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Research article

ASSESSMENT OF A PROBABLE RELATIONSHIP BETWEEN INFLUENCE OF HARMFUL AND (OR) HAZARDOUS WORKING CONDITIONS, AMBIENT AIR POLLUTION AND THE INCIDENCE OF MALIGNANT NEOPLASMS OF THE TRACHEA, BRONCHI, AND LUNGS (C33, C34) IN THE MALE POPULATION OF THE RUSSIAN FEDERATION

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In 2021, in the Russian Federation, malignant neoplasms (MN) of the trachea, bronchi, lungs (ICD – C33, C34) occupied the first place in the structure of MN in men accounting for 16.4 %. Many studies show the existence of a potential connection between impacts of occupational factors and MN development; however, in Russia, the occupational genesis of MN is rarely recognized.

The aim of this study was to identify a relationship between working conditions, volumes of pollutants emitted into ambient air and the incidence of tracheal, bronchial, and lung MN in men.

The data were obtained from Form No. 7 "Information on malignant neoplasms", the Report "The state of working conditions for workers employed by economic entities operating in the Russian Federation as per specific types of economic activity", and Form No. 2-TP (air) "Information on the protection of ambient air" of Rosstat. We analyzed incidence rates of malignant neoplasms of the trachea, bronchi, and lungs among working age males, as well as males aged between 40 and 65 years in 2011–2021. The study involved quartile analysis (incidence rates were standardized with the direct method); correlation analysis (Kendall rank correlation); as well as multiple regression analysis. The latter was carried out to study effects of predictors (volumes of pollutants emitted into ambient air) on the selected criterion (MN incidence). The research data were statistically analyzed using MS Office Excel 2019, IBM SPSS Statistics 26.

A downward trend was established for the analyzed incidence rates in Russia. A moderate positive correlation ($\tau = +0.31$) was obtained between the proportion of workers employed in harmful or hazardous working conditions and the incidence of MN of the specified localization. A predictive regression model was developed.

The obtained results of the correlation analysis require more in-depth consideration in subsequent studies. In our opinion, oncologists need to study occupational routes of their patients. Employers should focus on primary MN prevention within corporate practices of enterprises.

Keywords: *occupational malignant neoplasms, trachea cancer, bronchus cancer, lung cancer, oncology, harmful working conditions, incidence rates, correlation analysis, prognostic regression model.*

In 2011, 1.09 million cases of malignant neoplasms (MNs) of lung were registered in men worldwide according to the GLOBOCAN, an interactive web-based platform presenting global cancer statistic. They held the first rank place in the total MNs incidence and the trend persisted over the whole analyzed period between 2011 and 2021. Thus, in 2020, 1.43 million of lung cancer cases were registered in men for the first time[1] [1, 2]. In 2020, MNs of

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[1] Cancer today. Data visualization tools for exploring the global cancer burden in 2020. *Global Cancer Observatory IARC*, 2023. Available at: https://gco.iarc.fr/today/home (July 11, 2023).

lungs were also the leading cause of death from cancer among men in 93 countries mostly due to their high fatality rate [3]. The total number of new trachea, bronchus and lung cancer cases grew by 23.3 % worldwide between 2010 and 2019 (95 % *CI*: 12.9–33.6 %) [4]. The situation in the Russian Federation is similar to the global trends. Thus, in 2011, approximately 46 thousand cases of trachea, bronchus and lung (TBL) cancer were registered in men in Russia and this cancer also holds the first rank place in the total MNs incidence accounting for 18.9 %. In 2021, 37.3 thousand cases of TBL cancer were first diagnosed in men; this also corresponded to the first rank place in the total MNs structure accounting for 16.4 %. In 2021, 47.2 % of patients with diagnosed TBL cancer (C33, C34) died during the first year after the diagnosis was put in accordance with data provided in the Federal Statistical Form No. 7 'Information on malignant neoplasms' [2].

Large-scale global studies report that 80.3 % (95 % *CI*: 77.5–83.2 %) of all deaths due to MNs of trachea, bronchus and lung in 2019 were associated with exposure to risk factors.

Smoking occupied the first rank place as per its contribution and caused 64.2 % (61.9–66.4 %) of all deaths from TBL cancer among patients of both sexes.

Despite this fact, approximately 25 % of patients with lung cancer never smoked [5]. This means the disease might be caused by other factors. Ambient particulate matter pollution is the second-highest specific risk factor that causes 15.6 % (95 % *CI*: 11.7–19.6) of deaths from TBL cancer for men and 13.9 % (95 % *CI*: 10.3–17.6) of TBL cancer deaths for women [4, 6, 7].

Occupational exposure to asbestos is the third-highest specific risk factor for deaths from tracheal, bronchus, and lung cancer in 2019 causing 12.4 % (95 % *CI*: 8.3–16.6) of deaths from TBL cancer for men and only 4.0 % (95 % *CI*: 2.4–5.5) for women. Indeed, occupational factors have significant effects on development of MNs of this localization. The above-mentioned study reports that 9 out of 16 leading risk factors can be considered occupational (exposure to asbestos, silica, diesel engine exhaust, arsenic, nickel, polycyclic aromatic hydrocarbons, chromium, cadmium, and beryllium) [4]. According to the International Labor Organization estimates, 2 million out of 2.5 billion workers worldwide annually die due to occupational injuries or diseases; TBL cancer and interstitial lung diseases account for one third of the latter. It is worth considering that the accomplished studies reveal a significant growth in risks of trachea, bronchus and lung cancer under simultaneous exposure to harmful and (or) hazardous occupational factors and smoking [8–10].

Despite the foregoing, malignant neoplasms are very rarely considered to be occupational by experts in the Russian Federation [11]. An occupational disease is diagnosed in conformity with the Labor Code of the Russian Federation No. 197-FZ issued on December 30, 2001, the Federal Law on Mandatory Social Insurance from Occupational Injuries and Diseases No. 125-FZ issued on July 24, 1998, the Federal Law On Essentials of Citizen's Health Protection No. 323-FZ issued on November 21, 2011, the RF Government Order issued on July 05, 2022 No. 1206 On the Procedure for Investigating and Keeping Records of Occupational Diseases among Workers, the Order by the RFD Ministry of Health and Social Development dated April 27, 2012 No. 417n On Approval of the List of Occupational Diseases. A preliminary diagnosis can be put by any certified healthcare organization a worker has applied to for medical aid. Further expertise is conducted by a Center for Occupational Pathologies.

A remarkable fact is that only 497 cases of occupational cancer were established in Russia over the period between 2002 and 2014. Most of them were identified in the Urals and Siberia Federal Districts. However, in France, for example, 1030 cases of occupational MNs of lungs and bronchus (C34) were registered solely in 2019 [12]. For several years, data in the State Reports 'On Sanitary-Epidemiological Welfare of the Population in the Russian Federation' indicate that equipment and machinery are extremely worn out at many industrial enterprises, a lot of companies still use outdated technologies and often do not have a system for hazard prevention and control in workplace settings thus failing to conform to the Labor Code requirements.

Given all the foregoing, it is rather doubtful that rates of occupational MNs are actually so low. Some research data clearly indicate that more than 20 thousand MNs per year in Russia are likely to be associated with occupational factors; however, there are no system records on them in Russia and the actual prevalence of occupational MNs is assumed to be considerably higher. Difficulties in identification of occupational MNs can be caused by several reasons including ineffective preliminary and periodical health examinations (PHEs) (insufficient attention paid to collecting data relevant for an occupational case history) especially in small and medium-sized businesses; absence of specialized scientific research institutions; peculiarities of the valid regulatory documents that do not provide a precise system of relevant criteria for expert decision-making[2] [13–19].

A study conducted in the RF relying on 2016 data revealed the total economic burden of lung cancer to be equal to 14.77 billion rubles or approximately 0.2 % of the country GDP in the same period. Indirect costs on one potentially employed patient with lung cancer were established to be the highest against the same socioeconomic burden due to other MNs (kidney, prostate, breast, ovaries, or melanoma). In 2015, 4.00 billion rubles were paid to disabled people with diagnosed lung cancer; in 2016, 5.16 billion rubles [20, 21].

Given all the above stated, it is necessary to establish an association between cancer and an occupational factor in case it truly exists and, consequently, to increase a number of diagnosed occupational cancer cases. This will help workers receive due compensations and cover rehabilitation costs at en employer's expense thereby providing even distribution of economic burden associated with cancer treatment between the state and an employer.

Therefore, the **aim** of this study was to identify a relationship between working conditions, volumes of pollutants emitted into ambient air and the incidence of tracheal, bronchial, and lung MN (C33, C34) in men in 2021.

Materials and methods. Data on the first diagnosed cases of trachea, bronchus and lung cancer (C33, C34) in the period between 2011 and 2021 were taken from the Federal Statistic Form No. 7 'Information on malignant neoplasms'. 'Rough' incidence rates for trachea, bronchus and lung cancer in working age men and men aged between 40 and 65 years were calculated based on these data and then standardized using the direct standardization method (the standard is an age-specific structure of male population within the respective age range in RF in 2011). 95 % confidence intervals (95 % *CI*) were calculated as well. This age range was selected due to a latent period in cancer development and duration of exposure to adverse occupational and environmental factors. Quartile analysis was conducted in order to divide the indicators into quartiles for further creation of data maps. Data on shares of workers with harmful and (or) hazardous conditions at their workplaces were taken from the Report 'The state of working conditions for workers employed by economic entities operating in the Russian Federation as per specific types of economic activity in 2021' issued by the Federal State Statistic Service (Rosstat). Data on pollutant emissions were taken from the Form No. 2-TP (air) 'Information on the protection of ambient air' of Rosstat. We performed a correlation analysis to estimate a potential correlation between standardized incidence rates in men of working age in the RF in 2021 and a share of male workers exposed to harmful and hazard-

[2] Health and safety at work. Details by NACE. *Eurostat: Data Browser*, 2019. Available at: https://ec.europa.eu/eurostat/databrowser/explore/all/popul?lang=en&subtheme=hlth.hsw&display=list&sort=category&extractionId=HSW_N2_01__custom_2403901 (July 30, 2023).

ous conditions in their workplace settings, a share of workers exposed to predominantly fibrogenic aerosols; a share of smokers (%) (among men older than 15 years); the amount (tons) of pollutants emitted into ambient air in 2021 including cadmium oxide, nickel and its compounds, chromium (recalculated as per chromium (VI) oxide), arsenic (inorganic compounds (recalculated as per arsenic)), benzo(a)pyrene, inorganic dust with SiO_2 > 70 %, inorganic dust with 70–20 % SiO_2, volatile organic compounds (VOC). The analysis relied on using the Kendall rank correlation. The method was selected due to analyzed indicators not being distributed normally. In a regression analysis, we estimated a linear relationship between the standardized incidence rate of TBL cancer (C33, C34) in working age males in the RF and all the foregoing parameters. Factors were selected by excluding statistically insignificant ones; a predictive regression model was created later on. Statistical data analysis was conducted using MS Office Excel 2019 and IBM SPSS Statistics 26.

Results and discussion. In the Russian Federation, 256,421 new cases of trachea, bronchus and lung cancer (C33, C34) were registered in men aged between **40 and 65** years between 2011 and 2021; this accounts for 50.44 % of all first diagnosed MNs of the said localization in men of all age groups over the same period. Most TBL cancer (C33, C34) cases were identified between 2011 and 2021in men aged 60–64 years.

The standardized incidence rate of trachea, bronchus and lung cancer (C33, C34) in men aged between 40 and 65 years was 109.47 (95 % *CI*: 108.11–110.84) in the RF in 2011 and 80.89 (95 % *CI*: 79.73–82.05) in 2021. A downward trend in the TBL cancer (C33, C34) incidence was identified in the RF in the analyzed period with its annual decline rate being -2.92 %.

The greatest annual decline rate was established in the North Caucasian Federal District in 2011–2021 where it equaled -4.04 %; the lowest decline rate among all Federal Districts was identified in the Siberian Federal District where it equaled -2.30 %.

Among the RF regions, the greatest annual decline rate in 2011–2021 was identified in Chechnya, -7.77 %; the lowest decline rate, Khakassia, -0.17 % (Figure 1).

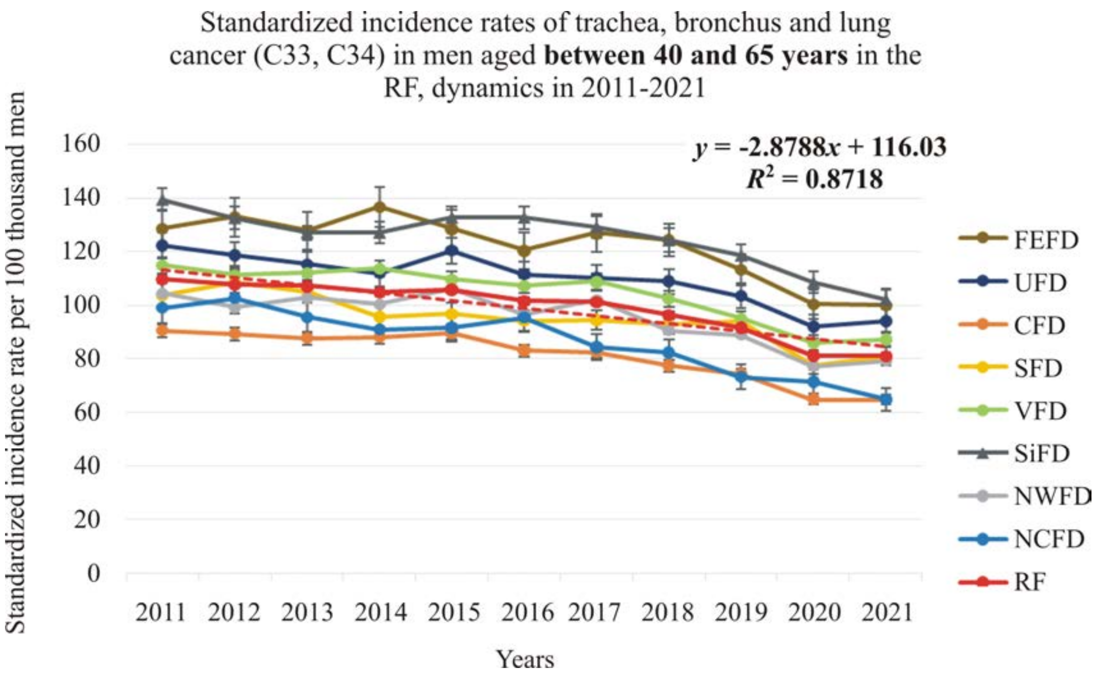

Figure 1. Standardized incidence rates of trachea, bronchus and lung cancer (C33, C34) in men aged **between 40 and 65 years** in the RF, dynamics in 2011–2021

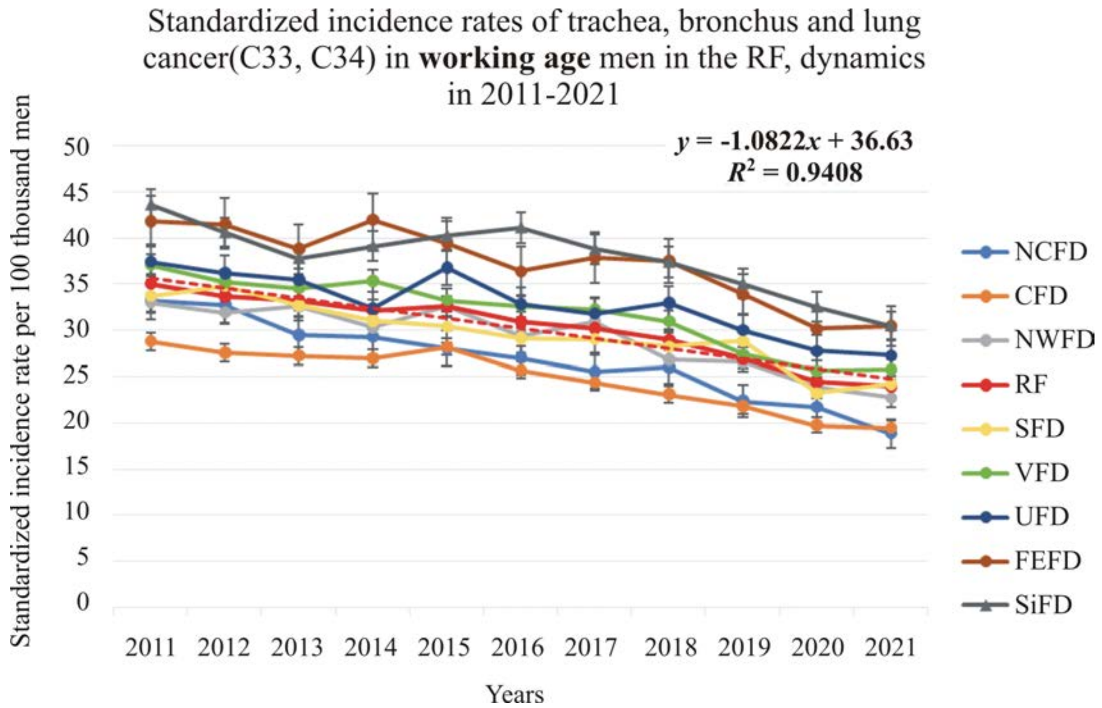

Figure 2. Standardized incidence rates of trachea, bronchus and lung cancer (C33, C34) in **working age** men in the RF, dynamics in 2011–2021

Between 2011 and 2021, 150,149 TBL cancer (C33, C34) cases were diagnosed in **working age** men, which accounts for 29.54 % of all MNs of the said localization in men over the analyzed period. In the RF, the standardized incidence rate of TBL cancer (C33, C34) in working age men was 34.93 (95 % *CI*: 34.39–35.47) in 2011 and 23.93 (95 % *CI*: 23.47–24.40) in 2021; the annual decline rate was -3.37 %. The highest annual decline rate equaling -4.60 % was identified in the North Caucasian Federal District; the lowest equaling -2.53 %, in the Siberian Federal District.

Among the RF regions, the greatest annual decline rate was established in Chechnya where it equaled -10.85 %. The annual growth in the indicator was established in the Murmansk oblast, +0.31 %. (Figure 2).

‘Rough’ and standardized incidence rates for trachea, bronchus and lung cancer (C33, C34) in men aged between 40 and 65 years as well as working age men were divided into four quartiles at the next stage in our study. RF regions with lowest rates were included into the 1st quartile; the highest rates, the 4th quartile (Tables 1 and 2, Figures 3 and 4). Shares of workers exposed to harmful and (or) hazardous conditions in workplace settings were also divided into quartiles. Interestingly, there is partial coincidence of territories with high incidence rates and territories with prevailing shares of workers exposed to harmful and (or) hazardous conditions in workplace settings (Figures 3–5).

Next, we conducted a correlation analysis using the Kendall rank correlation. As a result, we established an authentic ($p < 0.01$) moderate positive correlation ($\tau = + 0.31$) between the standardized incidence rates of trachea, bronchus and lung cancer (C33, C34) in working age men in the RF in 2021 and the share of male workers exposed to harmful and hazardous working conditions in 2021. We did not identify any significant correlation between the analyzed incidence rates and indicators that described ambient air pollution (Figure 6).

Table 1

Quartile distribution of rough and standardized incidence rates of trachea, bronchus and lung cancer (C33, C34) per 100 thousand working age men in the RF in 2011–2021

'Rough' incidence rates of trachea, bronchus and lung cancer (C33, C34) in working age men in the RF (per 100 thousand men)					
Year \ Quartile	**0**	**1**	**2**	**3**	**4**
2011	8.78	32.59	39.28	44.30	56.31
2012	17.14	32.91	37.63	42.28	54.28
2013	13.98	32.44	38.73	44.35	64.74
2014	16.30	30.93	36.29	43.10	85.95
2015	14.68	32.07	37.39	42.34	62.12
2016	16.75	30.16	34.91	40.50	63.45
2017	16.90	29.17	34.93	40.27	80.81
2018	9.99	30.04	33.43	37.91	54.74
2019	7.37	25.70	31.42	34.53	46.46
2020	10.87	23.86	27.88	33.56	40.90
2021	8.33	22.85	27.40	30.96	49.04
Standardized incidence rates of trachea, bronchus and lung cancer (C33, C34) in working age men in the RF (per 100 thousand men)					
Year \ Quartile	**0**	**1**	**2**	**3**	**4**
2011	11.72	32.73	38.49	41.99	63.49
2012	14.09	32.79	36.25	40.54	56.53
2013	14.88	31.63	37.10	42.16	69.06
2014	17.60	29.74	34.80	41.82	80.17
2015	18.82	30.54	35.06	40.01	54.88
2016	17.58	29.16	33.46	39.18	70.39
2017	16.87	28.25	32.78	38.43	73.63
2018	12.88	28.25	32.07	36.72	52.02
2019	7.25	25.55	29.71	33.97	46.58
2020	12.85	23.41	27.30	32.24	44.80
2021	7.58	23.19	27.37	30.71	52.13

Table 2

Quartile distribution of rough and standardized incidence rates of trachea, bronchus and lung cancer (C33, C34) per 100 thousand men aged between 40 and 65 years in the RF in 2011–2021

'Rough' incidence rates of trachea, bronchus and lung cancer (C33, C34) in men aged between 40 and 65 years in the RF (per 100 thousand men)					
Year \ Quartile	**0**	**1**	**2**	**3**	**4**
2011	38.01	103.93	122.59	134.76	173.39
2012	53.18	103.78	119.07	130.89	187.27
2013	42.01	103.63	121.95	140.98	212.42
2014	49.69	101.57	116.47	141.17	212.59
2015	57.26	106.34	121.78	134.76	188.98
2016	54.89	104.91	115.10	131.82	209.41
2017	58.50	100.30	117.12	136.96	232.80
2018	49.02	97.91	114.95	126.95	175.45
2019	54.13	97.89	106.50	118.49	161.21
2020	41.85	84.23	94.29	106.41	135.99
2021	27.00	82.46	95.08	107.07	154.21

The End of Table 2

Standardized incidence rates of trachea, bronchus and lung cancer (C33, C34) in men aged between 40 and 65 years in the RF (per 100 thousand men)					
Year \ Quartile	**0**	**1**	**2**	**3**	**4**
2011	48.90	105.40	120.57	131.57	172.90
2012	59.40	104.24	115.98	127.38	176.58
2013	54.45	103.08	118.18	135.31	210.44
2014	52.14	97.63	113.29	133.95	215.07
2015	61.71	100.47	117.55	127.47	172.18
2016	55.17	100.34	109.15	126.98	210.83
2017	58.55	96.70	109.41	128.37	244.02
2018	48.34	93.10	106.84	120.27	165.66
2019	53.22	89.47	100.80	111.48	147.98
2020	41.10	80.53	92.60	102.93	142.04
2021	26.42	79.20	91.46	101.86	156.95

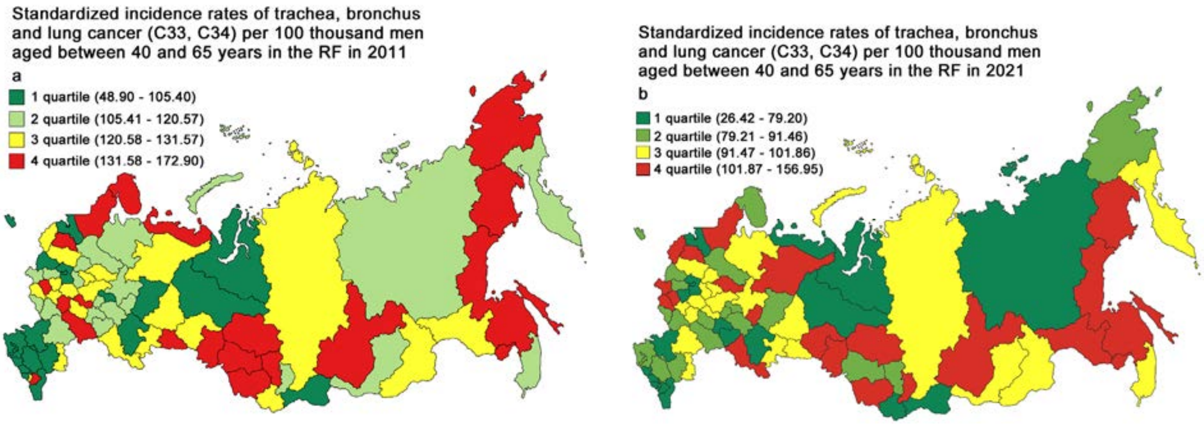

Figure 3. Data maps showing quartile distribution of standardized incidence rates of trachea, bronchus and lung cancer (C33, C34) per 100 thousand men aged between 40 and 65 years in the RF: a) in 2011; b) in 2021

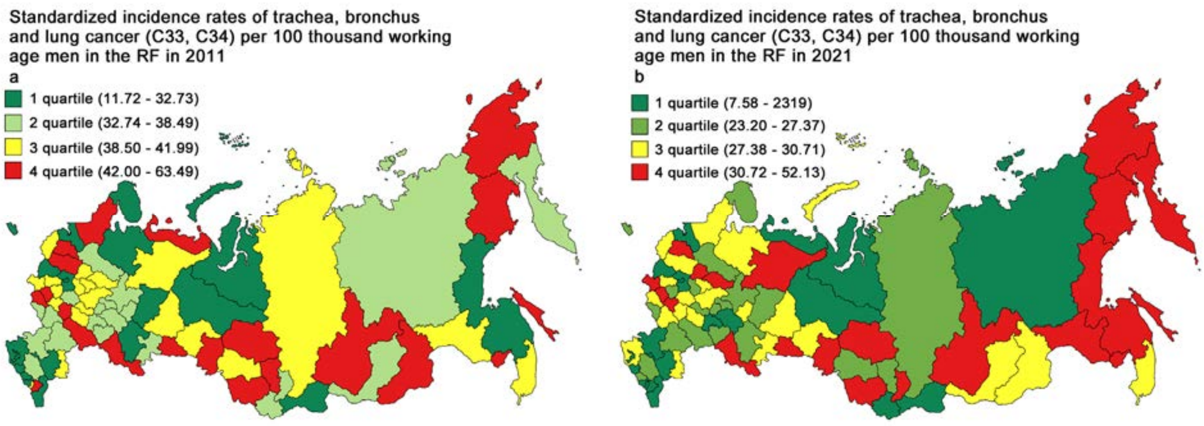

Figure 4. Data maps showing quartile distribution of standardized incidence rates of trachea, bronchus and lung cancer (C33, C34) per 100 thousand working age men in the RF: a) in 2011; b) in 2021

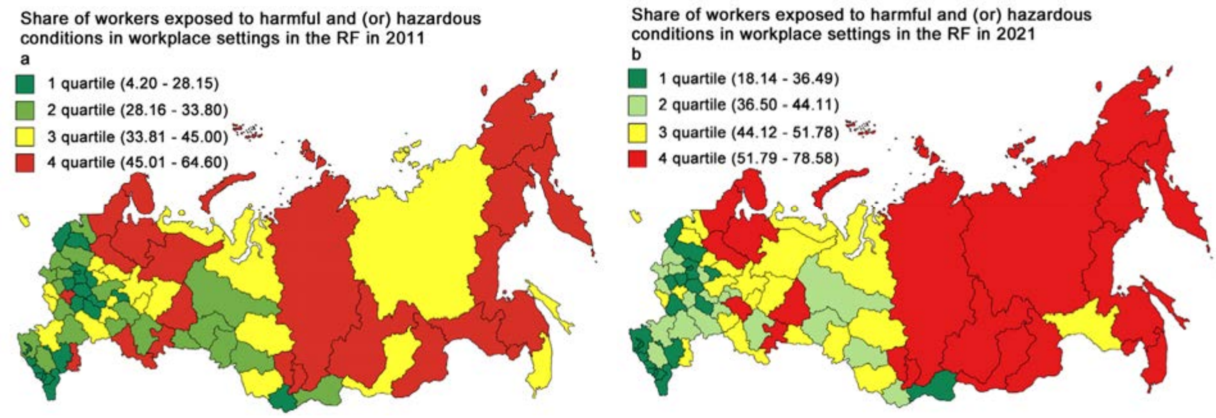

Figure 5. Data maps showing quartile distribution of shares of workers exposed to harmful and (or) hazardous conditions in workplace settings in the RF: a) in 2011; b) in 2021

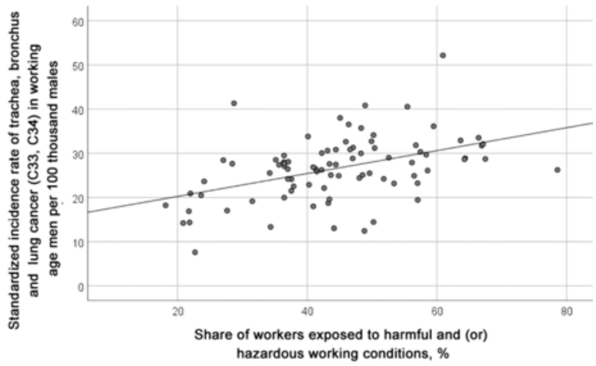

Figure 6. Correlation analysis results

The next stage in our study involved conducting a regression analysis. After relevant factors were selected by excluding statistically insignificant ones, we created a predictive regression model:

$$Y_{\text{C33, C34 incidence}} = 8.058 + 0.185X_{\text{harmful working conditions}} + 0.282X_{\text{smoking}},$$

where $Y_{\text{C33,C34 incidence}}$ is the standardized incidence rate of trachea, bronchus and lung cancer (C33, C34) in working age men in the RF in 2021, per 100 thousand people;

$X_{\text{harmful working conditions}}$ is the share of male workers exposed to harmful and (or) hazardous working conditions, %;

X_{smoking} is the share of smokers among men older than 15 years, %.

The resulting relationship was considered a statistically significant moderate correlation according to the Chaddock scale ($r_{xy} = 0.510$; $p < 0.001$). In accordance with the adjusted determination coefficient R^2 in the created model, 24.2 % of the dispersion of the standardized incidence rate for trachea, bronchus and lung cancer (C33, C34) in working age men was determined by the analyzed factors in the RF in 2021.

According to the values of the regression coefficient, an increase by 1 in the share of male workers exposed to harmful and (or) hazardous working conditions corresponded to an increase by 0.185 in the standardized incidence rate of trachea, bronchus and lung cancer (C33, C34) ($p < 0.001$). An increase by 1 in the share of smokers led to an increase by 0.282 in the analyzed incidence rate ($p < 0.001$).

Conclusion. Malignant neoplasms of trachea, bronchus and lung are a significant social issue. We analyzed standardized incidence rates for trachea, bronchus and lung cancer (C33, C34) in men in the RF in 2011–2021; as a result, a downward trend in it was established. However, it is worth noting that these rates still remain high, especially among men aged between 40 and 65 years.

The results obtained by the conducted correlation analysis indicate a potential correlation between incidence of MNs of the said localization and the share of workers exposed to harmful and (or) hazardous conditions in their workplace settings. This requires more in-depth consideration and analysis in subsequent studies.

Low numbers of established occupational MNs in the RF are due to underestimation of contributions made by harmful and (or) hazardous working conditions into MN development. In our opinion, oncologists need to study occupational routes of their patients carefully when they diagnose MNs in them. To protect workers' health, employers, in their turn, should focus on primary prevention of occupational MNs, for example, within corporate practices of enterprises.

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Competing interests. The authors declare no competing interests.

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