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INHALED NON-CARCINOGENIC RISKS BASED ON EVOLUTIONARY MODELS FROM DISEASES OF THE DIGESTIVE SYSTEM OF THE POPULATION OF KRASNOYARSK

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Abstract

The assessment methodology for epidemiological non-carcinogenic risks makes it possible to evaluate the potential consequences for human health of different variants of previous and predicted exposures to pollutants. The article considers the influence of pollution in the atmospheric air of Krasnoyarsk on the formation of mortality risks from diseases of the digestive system.

Keywords: non-carcinogenic risk, evolutionary models, atmospheric air

I. Introduction

Industrial enterprises are one of the problems of atmospheric air pollution in the city of Krasnoyarsk. They are involved in the formation of high concentrations of chemicals through the emission of specific hydrocarbons into the atmospheric air, from which carcinogenic and neurotoxic substances are synthesized. This leads to increased risks of disease and mortality from changes in the state of the nervous, endocrine, immune, genitourinary, digestive, cardiovascular, and respiratory systems. The objective of the study was to assess the risks of diseases of the digestive system from inhalation effects associated with the presence of sulfur dioxide in the atmospheric air of Krasnoyarsk in the period from 2013 to 2019, received at the posts of the state monitoring network.

The essence of the problem of the methodology of risk analysis is to assess the potential consequences for human health of different variants of previous, existing, or possible future exposures to harmful factors. It also consists of comparative characteristics of various factors, sources of their education, and the medical, social, and economic efficiency of various management decisions.

II. Methods

To assess inhalation risks, it is necessary to build a paired mathematical model reflecting the effect of exposure to chemicals on the violation of the digestive system. In solving this problem, were used data on monthly concentrations of sulfur dioxide in the atmosphere of the city of Krasnoyarsk, obtained at the posts of the Central Siberian Department for Hydrometeorology and Environmental Monitoring [1]. Sulfur dioxide is one of the main components of emissions from industrial enterprises whose activities are associated with the burning of coal, fuel oil, and sulfur-containing petroleum products. The respiratory organs are most sensitive to the negative effects of sulfur dioxide, especially in people with chronic diseases of the respiratory system and allergic diseases. There is evidence that the inhalation effect of the substance has an impact on the digestive organs.

Assessment of non-carcinogenic risk based on evolutionary models for the inhaled effects of pollutants allows us to assess the accumulative impact on the health of the population. When constructing the model, the processes of accumulation of functional disorders in the body due to natural causes are taken into consideration. The prediction of the risk of health disorders in the model is made through the calculated risk value at the current time. At the initial time, the risk value is taken to be equal to 0.01. Based on paired 'exposure-effect' models, which are elements of the evolutionary model, it is possible to assess the temporal dynamics of the risk of organ and system disorders [2].

Epidemiological models were used to assess the accumulation of risks, as recommended by MP 2.1.10.0062-12.

The research also used the primary database of deaths and life expectancy of the population of the city of Krasnoyarsk from 2013 to 2019, including data on deaths from diseases of the digestive system.

III. Results

As a result of the research, characteristic features are identified and described, which include the sequential implementation of the following steps:

- collecting information on the mortality of the population of the city of Krasnoyarsk from diseases of the digestive system in the period from 2013 to 2019 and forming a data table of agreed values 'exposure marker – response marker' (Table 1);
- calculation of the probability of deviation of the response marker from the norm for each observation in the data table;
- assessment of the parameters of a mathematical model reflecting the dependence of the probability of deviation of the response marker from the norm of the exposure marker.

Table 1: *Data for constructing paired models*

Case number	Exposure value (x)	Response value (y)
1	2013	47000
2	2014	67300
3	2015	63300
4	2016	72900
5	2017	61200
6	2018	60000
7	2019	61300

For a more complete description of the issue under consideration, a result was obtained that leads to the following conclusion: the mortality rate of the population of the city of Krasnoyarsk from diseases of the digestive system in 2016 was the highest compared to 2013, as shown in Fig.1.

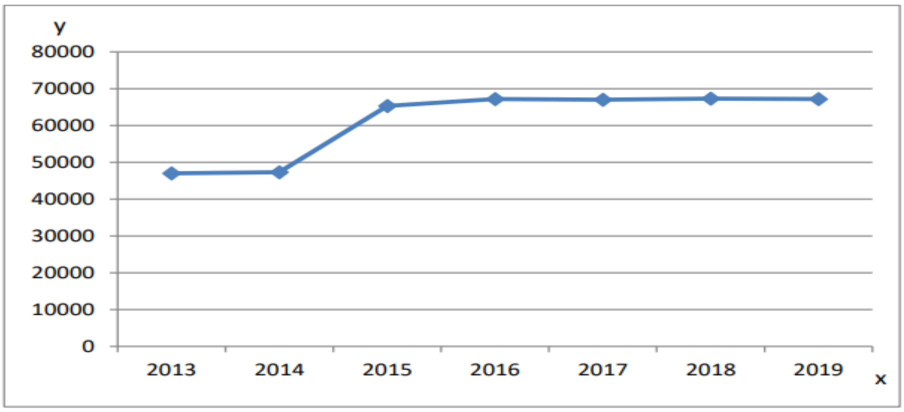

Fig. 1: *Mortality of the population of the city of Krasnoyarsk from diseases of the digestive system*

The calculation of the probability of deviation of the response marker from the norm for each observation in the data table is carried out using the 'sliding window' technology.

To do this, for each monitoring in the data table (each value of the exposure marker xi) an estimate of the probability of deviation of the response marker from the norm (pi) calculated for the range ('sliding window') is put in accordance [4]:

$$x_i - \delta < x \le x_i + \delta \quad (1)$$

Here δ is the width of the 'sliding window', which is determined from the ratio:

$$2\delta = \frac{10x_{max} - x_{min}}{N} \quad (2)$$

N is the total number of studies for the whole population.

The probability of deviation of the response marker from the norm is estimated according to the classical probability formula:

$$p_i = \frac{m_i}{n_i} \quad (3)$$

m_i is the number of studies deviating from the norm for the range xi – δ < x ≤ xi + δ;

n_i is the total number of studies for the range xi – δ < x ≤ xi + δ.

As a result, an estimate was received of the probability of deviation of the response marker from the norm using a 'sliding window' (Fig.2.).

When modeling the 'exposure–respons' dependencies, when assessing non-carcinogenic risk, the principle of threshold action is laid, according to which negative effects or responses from the health side are manifested, starting from the reference level. The probability of negative effects is determined using regional models that are suitable for a specific complex of chemical factors [4].

Paired models reflecting the 'exposure–response' relationship allow us to calculate the probability of developing specific responses (diseases and death) from exposure to a chemical substance.

The estimation of parameters of the paired model reflecting the dependence 'exposure – probability of response' is carried out by the method of constructing a logistic regression model [4]:

$$p = \frac{1}{1+e^{-(b_0+b_{1x})}} \quad (4)$$

p is the probability of deviation of the response from the norm;

x is the exposure level;

b_0, b_{1x} – parameters of the mathematical model.

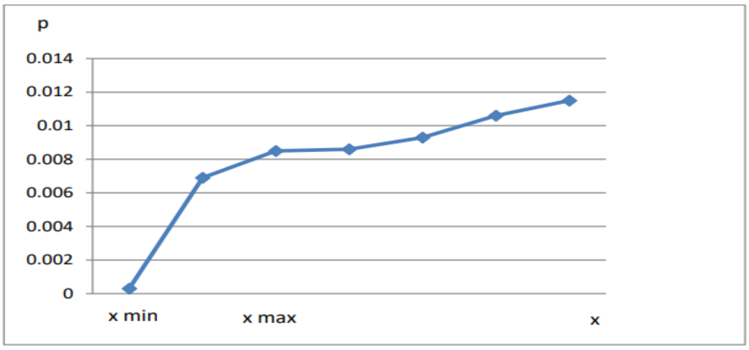

Fig. 2: *Assessment of the probability of deviation of the marker from the norm*

To construct the model, the values of the data exposure markers are used (Table 1) and their respective probability values.

Based on the results received, the exposure of the response probability was identified in order to justify the examination of the obtained dependencies to assess their biological relevance.

When modeling the risk of non-carcinogenic effects from chemical factors using evolutionary models of risk accumulation, the concept of an increase in the risk of violations of the body system caused by the action of a chemical substance over the time determined by the objectives of the study is used [4]:

$$\Delta R = g\ \langle p(x) - p(x_0) \rangle \quad (5)$$

Where, *R* is an increase in the risk of violations of the critical system of the body due to the action of chemical substance for the time determined by the objectives of the study;
g is a coefficient that characterizes the severity of violations of the critical system in relation to performing the functions of the body. The g coefficient is estimated based on the ratio of mortality and morbidity due to the same cause of dysfunction of an individual organ/system; x0 is the reference level for the exposure marker;
< > – Macaulay brackets, which take the values x = 0 for x < 0 and x = x for x ≥ 0.

The x_0 calculation algorithm is based on the construction of regression models reflecting the influence of the exposure level on the 'odds ratio' (OR) indicator, which characterizes the strength of the relationship between the exposure level values and the response. The requirement of OR ≥ 1 [4] is accepted as a criterion for the presence of a connection.

Based on the above mentioned ratios, a calculation is conducted for each observation as an indicator of the odds ratio, which is carried out by conditionally dividing the sample into two parts: below and above the current exposure marker level ([x_{min}, xi] and [x_i, x_{max}] (Fig.3). Accordingly, here xi is the current level of the exposure marker. For both ranges, a value is calculated that characterizes the probability of deviation of the response marker from the norm pi- and i+, respectively, as the ratio of the number of observations that differ from the norm to the total number of observations.
The estimation of the parameters of the dependence of the odds ratio indicator on the exposure value is carried out by constructing a regression model in the form of an exponential function [4]:

$$OR = e^{a_0 + e^{a_1 x}} \quad (6)$$

a0, a1 are the model parameters determined by the regression analysis method.
The calculation of the reference level of the exposure factor (x0) in relation to the type of response is carried out based on the condition OR = 1, according to the formula:

$$x_0 = \frac{a_0}{a_1} \quad (7)$$

The suggested method makes it possible to calculate the risk at any given time by predicting the accumulation of risk effects, taking into account the duration of exposure and age. On this basis, it is possible to predict life expectancy and its reduction under the influence of risk factors.

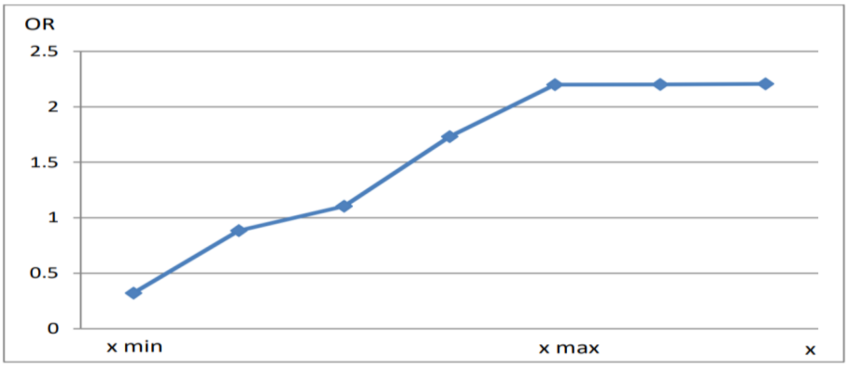

Fig. 3: *Increase in the risk of violations of the critical system of the body*

To describe the dependencies of the occurrence of adverse effects on human health due to malnutrition, a threshold logistic relationship between the increase in the risk of disease and the value of the indicator was used [5]:

$$\Delta R_{t\,ij} = b_{ij}\left[\frac{1}{1+e^{-b_{ij_0}x_i^j}} - \frac{1}{1+e^{-b_{ij_0}}}\right] \tag{8}$$

Where x_t^j is the normalized value of the j-th indicator in the time period t; b_{ij}, b_0^{ij}, b_1^{ij} are the parameters of the threshold logistic dependence.

The integral risk of developing health disorders for all systems associated with exposure to adverse factors is calculated by the formula [6]:

$$R_{t\,int} = 1 - \prod_i^n = 1\,(1 - R_t^i) \tag{9}$$

Based on the data obtained (Table 2) paired models have been compiled, where the following evaluation scale of the given risk index is used:

– unacceptable is the level of risk established by the administration of the enterprise or regulatory authorities as the maximum allowed, which does not lead to deterioration of the economic activity of the enterprise or the quality of life of the population under existing socio-economic conditions (risk level >10^{-6});

– acceptable is the level of risk that society as a whole is ready to tolerate in order to obtain certain benefits or benefits as a result of its activities (10^{-6} < risk level <10^{-8});

– negligible is the level of risk established by administrative or regulatory authorities as the maximum, above which it is necessary to take measures to eliminate it;

Since the natural risk boundaries for a person are the range between 10^{-2} (the probability of morbidity per capita) and 10^{-6} (the lower level of risk from a natural disaster or other serious danger), technogenic risk is considered acceptable if it is less than 10^{-6} [7].

Table 2: *Paired 'Exposure-effect models'*

Target organs	Pollutants															
	Carbon monoxide				Sulfur dioxide				Nitrogen dioxide				Suspended solids			
	R_t^i	α_i	ΔR_t^i	ΔR_t^j	R_t^i	α_i	ΔR_t^i	ΔR_t^j	R_t^i	α_i	ΔR_t^i	ΔR_t^j	R_t^i	α_i	ΔR_t^i	ΔR_t^j
RS	10^{-2}	10^{-4}	10^{-4}	10^{-4}	10^{-2}	10^{-4}	10^{-6}	10^{-5}	-	-	-	-	10^{-2}	10^{-4}	10^{-6}	10^{-5}
CVC	10^{-2}	10^{-2}	10^{-2}	10^{-3}	-	-	-	-	-	-	-	-	10^{-2}	10^{-2}	10^{-6}	10^{-6}
CS	-	-	-	-	10^{-2}	10^{-3}	10^{-2}	10^{-2}	-	-	-	-	-	-	-	-
DS	-	-	-	-	10^{-3}	10^{-4}	10^{-6}	10^{-5}	-	-	-	-	-	-	-	-

Notes: RS is respiratory system; CVC is cardiovascular system; CS is circulatory system; DS is the digestive system.

Coefficients that take into consideration the evolution of risk due to natural causes (ai) are determined based on the background indicators of morbidity and mortality for classes of diseases reflecting functional disorders of critical organs and systems. Health indicators typical for the most prosperous regions from the point of view of environmental pollution are selected as background levels. The empirical values of the coefficients take into consideration both the severity of the clinical course and outcomes of diseases, and the degree of disruption of the functional systems of the body.

The values of the coefficients of risk evolution due to natural causes for critical body systems are given in (Table 3).

Table 3: *Values of risk evolution coefficients due to natural causes*

Critical system	risk evolution coefficient
Cardiovascular system	0,05
Respiratory system	0,0515
Circulatory system	0,051
Digestive system	0,035

Based on the obtained values of the coefficients of risk evolution due to natural causes, it is estimated:

– the value is less than 0.05, which can be assessed as a negligible risk (acceptable, permissible), not different from ordinary, everyday risks;

– the value is in the range of more than 0.05–0.35, which can be assessed as a moderate risk. Measures for the organization of constant monitoring of the structure of nutrition are recommended;

– the value is in the range of more than 0.35–0.6, which is assessed as a high risk. Measures to reduce the impact of the negative factor are recommended;

– the value exceeds the level of 0.6, which is assessed as a very high risk. Measures are recommended to immediately stop the abnormal consumption of nutrients and trace elements.

The evolutionary model allows you to calculate the risk at any given time. The prediction of the risk of health disorders in the model is carried out through the calculated risk value at the current time. At the initial time, the risk value is assumed to be 0.01. Based on the known changes in the exposure of chemicals over time, it is possible to determine a long-rang prediction for the period of the expected duration of the upcoming life.

Initial risk levels can be estimated based on the frequency and severity of morbidity and mortality at the start of the calculation.

As a result of the research, a model of recurrent ratios for individual body systems was obtained, reflecting the influence of individual environmental factors on the evolution of the risk of functional disorders of critical systems.

The risk of developing disorders of the digestive system of varying severity from exposure to sulfur dioxide at time t:

$$R_{t+1}^{\text{ПС}} = R_t^{\text{ПС}} + (0{,}035 \cdot R_t^{\text{ПС}} + 0{,}72 \cdot \langle e^{-0{,}000106} - e^{-0{,}000152 \cdot x} \rangle \cdot C \quad (10)$$

Where $Rt+1^{\text{ПС}}$ is the risk of violations of the body system at time t+1;

$Rt^{\text{ПС}}$ is the risk of violations of the body system at time t;

C is the time empirical coefficient taken in accordance with Table 3.

IV. Discussion

In the structure of morbidity in Krasnoyarsk, the leading place is occupied by respiratory diseases – 376.1 (territory - 334.7 cases per thousand population, SFD - 392.5 per 1000 population, in the Russian Federation – 403.2), in the second place diseases of the circulatory system – 326.5, in the third place diseases of the digestive system – 72.9 per thousand population.

Based on the calculations carried out, it can be concluded that the highest rate of the increase is noted in the class of diseases of the digestive system from sulfur dioxide (93.8%), mostly due to diseases characterized by oncological diseases (the incidence rate increased by 2 times). The incidence of oncological diseases is 35.4 per thousand of the population. This trend can be traced across most territories. In 2016, compared with 2013, the diseases of the region's population with gastric cancer increased. During 2018-2019, the dynamics of the increase in the incidence of malignant neoplasms among the population is observed (the growth rate was 11.1%).

Methodological approaches to assessing the risk of exposure to heterogeneous environmental factors allow us to evaluate its categories in accordance with the proposed scale and simulate changes in the risk of dysfunction of organs and systems of the human body during life. Further calculations can serve as a basis for the organization of in-depth examinations of the influence of environmental factors on the health of medical and preventive measures.

The calculations performed allow us to conclude that modeling the evolution of risk is a suitable method for assessing the impact of heterogeneous environmental factors on the health of the population, which makes it possible to quantify the indicators of additional and population risk, including a reduction in projected life expectancy.

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