 2020, thousand rubs	% of the funds provided for 5 months 2020	% growth by 2019
Russian Federation	67,693,563.7	110,360,166.5	97.6	163.0
Sverdlovsk region	1,492,383.5	3,274,515.9	103.4	219.4
Vladimir region	500,777.3	948,915.5	106.4	189.5
Tyumen region	701,581.3	1,276,484.3	116.2	181.9
Moscow region	3,978,049.6	7,193,935.4	128.9	180.8
Samara region	1,201,143.4	2,122,693.7	102.7	176.7
Ryazan region	508,501.8	789,224.2	110.5	155.2
Krasnoyarsk region	1,917,271.0	2,902,619.7	102.8	151.4
Orenburg region	987,511.0	1,492,923.6	103.0	151.2
Rostov region	1,851,908.2	2,711,643.8	103.5	146.4
Nizhny Novgorod region	1,628,569.6	2,223,103.6	106.9	136.5

5.1 Predictive modeling values of the outpatient state of the model for the treatment of patients with malignant neoplasms of the bronchi and lungs

The sample for predicting the outpatient stage included all 1,717 patients, because they were diagnosed during their lifetime according to the data of the P.A. Hertsen Moscow Oncology Research Center.

In the first year, the total number of medical services to diagnose the disease will amount to 22,419, of which primary appointments with specialist physicians – 1,513 services (6.75 %), laboratory tests – 8,928 services (39.83 %), instrumental methods – 8,853 services (39.49 %), molecular and genetic studies in outpatient conditions – 3,125 services (13.94 %).

Total costs amounts of funding to pay for all of the above outpatient services in the first year from the date of diagnosis of MN of the bronchi and lung disease will amount to 68,405.29 thousand rubs, including primary appointments of specialists – 1,116.03 thousand rubs (1.63 %), laboratory methods of examination – 7,863.59 thousand rubs (11.50 %), instrumental methods of examination – 38,123.26 thousand rubs (55.73 %), molecular and genetic studies – 21,302.41 thousand rubs (31.14 %).

Of the total number of primary appointments of specialist doctors, 1,408 (93.08 %) are consultations of an oncologist, 60 (3.97 %) are consultations of a neurologist and 45 (2.95 %) are consultations of a cardiologist.

Of laboratory methods of research, the number of pathologoanatomical studies of biopsy material, cytological studies of tissue micropreparations, clinical and biochemical blood analysis, general urinalysis and coagulogram will be performed of 1,374 services (15.38 %), and pathologoanatomical studies of biopsy material of tissues using immunohistochemical methods – 687 services (7.69 %).

Of the instrumental studies performed at the outpatient stage in the first year from the moment of diagnosis of MN of the bronchi and lung 1,528 (17.26 %) – registration of electrocardiograms, 1,374 (15.52 %) – videotracheobronchoscopy with biopsy, ultrasound studies of lymph nodes and ultrasound studies of abdominal cavity organs. Magnetic resonance imaging of the brain with intravenous contrast will be performed of 1,236 (13.96 %) studies. Positron emission tomography combined with computed tomography with tumorotropic radiopharmaceuticals with contrast – 824 (9,31 %) studies. Computed tomography of the chest and brain organs with intravenous contrast will be performed of 549 (6.21 %) studies, as well as a whole-body bone scintigraphy (Table 28).

Table 28 – Volume and funding to pay for medical care in the "oncology" profile for patients with malignant neoplasms of the bronchi and lung in outpatient conditions in the first three years from the moment of diagnosis establishment

Medical services to diagnose a disease, condition	Number of medical services	Amount for medical services, thousand rubs
1. Medical services to diagnose a disease, condition in the first year of observation		
1.1. Reception (examination, consultation) of a specialist doctor	1,513	1,116.03
1.2. Laboratory methods of examination	8,928	7,863.59
1.3. Instrumental methods of examination	8,853	38,123.26
1.4. Molecular genetic studies in outpatient conditions	3,125	21,302.41
Total in the first year of diagnosis	22,419	68,405.29
2. Medical services for treatment of a disease, condition, and of treatment, 2 and 3 years of observation		
2.1. Reception (examination, consultation) and supervision of a specialist doctor	4,914	3,697.54
2.2. Instrumental methods of examination	10,810	16,353.73
Total for 2–3 years from the moment of diagnosis	15,724	20,051.27
Total for three years of observation	38,143	88,456.56

Of the molecular genetic studies, 876 (28.02 %) each will account for the determination of PDL1 protein expression by immunohistochemical method and the study of mutations in the EGFR gene in biopsy material. Immunocytochemical study of biological material will be performed in 515 (16.48 %) cases, ALK gene translocation study and ROS1 gene translocation study will be performed in 343 cases (10.99 %) each. Molecular genetic study of mutations in the BRAF gene – 172 (5.49 %) cases.

Out of the total budget required to pay for the outpatient state of the clinical model first year from the moment of diagnosis of MN of the bronchi and lung, modeled on the basis of clinical recommendations in 2021, 25.70 % will be required to pay for positron emission tomography combined with computed tomography with tumorotropic radiopharmaceuticals with contrast – 17,581.80 thousand rubs, the second place is 15.59 % – molecular biological research for determination of PDL1 protein expression by immunohistochemical method, its costs will amount to 10,665.66 thousand rubs. The third place – 13.91 % in terms of costs – belongs to magnetic resonance imaging of the brain with contrast – 9,517.81 thousand rubs (Table D.1 of Appendix D).

In accordance with clinical guidelines, based on modeling of the second and third years of treatment and observation of MN of the bronchi and lung patients, taking into account the exclusion from the group of the number of those who died and moved to the "last contact" stage in the previous year, we obtained that the number of medical services in the second year of observation would be 9,101 cases for 11,605.80 thousand rubs, and in the third year – 6,623 cases for 8,445.47 thousand rubs. During both years of observation, 4,914 oncologist appointments and lung ultrasound examinations will be performed for 3,697.54 thousand rubs and 1,830.35 thousand rubs, respectively, 4,422 computed tomography scans of thoracic cavity organs for 9,821.95 thousand rubs.

Whole body bone scintigraphy, magnetic resonance imaging of the brain and lung radiography will be performed for 491 studies for 3,560.92 thousand rubs, 971.93 thousand rubs and 168.59 thousand rubs, respectively. A more detailed distribution of the required number of medical services for MN of the bronchi and lung patients and the required amount of funding for outpatient conditions in the second and third year of observation is presented in the Appendix (Table D.2 of Appendix D).

5.2 Results of modeling medical care received during inpatient treatment by patients with malignant neoplasms of the bronchi and lungs

Forecasting, taking into account the created clinical model of a patient with MN of the bronchi and lung allows to put into the program different values of scenarios, as an increase in the share of patients with early stages of MN of the bronchi and lung, as well as an increase in the absolute number of patients, for example, with the introduction of the screening programs described above. Therefore, we have created two scenarios of the model:

– maintaining the current proportion of patients with stages I and II (33.3 %) according to the data of P.A. Hertsen Moscow Oncology Research Center for 2019;

– increasing the proportion of stages I and II MN of the bronchi and lung patients to 58 %, for example, when CT screening is introduced, as calculated by Diederich et al. 2002 [109].

The modeling horizon was 3 years, based on the program of state guarantees of free medical care for citizens, which is annually approved for the relevant period (Resolution of the Government of the Russian Federation No. 2505 dated December 28, 2021 "Program of state guarantees of free medical care to citizens for 2022 and for the planned period of 2023 and 2024" and Methodological recommendations on methods of payment for medical care at the cost of compulsory medical insurance, approved by the Ministry of Health of the Russian Federation and the Federal Compulsory Medical Insurance Fund No. 11-7/I/2-1619, 00-10-26-2-06/750 dated February 2, 2022).

5.2.1 Predictive values for modeling stationary conditions of treatment of patients with malignant neoplasms of the bronchi and lungs with current key indicators

The sample for predicting inpatient care in the “oncology” profile included 1 659 patients, because according to the data of the P.A. Hertsen Moscow Oncology Research Center, 3.40 % (58 patients out of 1 717) have no stage of disease and there is no possibility to assign them to a subgroup by stage, on which survival depends [62].

When analyzing the first three years from the diagnosis of MN of the bronchi and lung, more than 78 % (4 435) of hospital admissions occurred in the first year in the group of patients newly diagnosed with MN of the bronchi and lung (Figure 25) [97].

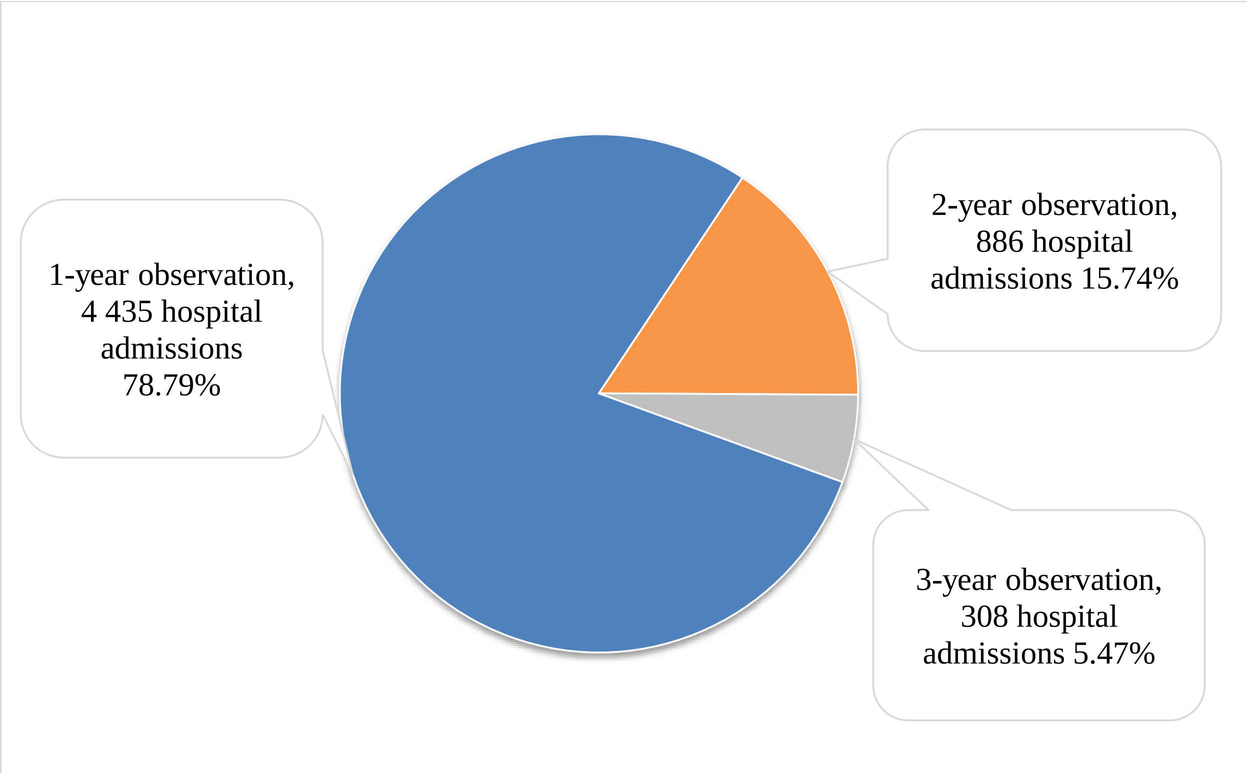


Figure 25 – Number of hospital admissions of patients with stage I–IV malignant neoplasm of the bronchi and lung over three years from the moment of diagnosis

On average, there are 3 hospitalizations per 1 patient diagnosed with MN of the bronchi and lung in the first year from the moment of diagnosis (stages I and II – 2, stages III and IV – 3). If we apply the "Indicator of the frequency of medical service provision" proposed in the clinical guidelines to the selected groups of inpatient treatment, the highest frequency of service provision in the group of patients with stage I of the disease falls on hospital admissions for major surgical treatment and is 0.65; for groups of patients with stages II–IV these are hospital admissions for chemotherapy treatment with the frequency of service provision II – 1.31, III – 2.42, IV – 1.89 [25].

Of the total 1-year hospital admissions, 2,853 were for chemotherapy treatment – 64.33 %. The second place is occupied by hospital admissions allocated to the state of therapeutic symptomatic treatment in inpatient facility related to previous treatment or course of the underlying disease – 549 hospital admissions (12.39 %).

The third place is hospital admissions to the condition model – “surgical treatment for the purpose of basic surgical treatment” 493 hospital admissions (11.11 %) (Figure 26).

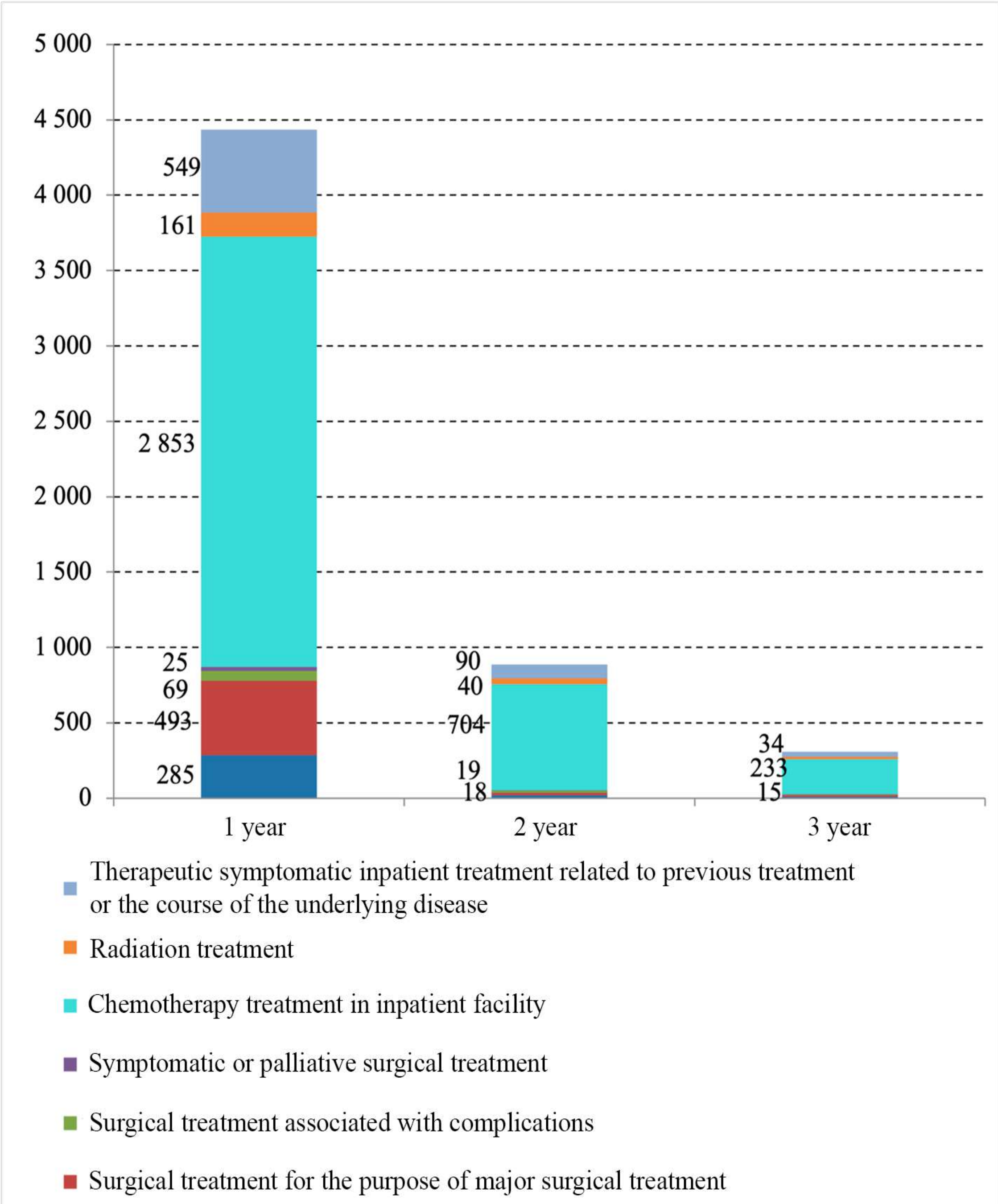


Figure 26 – Number of hospital admissions of patients with stage I–IV malignant neoplasm of the bronchi and lung over three years from the moment of diagnosis for each state of inpatient treatment

When forecasting the necessary funding to pay for inpatient treatment of patients newly diagnosed with MN of the bronchi and lung (according to the data of P.A. Hertsen Moscow Scientific and Research Oncological Institute of 2019) on the basis of the 2022 FCHIF tariffs for three years 848,401.56 thousand rubs will be required, excluding indexation and changes in tariffs for inpatient treatment. Almost 77 % of this amount falls on the first year of treatment (653,199.78 thousand rubs) (Figure 27).

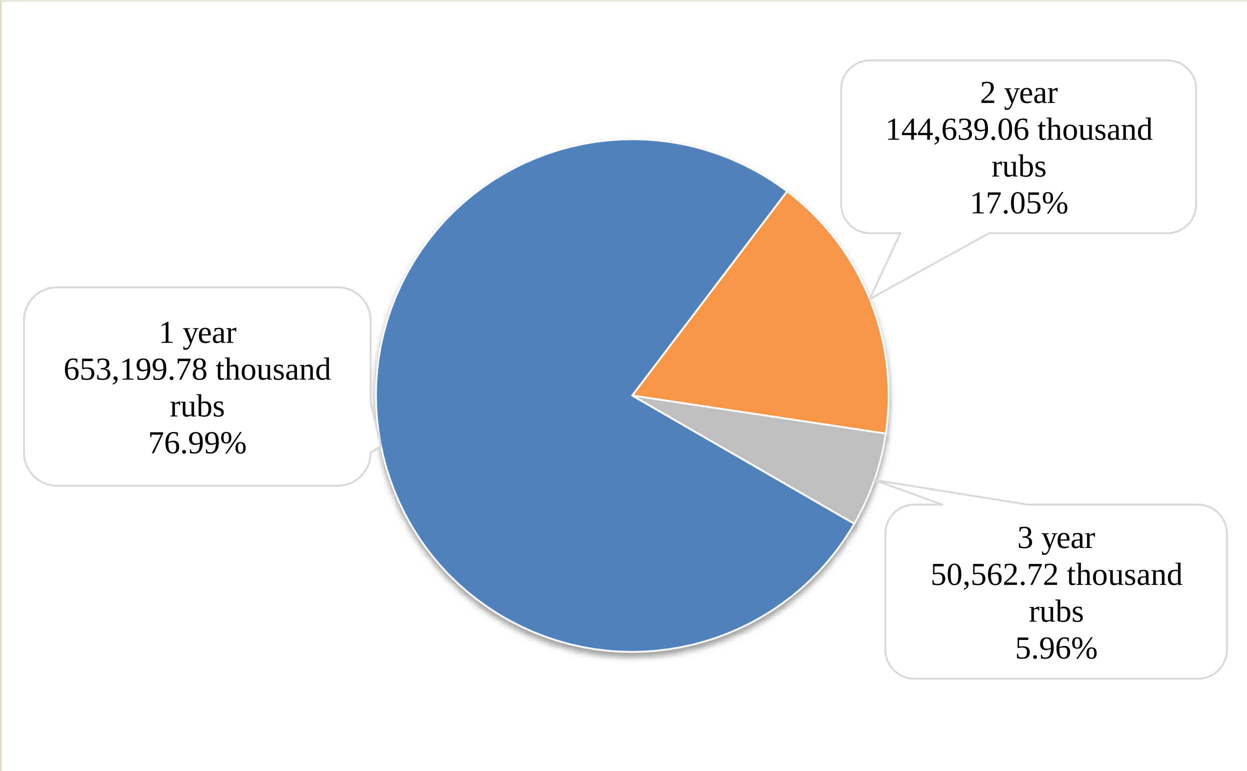


Figure 27 – Financing to pay for inpatient treatment of patients with stages I–IV malignant neoplasms of the bronchi and lung over three years from the moment of diagnosis

The first place in volume of financing is occupied by payment for chemotherapeutic treatment 80.79 % (527,703.38 thousand rubs) of the total budget in the first year of treatment, the second place in terms of the amount needed to pay for medical care in the first year – 71,663.04 thousand rubs belong to hospital admissions for the purpose of basic surgical treatment – 10.97 %, while in terms of the number of admissions this model state is in third place (493) (Figure 28) [94, 95, 97].

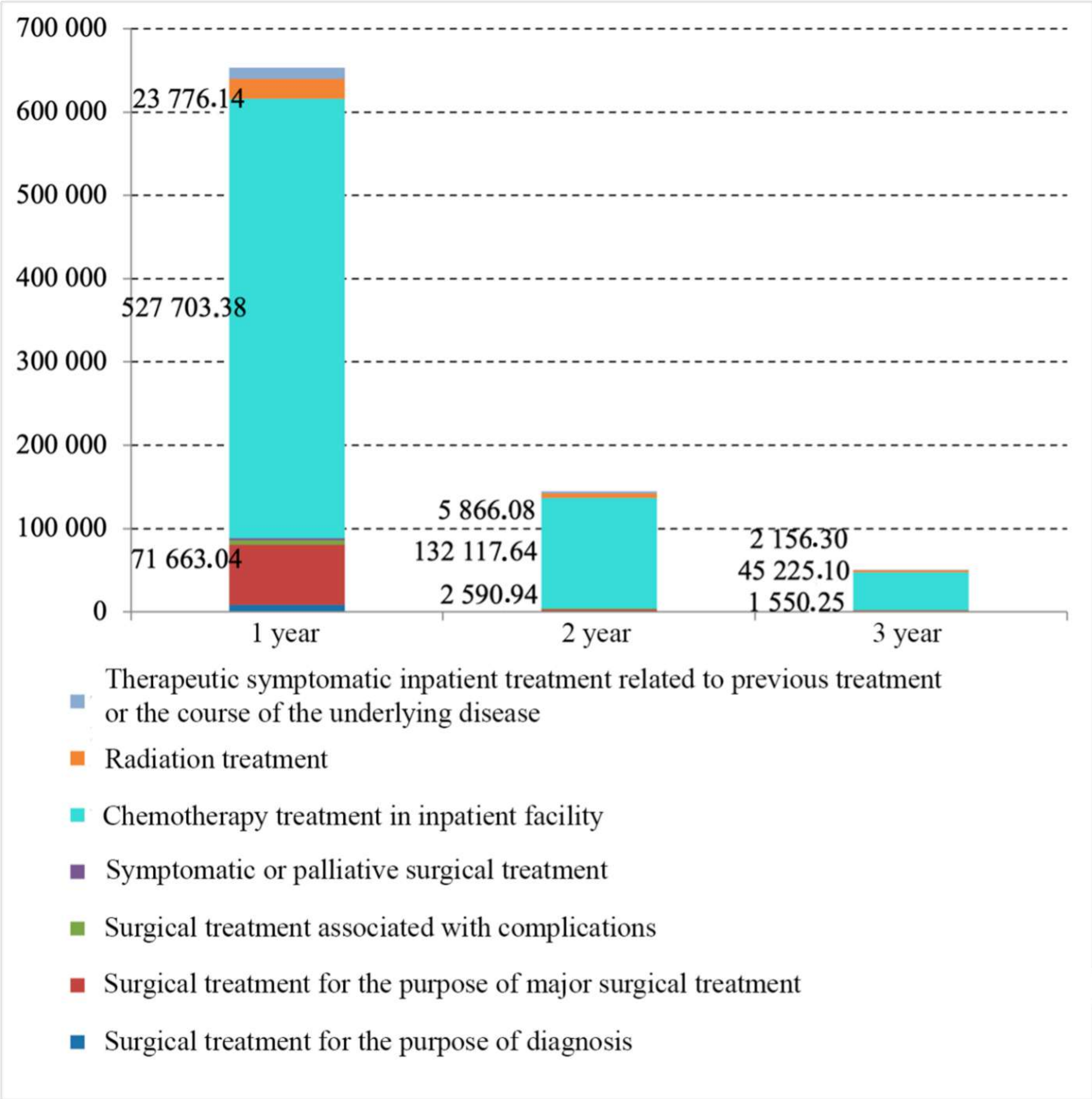


Figure 28 – Financing to pay for inpatient treatment of patients with malignant neoplasm of the bronchi and lungs of stages I–IV over three years, from the moment of diagnosis in the group of newly diagnosed, thousand rubs

The created clinical model allows to predict the necessary resources for the group of patients newly diagnosed with MN of the bronchi and lung, to take into account the resources necessary resources for a group of newly diagnosed patients. To take into account the resources necessary to provide medical care in the “oncology” profile to the accumulated contingent, it is necessary to model previous years also by the number of newly diagnosed ones and add up the periods of interest. This will allow a more detailed and complete calculation of the required resources.

5.2.2 Predictive modeling values of the inpatient stage of treatment of malignant neoplasm of the bronchi and lung patients with an increase in the proportion of early stages

Predictive increase in the proportion of MN of the bronchi and lung patients at early (I and II) stages is possible with the development and implementation of new diagnostic methods, screening programs or more sensitive laboratory tests. Thus, according to the calculations of Diederich et al. (2002) in a study in 2002 [109], using CT as one of the stages of early screening may increase early stages of MN of the bronchi and lung up to 58 %. We tried to predict how will the workload on medical personnel providing medical care in inpatient settings change, which treatment will become predominant – surgical or chemotherapeutic, and in what ratio, according to the created clinical model. These changes need to be built in at the screening planning stage and the healthcare system needs to be prepared in advance.

The results obtained are given in a comparative version with the current distribution by stages and without taking into account the increase in the number of MN of the bronchi and lung patients, i.e., the total number of newly diagnosed with MN of the bronchi and lung patients is 1,717 patients. Changes were made to the model only taking into account changes in the stages of the disease, increasing I–II stages to 58 % and maintaining the proportion of patients without stages within 3.40 % or taking into account the fact that their share will be equal to 0 %. The data is presented in table 29.

As a result, the total number of hospital admissions for three years in the II modeling option was 5,149 cases, which is 9.33 % less than in the I modeling option (5,630 admissions) when distributing patients by stages based on the data of the P.A. Hertsen Moscow Oncology Research Center for 2019. This decrease in the number of hospital admissions arises from their decrease in all states of the model, except for "surgical treatment for the purpose of basic surgical treatment", here, on the contrary, a significant increase of 31.7 % was observed compared to the 2019 model (from 521 cases in option I, to 687 cases in option II).

Table 29 – Distribution of malignant neoplasms of the bronchi and lung patients with a newly diagnosed malignant neoplasm of the bronchi and lung according to the modeled parameters

Stages	According to 2019 [1]		With the proportion of early stages increasing to 58 %			
	Model option I		Model option II		Model option III	
	distribution of patients with MN of the bronchi and lung, %	number of patients	distribution of patients with MN of the bronchi and lung, %	number of patients	distribution of patients with MN of the bronchi and lung, %	number of patients
I–II	33.3 %	572	58.0 %	996	58.0 %	996
III–IV	63.3 %	1,087	38.6 %	663	42.0 %	721
No stage	3.4 %	58	3.4 %	58	0 %	0

Note: [1] - data of the P.A. Hertsen Moscow Oncology Research Center

The required amount of funding for group II for the first three years of inpatient treatment from the moment of diagnosis decreased by 7.22 % (from 848,401.56 thousand rubs in option I, to 791,297.08 thousand rubs in option II). More detailed modeling of all three options is presented in Table 30.

If the share of early stages increases to 58 %, the workload of chemotherapy departments will drop significantly (by 521 hospital admissions), but the number of admissions with radical surgery will increase significantly (by 165 cases).

If we consider the model of option III with increase of early stages up to 58 % and exclusion of the group of patients without disease stage, the number of hospital admissions for three years will make 5,376, which is by 4.71 % less than in option I of modeling (5,630 admissions) at distribution of patients by stages on the basis of data of P.A. Hetsen Moscow Scientific and Research Oncological Institute for 2019. An increase in the number of hospital admissions was noted in "surgical treatment for the purpose of basic surgical treatment" – by 176 cases, and a decrease in "chemotherapeutic treatment in hospital" – by 358 cases.

Table 30 – Distribution of malignant neoplasm of the bronchi and lung patients with a newly diagnosed malignant neoplasm of the bronchi and lung according to the modeled parameters

States of inpatient treatment according to the model of a patient with MN of the bronchi and lung	Model option I		Model option II		Model option III	
	Number of cases	Required amount (thousand rubs)	Number of cases	Required amount (thousand rubs)	Number of cases	Required amount (thousand rubs)
First, second and third year of observation (total data for the first 3 years of observation from the diagnosis of MN of the bronchi and lung)						
Surgical treatment for the purpose of diagnosis	314	9,686.76	282	8,703.99	295	9,096.10
Surgical treatment for the purpose of basic surgical treatment	521	75,804.23	687	99,859.18	697	101,337.32
Surgical treatment associated with complications	82	7,133.05	69	5,990.60	73	6,298.64
Symptomatic or palliative surgical treatment	33	2,548.58	28	2,144.71	29	2,253.61
Chemotherapeutic treatment in inpatient facility	3,790	705,046.12	3,269	630,611.07	3,432	660,022.28
Radiation treatment	215	31,798.52	196	28,934.07	205	30,240.93
Therapeutic symptomatic treatment in inpatient facility associated with previous treatment or the course of the underlying disease	673	16,384.31	619	15,053.46	646	15,705.70
Total	5,630	848,401.56	5,149	791,297.08	5,376	824,954.58

The financing to pay for the treatment of patients with MN of the bronchi and lung in the first three years from the moment of diagnosis according to the predicted option III will amount to 824,954.58 thousand rubs, which is 23,446.99 thousand rubs less than in option I. When comparing option III with option I, an increase in the required budget in the "surgical treatment for the purpose of basic surgical treatment" model group was noted (by 25,533.09 thousand rubs).

A decrease in the required funding was established in the conditions of "chemotherapeutic treatment in inpatient facility" (by 45,023.83 thousand rubs) and "radiation treatment" (by 1,557.59 thousand rubs), other conditions a decrease was also noted, but to a lesser extent.

5.3 Model limitations

The absence of uniform patient identifiers in all of the above record systems creates difficulties in tracing the actual clinical pathway of a patient, also for this reason, patients without stage or morphology of MN of the bronchi and lung were not included in the model, in 2019 their share amounted to 9.62 %, in 2020 – 15 %. It is not possible to take into account the personal expenses of citizens for diagnosis and treatment and to determine their approximate volume of both medical care and financial costs [84]. If incorrect information about the proportion of MN of the bronchi and lung stages is entered into the model (e.g., overestimation of the proportion of early stages), the estimated prediction will also be incorrect. Separately, it is not currently possible to incorporate into the model such risk factors as severe comorbidities, such as chronic obstructive pulmonary disease or asthma, which may provoke or aggravate the course of MN of the bronchi and lung.

There is also no possibility of individual accounting of oncoimmunological factors that determine the tactics of treatment due to the lack of a record-keeping system:

1) EGFR, KRAS, HER2, BRAF, MET mutations;
2) ALK, ROS1 translocations;
3) FGFR1 amplification.

Based on the oncoimmunologic results, a personalized approach to treatment is applied with the use of targeted drugs, which can significantly improve survival rates due to their high efficiency and, as a consequence, increase in drug therapy costs [75, 89, 127].

Summary of Chapter 5

In the first year, the total number of medical services to diagnose the disease will amount to 22,419: primary appointments with specialists – 1,513 services, laboratory tests – 8,928 services, instrumental methods of research – 8,853, molecular genetic research – 3,125 services.

The total amount of funding to pay for outpatient medical care in the model in the first year will amount to 68,405.29 thousand rubs, including: primary appointments of specialists – 1,116.03 thousand rubs, laboratory methods of research – 7,863.59 thousand rubs, instrumental methods of research – 38,123.26 thousand rubs, molecular genetic research – 21,302.41 thousand rubs.

In the second and third years of treatment and observation, taking into account the exclusion of those who died and moved to the "last contact" stage, the number of medical services in the second year of observation will amount to 9,101 cases for 11,605.80 thousand rubs, and in the third year – 6,623 cases for 8,445.47 thousand rubs.

To pay for medical care received in an inpatient setting by patients with MN of the bronchi and lungs, based on the data of the P.A. Hertsen Moscow Scientific and Research Oncological Institute for 2019, 848,401.56 thousand rubs (5,630 hospital admissions) will be required from the health budget during the first 3 years, which is 57,104.48 thousand rubs more than the necessary costs for the same number of newly diagnosed with MN of the bronchi and lung patients, with an increase in early stages from 33.30 % to 58 % and the same proportion of patients without stage 791,297.08 thousand rubs (5,149 hospital admissions).

The created clinical model of the MN of the bronchi and lung patient allowed us to establish that in the case of increasing the proportion of patients detected at early stages up to 58 % in the first year from the moment of diagnosis, there is an increase in the number of hospital admissions in the model condition – “surgical treatment for the purpose of basic surgical treatment (basic surgery)” by 31.73 % (by 165 admissions), a decrease in chemotherapeutic treatment by 13.75 % (by 521 admissions) and radiation treatment by 9.00 % (by 19 admissions).

As a result of modeling based on the reference materials of the P.A. Hertsen Moscow Oncology Research Center for 2019, 38,143 outpatient services (specialist consultations, laboratory and instrumental, molecular genetic studies), 5,630 hospital admissions (4,435 of them in the first year of the disease) will be performed in the first three years from the moment of diagnosis of MN of the bronchi and lung, with a total budget for payment of these services of 936,858.12 thousand rubs.

The resulting clinical model of MN of the bronchi and lung patient allows to change the initial data (to increase and decrease the shares by stages and morphology) when introducing new screening methods, in-depth examination of risk groups aimed at combating MN of the bronchi and lung or vice versa, the emergence of situations that prevent early detection. To provide medical care to the accumulated patient population, it is necessary to model previous years also by the number of newly detected and add up the periods of interest. This will allow a more detailed and complete calculation of the necessary material, labor and financial resources.

Based on the above, the clinical model of a patient with MN of the bronchi and lung can be used in the healthcare system to make managerial decisions in terms of advance distribution of material, labor and financial resources for the full provision of medical care to patients in the “oncology” profile in accordance with the initial data on the incidence of MN of the bronchial and lung cancer, which will avoid the risk of a shortage of medical personnel, beds, equipment, chemotherapy drugs, etc.

FINDINGS

Thus, based on the conducted research, we have made the following conclusions:

1. In terms of the incidence of malignant neoplasms of the bronchi and lung, the Russian Federation is in 50th place out of 70 countries represented in the IARC (2013–2017) (among the male population – among the top ten countries – 49.9 $^{0}{}_{/0000}$, female – 7, 7 $^{0}{}_{/0000}$ – in 64th place), in terms of mortality it is among the top twenty leaders of GLOBOCAN 2022 (38.11 $^{0}{}_{/0000}$ – among the male population and 5.91 $^{0}{}_{/0000}$ – among the female population). There was a decrease in the reliability index for recording patients with malignant neoplasms of the bronchi and lungs from 0.93 in 2000 to 0.83 in 2021, which indicates a continuing process of incomplete registration of patients.

2. Since 2014, the diagnosis of malignant neoplasm of the bronchi and lung is established most often in stage IV of the disease, previously stage III prevailed, the proportion of early stages in St. Petersburg for the period 2011–2020 ranged from 26.4 % to 32.2 %, in 2022 reached a maximum value of 36.74% (for the first time in 12 years of observation).

3. Over 22 years of observation (2000–2021), a persistent decrease in the incidence of malignant neoplasms of the bronchi and lung was noted in the Russian Federation – 29.3 $^{0}{}_{/0000}$, and 20.82 $^{0}{}_{/0000}$, respectively, the same trend was established in St. St. Petersburg 22.9 $^{0}{}_{/0000}$ – 2007 and 19.52 $^{0}{}_{/0000}$ – 2021 (over 15 years of observation). The mortality rate from 2000 to 2019 in the Russian Federation decreased from 22.54$^{0}{}_{/0000}$ to 18.43 $^{0}{}_{/0000}$, in St. Petersburg 21.35 $^{0}{}_{/0000}$ – 2007 and 13.64 $^{0}{}_{/0000}$ – 2021 d. Over 20 years of observation (1997–2016) in St. Petersburg, there was an increase in one-year survival rate in patients with malignant neoplasms of the bronchi and lungs by 20.5% (from 35.2% to 42.4%), five-year survival by 12.9% (from 12.4% to 14.0%), a positive trend in median survival from 6.9 to 8.7 months was also noted.

4. We have found that despite the anti-tobacco program carried out in the Russian Federation and a decrease in the proportion of patients who smoke from 2013 to 2021, among patients diagnosed with malignant neoplasms of the bronchi and lung, there is an increase in the number of smokers by an average of 10 patients every year. The highest

percentage of smoking patients was identified among patients with malignant neoplasms of the larynx – 66.67%, malignant neoplasms of the esophagus – 53.20% and malignant neoplasms of the bronchi and lungs – 51.08%.

5. It was revealed that the COVID-19 pandemic had a negative impact on the detection of malignant neoplasms of the bronchi and lungs. Thus, in St. Petersburg in 2019, 2,236 cases of newly diagnosed diagnoses were identified (1,717 without posthumously recorded), in 2020 – 1,958 (1,523 without posthumously recorded), and in 2021 – 2,135 cases (1,534 cases without recorded posthumously), this is due to the restrictions being introduced, and therefore we should expect an increase in the late stages at which the disease is detected and the number of posthumously recorded cases. A more severe course of COVID-19 has also been confirmed in patients with malignant neoplasms of the bronchi and lungs.

6. For the first time, based on the combination of three databases – the territorial compulsory health insurance fund of St. Petersburg, the medical information and analytical center of St. Petersburg and the database of the population cancer registry of St. Petersburg – using the Markov mathematical model, a digital database containing information about 9 025 patients (2011–2020 year of diagnosis) included 34,268 records of medical care provided to them of the “oncology” profile in a hospital setting. The database contains information on the date of diagnosis, diagnostic studies, treatment and date of death (if any) for each patient with a malignant neoplasm of the bronchi and lung, providing 8 states in which the patient can be before moving to the finalpoints and 2 states, which are the final points of the model – “last contact”, “lethal outcome”.

7. The clinical model of a patient with a malignant neoplasm of the bronchi and lung during the observation period from 2011 to 2020, taking into account the stage of the disease and morphological type of tumor, had the following characteristics: 19.59 % of patients with stage I of the disease in the fourth week from the moment of diagnosis are inpatient treatment for such a model condition as “main surgical treatment” in patients with stage II - the condition “main surgical treatment” occurred in the period from 2 to 9 weeks (from 9.93 % to 11.74 %) from the moment of diagnosis , at 8–9 weeks the number of patients receiving chemotherapy treatment was maximum and amounted to 11.51 %.

8. For patients with stage III disease, only 5.1 % undergo primary surgical treatment at 3 weeks from diagnosis; chemotherapy treatment has a constant increase from 1 to 16 weeks from 4.25 % to 13.22 %. In stage IV, from the first week, almost 13 % of patients receive symptomatic therapy in a hospital setting; from weeks 5 to 18, the number of patients who died, i.e. those who have entered the “fatal outcome” model state increases weekly from 2.10 % to 3.13 %. It is with patients in the last group that by week 23, 50 % lose contact, and they move into the “last contact” or “lethal outcome” model state.

9. When modeling the necessary resources according to morbidity data in 2019, it was found that in the first year from the moment of diagnosis, the number of hospitalizations of patients with malignant neoplasms of the bronchi and lungs was 4,435, in the second – 886, in the third – 308, while out of the total number of hospitalizations 2,853 that occurred in the first year were in the “chemotherapeutic treatment” model state and accounted for 64.33 %. Hospitalizations allocated to the group “therapeutic symptomatic treatment in a hospital” associated with previous treatment or a complicated course of the underlying disease account for 12.39 %, hospitalizations for the purpose of primary surgical treatment – 11.11 %.

10. The developed and implemented clinical model of a patient with a malignant neoplasm of the bronchi and lung in an inpatient setting based on the generated digital database, including 9,025 patients with newly diagnosed disease for the period 2011–2020 in St. Petersburg, allows for strategic forecasting of the necessary material, labor and financial resources for making managemeny and organizational decisions in order to improve the provision of medical care to patients of the oncology profile, taking into account various options for distribution by stages and morphology of the disease(when planning the implementation of new screening programs or introducing restrictive measures due to the epidemiological situation).

PRACTICAL RECOMMENDATIONS

To create a clinical model of a patient that maximally takes into account all variants of the course of the MN of bronchial and lung cancer and treatment approaches, based on the work performed, we have established that it is necessary to complete the tasks presented below.

1. The Ministry of Health of Russia, when creating a unified digital circuit in healthcare based on a unified state health information system, have to take into account the possibility of registration for further analysis of the following data:

– individual characteristics of the patient (oncoimmunological factors);

– concomitant diseases (ICD, disease duration and severity);

– factors that aggravate the course of the disease (in our clinical model of the patient, this could be cigarette smoking indicating that the patient smokes, smoking history, the number of cigarettes smoked or harmful working conditions);

– accounting of medical services received at the expense of citizens' personal funds or voluntary health insurance is required for the diagnosis, observation or treatment of cancer, because at the moment this information is completely missing;

– it is necessary to individually record the preferential medications received by the patient and received by the patient on an outpatient basis.

2. When forecasting the necessary material, labor and financial resources, the created model must be adapted to the characteristics of the regions and areas for which calculations are required, therefore, the local health authorities need to take into account the incidence, distribution by stages of the disease and morphology, the availability of diagnostics and treatment facilities in theregion, preventive measures taken and patient specifics.

3. For patients with risk factors, it is mandatory to undergo clinical examination of certain groups of the adult population, and for patients with MN of the bronchi and lungs – clinical observation.

4. Taking into account the COVID-19 pandemic of 2019-2021 with the loss of some patients with MN of the bronchi and lungs as undercounted and the expected

increase in the number of late stages in 2023–2025, municipalities should prepare for more severe and extensive surgical operations, as well as the predominance of inpatient chemotherapy treatment, which will require the repurposing of beds and the need for additional supplies of chemotherapy drugs.

5. When implementing an anti-tobacco program, the Government of the Russian Federation needs to take a more targeted and individual approach to promoting smoking cessation in order to increase the motivation of smokers to give up this habit.

LIST OF ABBREVIATIONS AND SYMBOLS

ACI	accounting credibility index
C34	malignant neoplasm of the bronchi and lung according to the international classification of diseases
C77	secondary and unspecified malignant neoplasm of lymph nodes according to the international classification of diseases
C78	secondary malignant neoplasm of the respiratory and digestive organs according to the international classification of diseases
CHI	Compulsory health insurance – (medical care paid for from the means of compulsory health insurance)
CI	credibility interval
DB	database
FCHIF	Federal Compulsory Health Insurance Fund
HTMC	high-tech medical care paid for from the federal budget funds
HTMC from CHI	high-tech medical care paid for from compulsory health insurance funds
IARC	International Association for Cancer Research
ICD-10	International Classification of Diseases 10 revision
ID	unique identifier
MIAC	medical information and analytical center
MIS	medical information system
MN	malignant neoplasm
MO	medical organization
National Medical Research Center of Oncology named after N.N. Petrov	Federal State Budgetary Institution " National Medical Research Center of Oncology named after N.N. Petrov" of the Ministry of Health of the Russian Federation
NWFD RF	Northwestern Federal District of the Russian Federation
P.A. Hertsen MORC	P.A. Hertsen Moscow Oncology Research Center
PCR	population cancer registry
RF	Russian Federation
Rosstat	Federal State Statistics Service
SP	software product
SPb	Saint Petersburg
TCHIF	Territorial Compulsory Health Insurance Fund
TNM	international classification of stages of malignant neoplasms

TS	tobacco smoking, tobacco smokers
UIN	uniform insurance number
UIS	unified information system
UIS.CHI.HTMI.CHI	unified information system of the territorial fund for compulsory health insurance for issuing invoices for payment
WHO	World Health Organization

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APPENDIX A

(mandatory)

Data used to build the model

Table A.1 – Questionnaire of a patient with MN of the bronchi and lung for inclusion in the Markov model

Field	Patient information
ID_HISTORY from TCHIF SPb	10167515
CHI policy number	7849930832001604
Unique PCR code	abb-icrm5-de800
Date of birth	17.10.1960
Gender	M
Date of diagnosis in PCR	10.03.2016
Date of lethal outcome	26.02.2017
Morphological code	8070/3
Clinical stage according to TNM7	IV

Table A.2 – Data on received medical services

Date 1 (start date of service)	Date 2 (end date of service)	Diagnosis on a medical bill	Medical service code	Type of medical service	Tariff, rubs	Name of the MO	Type of medical care	Type of financing
1	2	3	4	5	6	7	8	9
12.02.2016	12.02.2016	C34.1	aOnkol	Oncology	532.70	SPB GBUZ "GKOD"	Outpatient	CHI
16.02.2016	16.02.2016	C34.1	aOnkol	Oncology	532.70	SPB GBUZ "GKOD"	Outpatient	CHI
19.02.2016	19.02.2016	C34.1	aOnkol	Oncology	532.70	SPB GBUZ "GKOD"	Outpatient	CHI
20.02.2016	20.02.2016	C34.1	iKlin	Clinical trial	71.90	SPB GBUZ "GKOD"	Outpatient	CHI
24.02.2016	25.02.2016	C34.0	mA001a	Biopsy of skin and mucous membrane neoplasms of various localizations m/a	2,639.10	SPB GBUZ "GKOD"	In a day inpatient facility	CHI
24.02.2016	25.02.2016	C34.0	501160	Stage I-III malignant neoplasm of the bronchi and lung	2,639.10	SPB GBUZ "GKOD"	In a day inpatient facility	CHI
10.03.2016	04.04.2016	C34.1	501170	Stage III-IV malignant neoplasm of the bronchi and lung	46,337.50	SPB GBUZ "GKOD"	Inpatient	CHI
05.04.2016	05.04.2016	C34.9	aOnkol	Oncology	532.70	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI
20.04.2016	20.04.2016	C34.9	aOnkol	Oncology	532.70	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI
22.04.2016	25.04.2016	C34.1	501170	Stage III-IV malignant neoplasm of the bronchi and lung	5,560.50	SPB GBUZ "GKOD"	Inpatient	CHI
28.04.2016	28.04.2016	C34.1	aOnkol	Oncology	532.70	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI
16.05.2016	17.05.2016	C34.1	501170	Stage III-IV malignant neoplasm of the bronchi and lung	1,853.50	SPB GBUZ "GKOD"	Inpatient	CHI

Continuation of Table A.2

1	2	3	4	5	6	7	8	9
18.05.2016	18.05.2016	C34.1	aOnkol	Oncology	532.70	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI
02.06.2016	02.06.2016	C34.9	aOnkol	Oncology	532.70	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI
06.06.2016	07.06.2016	C34.1	501170	Stage III-IV malignant neoplasm of the bronchi and lung	1,853.50	SPB GBUZ "GKOD"	Inpatient	CHI
17.06.2016	17.06.2016	C34.1	aOnkol	Oncology	532.70	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI
22.06.2016	22.06.2016	C34.8	aTerap	Therapy (general)	355.20	SPB GBUZ "CITY POLYCLINIC No.56"	Outpatient	CHI
27.06.2016	05.07.2016	C34.1	501170	Stage III-IV malignant neoplasm of the bronchi and lung	14,828.00	SPB GBUZ "GKOD"	Inpatient	CHI
07.07.2016	07.07.2016	C34.1	aOnkol	Oncology	532.70	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI
13.07.2016	13.07.2016	C34.9	aTerap	Therapy (general)	355.20	SPB GBUZ "CITY POLYCLINIC No.56"	Outpatient	CHI
14.07.2016	14.07.2016	C34.1	aOnkol	Oncology	532.70	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI
19.07.2016	28.07.2016	C34.1	501170	Stage III-IV malignant neoplasm of the bronchi and lung	16,681.50	SPB GBUZ "GKOD"	Inpatient	CHI
01.08.2016	01.08.2016	C34.1	aOnkol	Oncology	532.70	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI
08.08.2016	08.08.2016	C34.1	iElFiz	Electrophysiological examination	291.70	SPB GBUZ "GKOD"	Outpatient	CHI
08.08.2016	08.08.2016	C34.1	iBHim	Biochemical examination	25.40	SPB GBUZ "GKOD"	Outpatient	CHI
08.08.2016	08.08.2016	C34.1	iKlin	Clinical trial	71.90	SPB GBUZ "GKOD"	Outpatient	CHI

Continuation of Table A.2

1	2	3	4	5	6	7	8	9
12.08.2016	20.08.2016	C34.1	501170	Stage III-IV malignant neoplasm of the bronchi and lung	14,828.00	SPB GBUZ "GKOD"	Inpatient	CHI
22.08.2016	22.08.2016	C34.9	aOnkol	Oncology	532.70	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI
01.09.2016	01.09.2016	C34.1	iBHim	Biochemical examination	25.40	SPB GBUZ "GKOD"	Outpatient	CHI
01.09.2016	01.09.2016	C34.1	iKlin	Clinical trial	71.90	SPB GBUZ "GKOD"	Outpatient	CHI
01.09.2016	01.09.2016	C34.1	iElFiz	Electrophysiological examination	291.70	SPB GBUZ "GKOD"	Outpatient	CHI
02.09.2016	12.09.2016	C34.1	501170	Stage III-IV malignant neoplasm of the bronchi and lung	18,535.00	SPB GBUZ "GKOD"	Inpatient	CHI
26.09.2016	26.09.2016	C34.1	iBHim	Biochemical examination	25.40	SPB GBUZ "GKOD"	Outpatient	CHI
26.09.2016	26.09.2016	C34.1	iImmu	Immunological examination	156.20	SPB GBUZ "GKOD"	Outpatient	CHI
26.09.2016	26.09.2016	C34.1	iKlin	Clinical trial	71.90	SPB GBUZ "GKOD"	Outpatient	CHI
26.09.2016	26.09.2016	C34.1	iElFiz	Electrophysiological examination	291.70	SPB GBUZ "GKOD"	Outpatient	CHI
27.09.2016	04.10.2016	C34.1	501170	Stage III-IV malignant neoplasm of the bronchi and lung	9,885.33	SPB GBUZ "GKOD"	In a day inpatient facility	CHI
11.10.2016	11.10.2016	C34.9	aOnkol	Oncology	532.70	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI
14.10.2016	14.10.2016	C34.1	aOnkol	Oncology	532.70	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI
18.10.2016	18.10.2016	C78.0	uKRTbk	Services: computed X-ray tomography with bolus conformation	5,778.50	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI

Continuation of Table A.2

1	2	3	4	5	6	7	8	9
26.10.2016	26.10.2016	C34.1	iBHim	Biochemical examination	25.40	SPB GBUZ "GKOD"	Outpatient	CHI
26.10.2016	26.10.2016	C34.1	iImmu	Immunological examination	156.20	SPB GBUZ "GKOD"	Outpatient	CHI
26.10.2016	26.10.2016	C34.1	iKlin	Clinical trial	71.90	SPB GBUZ "GKOD"	Outpatient	CHI
26.10.2016	26.10.2016	C34.1	iRent	X-ray examination	323.70	SPB GBUZ "GKOD"	Outpatient	CHI
27.10.2016	01.11.2016	C34.1	501170	Stage III-IV malignant neoplasm of the bronchi and lung	7,414.00	SPB GBUZ "GKOD"	In a day inpatient facility	CHI
14.11.2016	14.11.2016	C34.1	iBHim	Biochemical examination	25.40	SPB GBUZ "GKOD"	Outpatient	CHI
14.11.2016	14.11.2016	C34.1	iKlin	Clinical trial	71.90	SPB GBUZ "GKOD"	Outpatient	CHI
23.11.2016	23.11.2016	C34.9	aSMP	SMP	3,071.76	SPB GBUZ "CITY POLYCLINIC No.56"	Outside MO	CHI
23.11.2016	23.11.2016	C34.1	iElFiz	Electrophysiological examination	291.70	SPB GBUZ "GKOD"	Outpatient	CHI
23.11.2016	23.11.2016	C34.1	iBHim	Biochemical examination	25.40	SPB GBUZ "GKOD"	Outpatient	CHI
23.11.2016	23.11.2016	C34.1	iKlin	Clinical trial	71.90	SPB GBUZ "GKOD"	Outpatient	CHI
23.11.2016	23.11.2016	C34.1	iImmu	Immunological examination	156.20	SPB GBUZ "GKOD"	Outpatient	CHI
25.11.2016	05.12.2016	C34.1	501170	Stage III-IV malignant neoplasm of the bronchi and lung	13,592.33	SPB GBUZ "GKOD"	In a day inpatient facility	CHI
30.11.2016	30.11.2016	C34.1	aOnkol	Oncology	532.70	SPB GBUZ "CITY POLYCLINIC No.109"	Outpatient	CHI
19.12.2016	19.12.2016	C34.1	iBHim	Biochemical examination	25.40	SPB GBUZ "GKOD"	Outpatient	CHI
19.12.2016	19.12.2016	C34.1	iKlin	Clinical trial	71.90	SPB GBUZ "GKOD"	Outpatient	CHI

Continuation of Table A.2

1	2	3	4	5	6	7	8	9
19.12.2016	19.12.2016	C34.1	iElFiz	Electrophysiological examination	291.70	SPB GBUZ "GKOD"	Outpatient	CHI
23.12.2016	23.12.2016	C34.9	aTerap	Therapy (general)	355.20	SPB GBUZ "CITY POLYCLINIC No.56"	Outpatient	CHI
26.12.2016	03.01.2017	C34.1	501170	Stage III-IV malignant neoplasm of the bronchi and lung	11,121.00	SPB GBUZ "GKOD"	In a day inpatient facility	CHI
09.01.2017	12.01.2017	C34.9	kTerap	Therapy (general) (at home)	621.70	SPB GBUZ "CITY POLYCLINIC No.56"	Outpatient	CHI
21.01.2017	21.01.2017	C34.1	aSMP	SMP	3,620.20	SPB GBUZ "CITY POLYCLINIC No.56"	Outside MO	CHI
21.01.2017	21.01.2017	C34.9	aTerUch	Visit to the district general practitioner	355.20	SPB GBUZ "CITY POLYCLINIC No.56"	Outpatient	CHI
27.01.2017	27.01.2017	C34.9	aTerUch	Visit to the district general practitioner	355.20	SPB GBUZ "CITY POLYCLINIC No.56"	Outpatient	CHI
10.02.2017	13.02.2017	C34.9	kTerap	Therapy (general) (at home)	621.70	SPB GBUZ "CITY POLYCLINIC No.56"	Outpatient	CHI
22.02.2017	26.02.2017	C34.1	301130	Malignant neoplasms of trachea, bronchi, lungs	26,368.50	GBU SPB RESEARCH INSTITUTE NAMED AFTER I.I. DZHANELIDZE	Inpatient	CHI
22.02.2017	26.02.2017	C34.1	431030	Reanimation of the 3rd category of complexity (from 4 to 5 days inclusive)	26,368.50	GBU SPB RESEARCH INSTITUTE NAMED AFTER I.I. DZHANELIDZE	Inpatient	CHI
22.02.2017	22.02.2017	C34.9	aSMP	SMP	3,620.20	SPB GBUZ "CITY POLYCLINIC No.56"	Outside MO	CHI

Table A.3 – Probabilities of transitions between model states in patients with non-small cell MN of the bronchi and lung stage I 1,659 patients

STAGE 1 (diagnosis)	TRANSITION (from which-to-which stage)	Establishing a diagnosis	Week of cycle from the time of diagnosis									
		0	1	2	3	4	5	6	7	8	9	10
1	2	3	4	5	6	7	8	9	10	11	12	13
outpatient stage	outpatient stage_outpatient stage	72.27%	89.82%	88.26%	85.09%	89.22%	88.24%	90.72%	92.66%	93.39%	92.65%	93.97%
outpatient stage	outpatient stage_ rays	72.27%	0%	0.09%	0.09%	0.09%	0.09%	0%	0.17%	0%	0.16%	0%
outpatient stage	outpatient stage_ last contact	72.27%	0.33%	0.18%	0.18%	0.18%	0.09%	0.44%	0.93%	0.25%	0.56%	0.56%
outpatient stage	outpatient stage_ symptomatic therapy hospital admission	72.27%	0.50%	1.32%	0.81%	0.55%	0.62%	0.44%	0.08%	0.33%	0.16%	0.16%
outpatient stage	outpatient stage_lethal outcome	72.27%	0%	0%	0%	0%	0%	0%	0%	0.08%	0.08%	0%
outpatient stage	outpatient stage_ chemotherapy	72.27%	3.34%	4.15%	4.40%	3.11%	4.07%	2.63%	1.52%	1.49%	1.36%	1.85%
outpatient stage	outpatient stage_ diagnostic surgery	72.27%	0.58%	0.71%	0.90%	0.82%	0.44%	0.61%	0.51%	0.17%	0.24%	0.48%
outpatient stage	outpatient stage_ surgery of complications	72.27%	0%	0.09%	0.09%	0.18%	0.18%	0.26%	0%	0.08%	0.08%	0.08%
outpatient stage	outpatient stage_ basic surgery	72.27%	5.42%	5.12%	8.36%	5.84%	6.19%	4.82%	4.13%	4.21%	4.64%	2.81%
outpatient stage	outpatient stage_ symptomatic surgery	72.27%	0%	0.09%	0.09%	0%	0.09%	0.09%	0%	0%	0.08%	0.08%
rays	rays_outpatient stage	0%	0%	0%	100%	0%	100%	0%	0%	50.00%	0%	33.33%
rays	rays_last contact	0%	0%	0%	0%	100%	0%	100%	0%	0%	0%	33.33%
rays	rays_rays	0%	0%	0%	0%	0%	0%	0%	0%	50.00%	100%	33.33%

Continuation of Table A.3

1	2	3	4	5	6	7	8	9	10	11	12	13
		11	12	13	14	15	16	17	18	19	20	21
rays	rays_chemotherapy	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
rays	rays_symptomatic surgery	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
rays	rays_diagnostic surgery	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
rays	rays_symptomatic therapy hospitalization	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
rays	rays_lethal outcome	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
last contact	last contact_last contact	0%	0%	100%	100%	100%	96.88%	100%	100%	100%	98.55%	100%
last contact	last contact_lethal outcome	0%	0%	0%	0%	0%	3.13%	0%	0%	0%	1.45%	0%
symptomatic therapy hospitalization	symptomatic therapy hospitalization_ outpatient stage	6.15%	4.90%	22.00%	27.71%	26.56%	46.00%	30.30%	23.08%	42.11%	37.50%	33.33%
symptomatic therapy hospitalization	symptomatic therapy hospitalization_ last contact	6.15%	0.98%	1.00%	2.41%	1.56%	0%	0%	0%	0%	0%	0%
symptomatic therapy hospitalization	symptomatic therapy hospitalization_ symptomatic therapy hospitalization	6.15%	92.16%	67.00%	65.06%	68.75%	50.00%	60.61%	69.23%	57.89%	56.25%	58.33%
symptomatic therapy hospitalization	symptomatic therapy hospitalization_ chemotherapy	6.15%	0%	0%	0%	1.56%	0%	0%	0%	0%	0%	8.33%

Continuation of Table A.3

1	2	3	4	5	6	7	8	9	10	11	12	13
		22	23	24	25	26	27	28	29	30	31	32
symptomatic therapy hospitalization	symptomatic therapy hospitalization_ diagnostic surgery	6.15%	0%	1.00%	0%	0%	2.00%	0%	0%	0%	0%	0%
symptomatic therapy hospitalization	symptomatic therapy hospitalization_ surgery of complications	6.15%	0%	1.00%	0%	0%	0%	0%	0%	0%	0%	0%
symptomatic therapy hospitalization	symptomatic therapy hospitalization_ basic surgery	6.15%	1.96%	8.00%	4.82%	1.56%	2.00%	9.09%	7.69%	0%	6.25%	0%
symptomatic therapy hospitalization	symptomatic therapy hospitalization_lethal outcome	6.15%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
symptomatic therapy hospitalization	symptomatic therapy hospitalization_rays	6.15%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
symptomatic therapy hospitalization	symptomatic therapy hospitalization_ symptomatic surgery	6.15%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
lethal outcome	lethal outcome_lethal outcome	0%	0%	0%	0%	0%	0%	100%	100%	100%	100%	100%
chemotherapy	chemotherapy_ outpatient stage	4.58%	51.32%	40.79%	24.69%	22.22%	17.80%	22.70%	26.87%	27.43%	30.30%	38.82%
chemotherapy	chemotherapy_last contact	4.58%	1.32%	2.63%	0%	0%	0%	0.71%	0%	0%	0%	0%

Continuation of Table A.3

1	2	3	4	5	6	7	8	9	10	11	12	13
		33	34	35	36	37	38	39	40	41	42	43
chemotherapy	chemotherapy_ chemotherapy	4.58%	47.37%	43.42%	71.60%	76.85%	80.51%	73.76%	70.90%	71.68%	68.69%	60.00%
chemotherapy	chemotherapy_ basic surgery	4.58%	0%	13.16%	3.70%	0.93%	1.69%	2.13%	2.24%	0.88%	1.01%	1.18%
chemotherapy	chemotherapy_ symptomatic therapy hospitalization	4.58%	0%	0%	0%	0%	0%	0.71%	0%	0%	0%	0%
chemotherapy	chemotherapy_lethal outcome	4.58%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
chemotherapy	chemotherapy_ diagnostic surgery	4.58%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
chemotherapy	chemotherapy_rays	4.58%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
chemotherapy	chemotherapy_ symptomatic surgery	4.58%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
chemotherapy	chemotherapy_ surgery of complications	4.58%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
diagnostic surgery	diagnostic surgery outpatient stage	2.65%	22.73%	28.95%	38.24%	26.67%	37.04%	35.00%	55.56%	21.43%	18.18%	58.33%
diagnostic surgery	diagnostic surgery_ last contact	2.65%	4.55%	0%	0%	3.33%	0%	0%	0%	0%	0%	0%
diagnostic surgery	diagnostic surgery_ diagnostic surgery	2.65%	70.45%	65.79%	58.82%	60.00%	51.85%	55.00%	44.44%	64.29%	81.82%	41.67%
diagnostic surgery	diagnostic surgery_ basic surgery	2.65%	2.27%	5.26%	2.94%	10.00%	11.11%	10.00%	0%	14.29%	0%	0%

Continuation of Table A.3

1	2	3	4	5	6	7	8	9	10	11	12	13
		44	45	46	47	48	49	50	51	52	53	54
diagnostic surgery	diagnostic surgery_ chemotherapy	2.65%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
diagnostic surgery	diagnostic surgery_rays	2.65%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
diagnostic surgery	diagnosic surgery_ symptomatic therapy hospitalization	2.65%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
diagnostic surgery	diagnostic surgery_ surgery of complications	2.65%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
diagnostic surgery	diagnostic surgery_ lethal outcome	2.65%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
diagnostic surgery	diagnostic surgery_ symptomatic surgery	2.65%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
surgery of complications	surgery of complications_ surgery of complications	0.42%	100%	100%	77.78%	87.50%	77.78%	66.67%	90.00%	77.78%	75.00%	71.43%
surgery of complications	surgery of complications_ outpatient stage	0.42%	0%	0%	22.22%	12.50%	11.11%	22.22%	10.00%	22.22%	25.00%	28.57%
surgery of complications	surgery of complications_ last contact	0.42%	0%	0%	0%	0%	11.11%	11.11%	0%	0%	0%	0%
surgery of complications	surgery of complications_ lethal outcome	0.42%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
surgery of complications	surgery of complications_ symptomatic therapy hospitalization	0.42%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
surgery of complications	surgery of complications_ basic surgery	0.42%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%

Continuation of Table A.3

1	2	3	4	5	6	7	8	9	10	11	12	13
		55	56	57	58	59	60	61	62	63	64	65
surgery of complications	surgery of complications_ diagnostic surgery	0.42%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
surgery of complications	surgery of complications_ chemotherapy	0.42%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
basic surgery	basic surgery_ outpatient stage	13.92%	0.87%	16.61%	28.16%	32.00%	30.10%	36.13%	24.46%	34.08%	22.11%	30.14%
basic surgery	basic surgery_ last contact	13.92%	0.87%	2.03%	0.32%	0.31%	0.69%	1.46%	3.00%	0.45%	2.51%	1.91%
basic surgery	basic surgery_ symptomatic therapy hospitalization	13.92%	0%	0.34%	0.32%	0%	0.35%	0%	0%	0.45%	0.50%	0%
basic surgery	basic surgery_ basic surgery	13.92%	98.27%	80.68%	70.89%	67.69%	68.51%	62.04%	72.53%	65.02%	74.87%	67.94%
basic surgery	basic surgery_ chemotherapy	13.92%	0%	0.34%	0.32%	0%	0%	0%	0%	0%	0%	0%
basic surgery	basic surgery_lethal outcome	13.92%	0%	0%	0%	0%	0.35%	0%	0%	0%	0%	0%
basic surgery	basic surgery_ surgery of complications	13.92%	0%	0%	0%	0%	0%	0.36%	0%	0%	0%	0%
basic surgery	basic surgery_ symptomatic surgery	13.92%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
basic surgery	basic surgery_ diagnostic surgery	13.92%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
basic surgery	basic surgery_rays	13.92%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
symptomatic surgery	symptomatic surgery_ symptomatic surgery	0%	0%	0%	100%	100%	50.00%	100%	66.67%	100%	50.00%	100%

Continuation of Table A.3

1	2	3	4	5	6	7	8	9	10	11	12	13
		66	67	68	69	70	71	72	73	74	75	76
symptomatic surgery	symptomatic surgery_ outpatient stage	0%	0%	0%	0%	0%	50.00%	0%	33.33%	0%	50.00%	0%
symptomatic surgery	symptomatic surgery_ basic surgery	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
symptomatic surgery	symptomatic surgery_symptomatic therapy hospitalization	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
symptomatic surgery	symptomatic surgery_ chemotherapy	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
symptomatic surgery	symptomatic surgery_ lethal outcome	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
symptomatic surgery	symptomatic surgery_ last contact	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
symptomatic surgery	symptomatic surgery_ rays	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%

Table A.4 – Outpatient state of the first year for MN of the bronchi and lung patients according to the Order of the Ministry of Health of the Russian Federation No.347n dated April 13, 2021

Medical service code	Name of medical service	The average indicator of the frequency of medical service provision	Average application rate	TCHIF tariff of SPb 2022, rubs
1	2	3	4	5
1. Medical services to diagnose a disease, condition				
1.1. Reception (examination, consultation) of a specialist doctor				
B01.015.001	Primary appointment (examination, consultation) with a cardiologist	0.026	1	540.00
B01.023.001	Primary appointment (examination, consultation) with a neurologist	0.035	1	540.00
B01.027.001	Primary appointment (examination, consultation) with an oncologist	0.82	1	752.50
1.2. Laboratory methods of examination				
A08.09.001	Pathologic-anatomical examination of biopsy (surgical) material of tracheal and bronchial tissues	0.8	1	1,706.21
A08.09.001.002	Pathologo-anatomical examination of biopsy (surgical) material of tracheal and bronchial tissues using immunohistochemical methods	0.4	1	3,947.27
A08.09.008	Cytological examination of micro-preparation of tracheal and bronchial tissues	0.8	1	895.00
B03.005.006	Coagulogram (indicative study of hemostasis system)	0.8	1	360.40
B03.016.003	General (clinical) blood test, detailed	0.8	1	117.81
B03.016.004	Biochemical blood analysis general therapeutic	0.8	1	612.79
B03.016.006	General (clinical) urine analysis	0.8	1	58.96

Continuation of Table A.4

1	2	3	4	5
1.3. Instrumental methods of examination				
A03.09.003.001 and A11.09.008	Videotracheobronchoscopy with Biopsy of trachea, bronchi during bronchoscopy	0.8	1	2,232.25
A04.06.002	Ultrasound examination of lymph nodes (one anatomical zone)	0.8	1	372.50
A04.10.002	Echocardiography	0.026	1	718.50
A04.16.001	Ultrasound examination of abdominal organs (complex)	0.8	1	372.50
A05.10.006	Electrocardiogram registration	0.89	1	309.20
A05.23.009.001	Magnetic resonance imaging of the brain with contrast	0.72	1	7,699.00
A06.09.005.002	Computed tomography of thoracic cavity organs with intravenous bolus contrasting	0.24	1	4,455.00
A06.23.004.006	Computed tomography of the brain with intravenous contrast	0.08	1	4,455.00
A07.03.001.001	Whole body bone scintigraphy	0.32	1	7,246.95
A07.30.043.001	Positron emission tomography combined with computed tomography with tumorotropic RFPs with contrasting	0.48	1	21,333.00
1.4 Molecular genetic studies in outpatient conditions				
A08.30.004	Immunocytochemical examination of biological material	0.3	1	2,130.53
A08.30.039	Determination of PDL1 protein expression by immunohistochemical method	0.51	1	12,180.00
A27.30.008	Molecular genetic examination of mutations in the BRAF gene in biopsy (surgical) material	0.1	1	5,508.00
A27.30.016	Molecular genetic examination of mutations in the EGFR gene in biopsy (surgical) material	0.51	1	5,500.00
A27.30.017	Molecular genetic examination of ALK gene translocations	0.2	1	5,500.00
A27.30.018	Molecular genetic examination of ROS1 gene translocations	0.2	1	5,500.00

Table A.5 – Outpatient state of the second and subsequent years of life for MN of the bronchi and lung patients in accordance with the Order of the Ministry of Health of the Russian Federation No.347n dated April 13, 2021

Medical service code	Name of medical service	The average indicator of the frequency of medical service provision	Average application rate	TCHIF tariff of SPb 2022, rubs
1	2	3	4	5
2 Medical services for the treatment of the disease, condition and control of treatment				
2.1. Reception (examination, consultation) and supervision of a specialist doctor				
B04.027.001	Dispensary appointment (examination, consultation) with an oncologist	1	3	752.50
2.2. Instrumental methods of examination				
A04.09.002	Ultrasound examination of the lungs	1	3	372.50
A05.23.009	Magnetic resonance imaging of the brain	0.3	1	1,978.00
A06.09.005	Computed tomography of the thoracic cavity organs	0.9	3	2,221.00
A06.09.007	Lung radiography	0.1	3	343.10
A07.03.001.001	Whole body bone scintigraphy	0.3	1	7,246.95

Table A.6 – Inpatient states of treatment a clinical model for MN of the bronchi and lung patients in accordance with the Order of the Ministry of Health of the Russian Federation No.347n dated April 13, 2021

Medical service code	Name of medical service	FCHIF tariff 2022, rubs	Average cost of the group in 2022, rubs.
1	2	3	4
1. Surgical treatment for the purpose of diagnosis			
A03.10.001	Thoracoscopy	37,370.85	30,818.43
A03.11.001	Mediastinoscopy	37,370.85	
A11.09.001	Radiosurgical transthoracic lung biopsy	24,266.00	
A11.11.002	Transbronchial puncture	24,266.00	
2. Surgical treatment for the purpose of basic surgical treatment - 197 694.23 rubs			
A16.06.004	Mediastinal lymphadenectomy	44,408.21	145,384.90
A16.06.004.001	Mediastinal lymphadenectomy using video endoscopic technology	91,728.44	
A16.08.032.006	Tracheal bifurcation resection	47,562.89	
A16.09.009	Lobectomy (removal of a lung lobe)	226,348.42	
A16.09.009.007	Extended bilobectomy for lung neoplasms	225,499.08	
A16.09.009.010	Lobectomy. Videothoracoscopic lung resection	124,973.93	
A16.09.014	Pneumonectomy	226,348.42	
A16.09.016	Anatomical segmentectomy of the lung	145,236.69	
A16.09.016.007	Video thoracoscopic lung segmentectomy	124,973.93	
A16.09.017	Bronchial resection	77,653.70	

Continuation of Table A.6

1	2	3	4
A16.09.018.001	Bronchial plasty. Reconstructive surgeries on the trachea and bronchi	124,973.93	
A16.09.013	Removal of lung neoplasm (atypical resection)	125,277.26	
A16.09.013.002	Combined operation of lung neoplasm removal and pleural cavity correction: thoracomyoplasty, diaphragmatic transposition	225,499.08	
A16.09.013.003	Removal of lung neoplasm (atypical resection). Pleural cavity correction surgeries: thoracomyoplasty, diaphragm transplantation	225,499.08	
A16.09.013.006	Removal of lung neoplasm (atypical resection) videothoracoscopy	145,236.69	
A16.09.015	Lung resection (more than one lobe)	145,236.69	
A16.09.016.005	Lung segmentectomy. Operations on a single lung	145,236.69	
A16.09.016.006	Lung segmentectomy. Extended polisegmental lung resection	145,236.69	
Tier I quota 20 group	Video-endoscopic intracavitary and video-endoscopic intraluminal surgical interventions, interventional radiologic interventions, minimally invasive organ-preserving interventions for MN Reconstructive-plastic, microsurgical, extensive cytoreductive, extended-combination surgical interventions, including with the use of physical factors (hyperthermia, radiofrequency thermoablation, PDT, laser and cryodestruction, etc.).	128,915.00	128,915.00
Tier II quota 21 group	Video-endoscopic intracavitary and video-endoscopic intraluminal surgical interventions, interventional radiologic interventions, minimally invasive organ-preserving interventions in MN	245,183.00	257,382.00
Tier II quota 22 group	Reconstructive-plastic, microsurgical, extensive cytoreductive, extended-combined surgical interventions, including those with the use of physical factors in MN	269,581.00	

Continuation of Table A.6

1	2	3	4
3. Surgical treatment associated with complications			
A16.09.004	Drainage of a pleural cavity or lung abscess	46,592.22	86,556.58
A16.09.036.001	Drainage of lung abscess under ultrasound control or using endoscopic equipment	77,653.70	
A16.09.006	Retoracotomy	46,592.22	
A16.12.035	Thrombectomy from the pulmonary artery, from the main veins	175,388.17	
4. Symptomatic or palliative surgical treatment – 148 229.18 rubs			
A16.09.005	Stopping bleeding from the lower respiratory tract, eliminating pain syndrome	37,370.84	77,584.37
A16.08.029	Tracheal recanalization	26,693.46	
A16.10.011.001	Performing pleural puncture or pericardial puncture with exudative pleurisy or pericarditis	89,605.09	
A16.11.003	Surgical treatment for pulmonary hemorrhage	77,653.70	
A16.09.006	Palliative surgery for massive tumor decay or secondary pneumonia	46,592.22	
A16.08.068	Stenting for tumor stenosis	47,562.89	
A16.09.030	Endoscopic bronchial stenting	124,973.93	
A16.08.028	Augmentation of tracheal and bronchial stenoses	119,331.90	
Tier I quota 20 group	Video-endoscopic intracavitary and video-endoscopic intraluminal surgical interventions, interventional radiologic interventions, minimally invasive organ-preserving interventions for MN Reconstructive-plastic, microsurgical, extensive cytoreductive, extended-combination surgical interventions, including with the use of physical factors (hyperthermia, radiofrequency thermoablation, PDT, laser and cryodestruction, etc.).	128,915.00	128,915.00
Tier II quota 21 group	Video-endoscopic intracavitary and video-endoscopic intraluminal surgical interventions, interventional radiologic interventions, minimally invasive organ-preserving interventions in MN	245,183.00	245,183.00

Table A.7 – State of the model - Chemotherapeutic treatment in inpatient facility for MN of the bronchi and lung patients according to the Order of the Ministry of Health of the Russian Federation No.347n dated April 13, 2021

Therapy	CS tariff, rubs	DS tariff, rubs	% distribution of application of XT regimens in 2021 adjuvant stage I–II	% distribution of application of XT regimens in 2021 neoadjuvant and adjuvant stage III–IV	Average cost of CS DS, rubs
1	2	3	4	5	6
5. Chemotherapeutic treatment in inpatient facility					
Etoposide 100-120 mg/m² on days 1-3 + carboplatin AUC 4-6 on day 1; cycle 21 days	18,564.61	6,900.53	11.87 %	9.59 %	12,732.57
Atezolizumab 1200 mg on day 1; cycle 21 days	252,012.40	240,258.99	10.26 %	8.29 %	246,135.69
Nivolumab 480 mg on day 1; cycle 28 days	425,785.31	392,066.43	7.85 %	6.34 %	408,925.87
Pembrolizumab 200 mg on day 1; cycle 21 days	343,998.14	392,066.43	7.38 %	5.97 %	368,032.28
Etoposide 100 mg/m² on days 1-3 + carboplatin AUC 5 on day 1 + atezolizumab 1200 mg on day 1; cycle 21 days	252,012.40	240,258.99	6.43 %	5.19 %	246,135.69
Pembrolizumab 200 mg on day 1 + paclitaxel 200 mg/m² on day 1 + carboplatin AUC 6 on day 1; cycle 21 days	343,998.14	392,066.43	4.82 %	3.89 %	368,032.28
Osimertinib 80 mg daily	0.00	301,821.00	3.74 %	3.03 %	301,821.00
Pembrolizumab 200 mg on day 1 + pemetrexed 500 mg/m² on day 1; cycle 21 days	425,785.31	392,066.43	3.47 %	2.80 %	408,925.87
Pembrolizumab 200 mg on day 1 + pemetrexed 500 mg/m² on day 1 + carboplatin AUC 5 on day 1; cycle 21 days	425,785.31	392,066.43	3.22 %	2.61 %	408,925.87
Etoposide 120 mg/m² on days 1-3 + cisplatin 60-80 mg/m² on day 1; cycle 21 days	9,755.50	6,900.53	3.17 %	2.56 %	8,328.01
Pemetrexed 500 mg/m² on day 1; cycle 21 days	69,979.89	70,613.44	3.15 %	2.55 %	70,296.66
Pemetrexed 500 mg/m² on day 1 + carboplatin AUC 5-6 on day 1; cycle 21 days	69,979.89	70,613.44	3.09 %	2.49 %	70,296.66

Continuation of Table A.7

1	2	3	4	5	6
Alectinib 1200 mg daily	0.00	301,821.00	2.81 %	2.27 %	301,821.00
Pembrolizumab 400 mg w/v on day 1; cycle 42 days	719,487.79	800,840.46	2.50 %	2.02 %	760,164.13
Nivolumab 240 mg on day 1; cycle of 14 days	202,853.71	240,258.99	2.28 %	1.84 %	221,556.35
Carboplatin AUC 4-7 on day 1; cycle 21 days	9,755.50	6,900.53	1.56 %	1.26 %	8,328.01
Pemetrexed 500 mg/m² on day 1 + cisplatin 75 mg/m² on day 1; cycle 21 days	69,979.89	70,613.44	1.42 %	1.15 %	70,296.66
Afatinib 40 mg daily	0.00	151,021.18	1.42 %	1.15 %	151,021.18
Paclitaxel 175-200 mg/m² on day 1 + cisplatin 60-80 mg/m² on day 1; cycle 21 days	26,189.83	34,066.83	1.28 %	1.04 %	30,128.33
Denosumab 120 mg p/k on days 1, 8, 15, 28 of the first month, then once every 28 days thereafter	26,189.83	34,066.83	1.21 %	0.98 %	30,128.33
Paclitaxel 175-200 mg/m² on day 1 + carboplatin AUC 5-6 on day 1 + bevacizumab 7.5-15 mg/kg on day 1; cycle 21 days	115,148.91	116,837.99	1.14 %	0.92 %	115,993.45
Vinorelbine 25-30 mg/m² on days 1, 8, 15; cycle 28 days	9,755.50	6,900.53	1.14 %	0.92 %	8,328.01
Atezolizumab 1200 mg on day 1 + paclitaxel 175-200 mg/m² on day 1 + carboplatin AUC 6 on day 1 + bevacizumab 15 mg/kg on day 1; cycle 21 days	343,998.14	392,066.43	1.01 %	0.82 %	368,032.28
Bevacizumab 7.5-15 mg/kg on day 1; cycle 21 days	91,130.95	86,830.39	1.01 %	0.81 %	88,980.67
Atezolizumab 1200 mg on day 1 + bevacizumab 7.5 mg/kg on day 1; cycle 21 days	343,998.14	392,066.43	0.92 %	0.74 %	368,032.28
Pemetrexed 500 mg/m² on day 1 + carboplatin AUC 5 on day 1 + bevacizumab 7.5 mg/kg on day 1; cycle 21 days	124,871.80	134,269.51	0.83 %	0.67 %	129,570.65
Gemcitabine 750-1250 mg/m² on days 1, 8; cycle 21 days	9,755.50	6,900.53	0.80 %	0.64 %	8,328.01
Atezolizumab 1200 mg on day 1 + bevacizumab 15 mg/kg on day 1; cycle 21 days	343,998.14	392,066.43	0.76 %	0.61 %	368,032.28
Pemetrexed 500 mg/m² on day 1 + bevacizumab 7.5 mg/kg once every 21 days; cycle 21 days	124,871.80	134,269.51	0.69 %	0.56 %	129,570.65

Continuation of Table A.7

1	2	3	4	5	6
Nivolumab 360 mg on days 1 and 22 + ipilimumab 1 mg/kg on day 1; cycle 42 days	252,012.40	301,821.00	0.66 %	0.54 %	276,916.70
Gemcitabine 1000-1250 mg/m² on days 1, 8 + cisplatin 25-40 mg/m² on days 1, 8; cycle 21 days	9,755.50	6,900.53	0.62 %	0.50 %	8,328.01
Crizotinib 500 mg daily	0.00	301,821.00	0.62 %	0.50 %	301,821.00
Nivolumab 3 mg/kg on day 1; cycle 14 days	202,853.71	204,426.52	0.60 %	0.49 %	203,640.12
Atezolizumab 1200 mg on day 1 + paclitaxel 175 mg/m² on day 1 + carboplatin AUC 5 on day 1 + bevacizumab 7.5 mg/kg on day 1; cycle 21 days	343,998.14	392,066.43	0.57 %	0.46 %	368,032.28
Nivolumab 3 mg/kg i.v. on day 1 + ipilimumab 1 mg/kg i.v. once every 42 days; cycle 14 days	252,012.40	301,821.00	0.51 %	0.41 %	276,916.70
Nintedanib 400 mg daily	0.00	173,525.41	0.42 %	0.34 %	173,525.41
Docetaxel 75 mg/m² on day 1 + bevacizumab 7.5 mg/kg on day 1; cycle 21 days	69,979.89	70,613.44	0.42 %	0.34 %	70,296.66
Etoposide 100 mg/m² on days 1-3 + cisplatin 100 mg/m² on day 1; cycle 28 days	9,755.50	6,900.53	0.41 %	0.33 %	8,328.01
Pemetrexed 500 mg/m² on day 1 + bevacizumab 15 mg/kg on day 1; cycle 21 days	173,050.85	204,426.52	0.38 %	0.31 %	188,738.69
Atezolizumab 840 mg on day 1; cycle 14 days	173,050.85	204,426.52	0.38 %	0.31 %	188,738.69
Gemcitabine 750-1000 mg/m² on days 1, 8 + carboplatin AUC 3-6 on day 1; cycle 21 days	9,755.50	6,900.53	0.31 %	0.25 %	8,328.01
Paclitaxel 60-100 mg/m² on day 1 + carboplatin AUC 2 on day 1; cycle 7 days	18,564.61	6,900.53	0.28 %	0.22 %	12,732.57
Gemcitabine 1000 mg/m² on days 1, 8, 15 + bevacizumab 7.5-15 mg/kg on day 1 every 3 weeks; cycle 28 days	65,593.47	43,487.91	0.24 %	0.20 %	54,540.69
Paclitaxel 50 mg/m² on days 1, 8, 15 + carboplatin AUC 2 on days 1, 8, 15; cycle 21 days	9,755.50	6,900.53	0.21 %	0.17 %	8,328.01
Pembrolizumab 200 mg on day 1 + pemetrexed 500 mg/m² on day 1 + cisplatin 75 mg/m² on day 1; cycle 21 days	425,785.31	392,066.43	0.21 %	0.17 %	408,925.87

Continuation of Table A.7

1	2	3	4	5	6
Gefitinib 250 mg daily	0.00	116,837.99	0.21 %	0.17 %	116,837.99
Pemetrexed 500 mg/m² on day 1 + cisplatin 75 mg/m² on day 1 + bevacizumab 7.5 mg/kg on day 1; cycle 21 days	124,871.80	134,269.51	0.21 %	0.17 %	129,570.65
Gemcitabine 800-1200 mg/m² i/v on days 1, 8, 15; cycle 28 days	9,755.50	6,900.53	0.21 %	0.17 %	8,328.01
Gemcitabine 750-1000 mg/m² on days 1, 8, 15; cycle 28 days	9,755.50	6,900.53	0.17 %	0.14 %	8,328.01
Dabrafenib 300 mg daily + trametinib 2 mg daily	0.00	392,066.43	0.14 %	0.11 %	392,066.43
Nivolumab 3 mg/kg on day 1 + ipilimumab 1 mg/kg on day 1; cycle 21 days	425,785.31	500,454.43	0.13 %	0.10 %	463,119.87
Erlotinib 150 mg daily	0.00	86,830.39	0.10 %	0.08 %	86,830.39
Oxaliplatin 85 mg/m² on day 1 + calcium folinate 200-400 mg/m² on day 1 + fluorouracil 400 mg/m² on day 1 + fluorouracil 2400 mg/m² (1200 mg/m² per day) 46-hour infusion on days 1-2 + bevacizumab 5 mg/kg on day 1; cycle 14 days	65,593.47	60,489.36	0.10 %	0.08 %	63,041.42
Gemcitabine 750-1000 mg/m² on days 1, 8 + oxaliplatin 100-130 mg/m² on day 1; cycle 21 days	18,564.61	6,900.53	0.10 %	0.08 %	12,732.57
Pembrolizumab 2 mg/kg on day 1; cycle 21 days	252,012.40	240,258.99	0.10 %	0.08 %	246,135.69
Ramucirumab 8 mg/kg on day 1; cycle 14 days	202,853.71	204,426.52	0.10 %	0.08 %	203,640.12
Pemetrexed 500 mg/m² on day 1 + cisplatin 75 mg/m² on day 1 + bevacizumab 15 mg/kg on day 1; cycle 21 days	173,050.85	204,426.52	0.07 %	0.06 %	188,738.69
Paclitaxel 45-50 mg/m² on day 1 + carboplatin AUC 1.5-2 on day 1; cycle 7 days	9,755.50	6,900.53	0.07 %	0.06 %	8,328.01
Gemcitabine 800-1200 mg/m² on days 1, 8, 15; cycle 21 days	9,755.50	6,900.53	0.07 %	0.06 %	8,328.01
Atezolizumab 1680 mg on day 1; cycle 28 days	343,998.14	392,066.43	0.06 %	0.05 %	368,032.28
Dabrafenib 300 mg daily	0.00	301,821.00	0.03 %	0.03 %	301,821.00

Table A.8 – Inpatient state of treatment f a clinical model for MN of the bronchi and lung patients in accordance with the Order of the Ministry of Health of the Russian Federation No.347n dated April 13, 2021

Medical service code	Name of medical service	FCHIF tariff 2022, rubs	Average cost of the group in 2022, rubs
1	2	3	4
6. Radiation treatment			
A07.30.009	Conformal remote radiation therapy (RT) is given at a dose of 2 Gy 5 days a week. The radiation volume includes the tumor, affected mediastinal lymph nodes, and the entire mediastinal volume up to the contralateral root. Supraclavicular areas are included in the radiation volume only if metastases are present. Total boost dose (TBD) - 60 Gy for the tumor and 46 Gy for the mediastinum. Hyperfractionation of RT is possible - irradiation 2 times a day with an interval of 4-6 h between fractions by 1.5 Gy up to TBD 45 Gy	27,664.13	147,747.75
A07.30.009.001	Conformal remote radiotherapy, including IMRT, IGRT, ViMAT, stereotactic	176,838.24	
Tier I quota 23 group	Conformal remote radiotherapy, including IMRT, IGRT, VMAT, stereotactic (1 - 39 Gy). Radio modification. Computed tomography and (or) magnetic resonance topometry. 3D - 4D planning. Fixing devices. Volumetric visualization of the target. Synchronization of breathing	85,395.68	
Tier I quota 24 group	Conformal remote radiotherapy, including IMRT, IGRT, VMAT, stereotactic (40-69 Gy). Radio modification. Computed tomography and (or) magnetic resonance topometry. 3D - 4D planning. Fixing devices. Volumetric visualization of the target. Synchronization of breathing	192,720.12	
Tier I quota 25 group	Conformal remote radiotherapy, including IMRT, IGRT, VMAT, stereotactic (70-99 Gy). Radio modification. Computed tomography and (or) magnetic resonance topometry. 3D - 4D planning. Fixing devices. Volumetric visualization of the target. Synchronization of breathing	256,120.58	
8. Therapeutic symptomatic treatment in inpatient facility associated with previous treatment or the course of the underlying disease			
-	Conservative hemostatic therapy for pulmonary hemorrhage, if it is impossible to perform surgical treatment	12,133.39	24,327.45
-	Metastatic lesion of the abdominal organs	29,362.80	
-	Metastatic brain damage	27,906.80	
-	Malignant neoplasm without special antitumor treatment	27,906.80	

APPENDIX B

(mandatory)

Questionnaire of a smoking patient who received inpatient treatment at the National Medical Research Center of Oncology named after N.N. Petrov

1. ID-outpatient card number ____

2. Gender: ☐ male ☐ female

3. Date of birth ____

4. Diagnosis of MN according to ICD 10 ____

5. The year of the first hospitalization in the National Medical Research Center of Oncology named after N.N. Petrov from 2013 to 2021__________________________

6. Smoking experience:

   ☐ from 1 year to 5 years ☐ from 6 to 10 years ☐ from 11 to 20 years old

   ☐ from 21 to 30 years old ☐ from 31 to 40 years old ☐ from 41 to 50 years old

   ☐ from 51 to 65 years old ☐ over 65 years old

7. Do you smoke now?

   ☐ yes ☐ no (quit)

8. What do you smoke?

   ☐ cigarettes ☐ pipe ☐ electronic cigarettes ☐ hookah

9. How many cigarettes do you smoke?

   ☐ 0.5 packs per day or less

   ☐ more than 0.5 and less than 1 pack per day (inclusive)

   ☐ more than 1 and less than 2 packs per day (inclusive)

   ☐ more than 2 and less than 3 packs per day (inclusive)

   ☐ more than 3 and up to 4 packs per day (inclusive)

APPENDIX C

(mandatory)

Questionnaire of a malignant neoplasm of the bronchi and lung patient who underwent COVID-19

1. Patient ID in the PCR database (unique code)
2. Gender: □ male □ female
3. Date of birth ______________________________
4. MN of the bronchi and lung stage:

   □ I □ II □ III □ IV □ without stage
5. Date of Covid diagnosis (confirmation) ______________________
6. Covid flow pattern:

   □ mild or satisfactory □ medium-severe (moderate)

   □ severe □ extremely severe □ unknown
7. Covid treatment was carried out:

   □ outpatient □ hospital admission for observation □ unknown
8. Exodus:

   □ recovery □ lethal outcome
9. Date of lethal outcome from Covid ______________________

APPENDIX D

(mandatory)

Results of modeling the outpatient phase of medical observation of malignant neoplasm of the bronchi and lung patients

Table D.1 – Results of modeling the outpatient state of diagnosis and medical observation of patients with MN of the bronchi and lung in the first year from the moment of diagnosis in accordance with the Order of the Ministry of Health of the Russian Federation No.347n, April 13, 2021

Medical service code	Name of medical service	Number of services	% of services by group	Required funding, thousand rubs	% of the funding by group
1	2	3	4	5	6
Reception (examination, consultation) of a specialist doctor					
B01.015.001	Primary appointment (examination, consultation) with a cardiologist	45	2.95 %	24.11	2.16 %
B01.023.001	Primary appointment (examination, consultation) with a neurologist	60	3.97 %	32.45	2.91 %
B01.027.001	Primary appointment (examination, consultation) with an oncologist	1,408	93.08 %	1,059.47	94.93 %
	Total for the group	1,513	6.75 %	1,116.03	1.63 %
Laboratory methods of examination					
A08.09.001	Pathologic-anatomical examination of biopsy (surgical) material of tracheal and bronchial tissues	1,374	15.38 %	2,343.65	29.80 %
A08.09.001.002	Pathologo-anatomical examination of biopsy (surgical) material of tracheal and bronchial tissues using immunohistochemical methods	687	7.69 %	2,710.99	34.48 %

Continuation of Table D.1

1	2	3	4	5	6
A08.09.008	Cytological examination of micro-preparation of tracheal and bronchial tissues	1,374	15.38 %	1,229.37	15.63 %
B03.005.006	Coagulogram (indicative study of hemostasis system)	1,374	15.38 %	495.05	6.30 %
B03.016.003	General (clinical) blood test, detailed	1,374	15.38 %	161.82	2.06 %
B03.016.004	Biochemical blood analysis general therapeutic	1,374	15.38 %	841.73	10.70 %
B03.016.006	General (clinical) urine analysis	1,374	15.38 %	80.99	1.03 %
	Total for the group	8,928	39.83 %	7,863.59	11.50 %
Instrumental methods of examination					
A03.09.003.001 and A11.09.008	Videotracheobronchoscopy with Biopsy of trachea, bronchi during bronchoscopy	1,374	15.52 %	3,066.22	8.04 %
A04.06.002	Ultrasound examination of lymph nodes (one anatomical zone)	1,374	15.52 %	511.67	1.34 %
A04.10.002	Echocardiography	45	0.50 %	32.08	0.08 %
A04.16.001	Ultrasound examination of abdominal organs (complex)	1,374	15.52 %	511.67	1.34 %
A05.10.006	Electrocardiogram registration	1,528	17.26 %	472.50	1.24 %
A05.23.009.001	Magnetic resonance imaging of the brain with contrast	1,236	13.96 %	9,517.81	24.97 %
A06.09.005.002	Computed tomography of thoracic cavity organs with intravenous bolus contrasting	412	4.65 %	1,835.82	4.82 %
A06.23.004.006	Computed tomography of the brain with intravenous contrast	137	1.55 %	611.94	1.61 %
A07.03.001.001	Whole body bone scintigraphy	549	6.21 %	3,981.76	10.44 %
A07.30.043.001	Positron emission tomography combined with computed tomography with tumorotropic RFPs with contrasting	824	9.31 %	17,581.81	46.12 %
	Total for the group	8,853	39.49 %	38,123.26	55.73 %

Continuation of Table D.1

1	2	3	4	5	6
Molecular genetic studies in outpatient conditions					
A08.30.004	Immunocytochemical examination of biological material	515	16.48 %	1,097.44	5.15 %
A08.30.039	Determination of PDL1 protein expression by immunohistochemical method	876	28.02 %	10,665.66	50.07 %
A27.30.008	Molecular genetic examination of mutations in the BRAF gene in biopsy (surgical) material	172	5.49 %	945.72	4.44 %
A27.30.016	Molecular genetic examination of mutations in the EGFR gene in biopsy (surgical) material	876	28.02 %	4,816.19	22.61 %
A27.30.017	Molecular genetic examination of ALK gene translocations	343	10.99 %	1,888.70	8.87 %
A27.30.018	Molecular genetic examination of ROS1 gene translocations	343	10.99 %	1,888.70	8.87 %
	Total for the group	3,125	13.94 %	21,302.41	31.14 %
	Total for all groups for the first year of observation	22,419		68,405.29	

Table D.2 – Results of modeling the outpatient stage of observation of patients with MN of the bronchi and lung in the 2d and 3d year from the moment of diagnosis in accordance with the Order of the Ministry of Health of the Russian Federation No.347n, April 13, 2021

Medical service code	Name of medical service	Number of services	% of services by group	Required funding, thousand rubs	% of the funding by group
1	2	3	4	5	6
Second year of observation					
Reception (examination, consultation) and supervision of a specialist doctor					
B04.027.001	Dispensary appointment (examination, consultation) with an oncologist	2,844	31.25 %	2,140.16	18.44 %
Instrumental methods of examination					
A04.09.002	Ultrasound examination of the lungs	2,844	31.25 %	1,059.41	9.13 %
A05.23.009	Magnetic resonance imaging of the brain	284	3.13 %	562.56	4.85 %
A06.09.005	Computed tomography of the thoracic cavity organs	2,560	28.13 %	5,685.01	48.98 %
A06.09.007	Lung radiography	284	3.13 %	97.58	0.84 %
A07.03.001.001	Whole body bone scintigraphy	284	3.13 %	2,061.08	17.76 %
	Results for the second year of observation	9,101	57.91 %	11,605.80	57.91 %
Third year of observation					
Reception (examination, consultation) and supervision of a specialist doctor					
B04.027.001	Dispensary appointment (examination, consultation) with an oncologist	2,070	31.25 %	1,557.38	18.44 %

Continuation of Table D.2

1	2	3	4	5	6
Instrumental methods of examination					
A04.09.002	Ultrasound examination of the lungs	2,070	31.25 %	770.93	9.13 %
A05.23.009	Magnetic resonance imaging of the brain	207	3.13 %	409.37	4.85 %
A06.09.005	Computed tomography of the thoracic cavity organs	1,863	28.13 %	4 136.95	48.98 %
A06.09.007	Lung radiography	207	3.13 %	71.01	0.84 %
A07.03.001.001	Whole body bone scintigraphy	207	3.13 %	1 499.84	17.76 %
	Results for the third year of observation	6,623	42.09 %	8 445.47	42.09 %
General data for the second and third year of observation		15 724		20,051.27	