RT&A, Special Issue № 4 (70)
Volume 17, November 2022

ASSESSMENT OF INHALATION NON-CARCINOGENIC RISKS BASED ON EVOLUTIONARY MODELS ON THE EXAMPLE OF KRASNOYARSK

Liubov Kalimanova[1], Olga Taseiko[1,2]

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[1]Reshetnev Siberian State University of Science and Technology, Russia
[2]Federal Research Centre for Information and Computational Technologies, Krasnoyarsk, Russia
kalimanova.l@mail.ru
taseiko@gmail.com

Abstract

The essence of the problem of the methodology for assessing non-carcinogenic risk is to assess the potential consequences for human health in different variants of previous and existing exposures in the future harmful factors. The article considers how atmospheric air pollution in Krasnoyarsk city affects human health.

Keywords: non-carcinogenic risk, chemicals, evolutionary models, atmosphere

I. Introduction

The city of Krasnoyarsk is a modern large industrial city, which is a complex multicomponent urbanized ecological system. The consequences of industrialization have led to the fact that the population of the city has been living in a crisis environmental situation for decades, that cannot but affect the health of residents. The main sources of air pollution by suspended substances are metallurgy, heat power engineering, building materials, municipal and industrial boilers, as well as secondary pollution. Sulfur dioxide pollution — companies of non-ferrous metallurgy, heat power engineering. Carbon monoxide pollution — municipal and industrial boilers, metallurgy, vehicles and forest fires. Nitrogen dioxide pollution — companies of heat power engineering, metallurgy, motor transport.

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

The aim of the study is to build a paired mathematical model that reflects the effect of exposure to the chemical substance sulfur dioxide on the risk of circulation system disorders.

II. Methods

The construction of a paired mathematical model that reflects the effect of chemical exposure on the probability of a response includes the sequential implementation of the following steps.

- Formation of a data table of agreed values "exposure marker — response marker"

- Calculate the probability of the response marker deviation from the norm for each observation in the data table.
- Evaluation 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

The data table is formed according to the data of paired models construction (Table 1).

Table 1: *Pair Model Building Data*

Observation number	Exposure value (x)	Answer value (y)
1	2013	17399
2	2014	17035
3	2015	36222
4	2016	35845
5	2017	35098
6	2018	35290
7	2019	35300

Evolutionary equations are constructed in the form of recurrence relations that allow organizing an iterative calculation procedure in time steps. These models make it possible to calculate the non-carcinogenic risk at any given point in time by predicting the accumulation of the risk of effects, taking into account the duration of exposure and age. This makes it possible to predict life expectancy (projected life expectancy) and reduce it under the influence of risk factors. The risk evolution model is a system of recurrent relationships for individual body systems, which include terms that reflect the influence of individual environmental factors on evolution risk of functional disorders of critical systems [1].

To assess the accumulation of risks, existing and developed epidemiological models were used in accordance with MR 2.1.10.0062-12 "Quantitative assessment of non-carcinogenic risk when exposed to chemicals based on the construction of evolutionary models".

When constructing an evolutionary model, the processes of accumulation of functional disorders in the body due to natural causes are taken into account. 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 point in time, the risk value is assumed to be 0.01. Based on paired exposition-effect models, which are elements of the evolutionary model, it is possible to assess the temporal dynamics of the risk of disorders of organs and systems.

To solve this problem, data on monthly concentrations of pollutants in the city of Krasnoyarsk, provided by the Regional State Budgetary Institution "Implementation Center Measures for Nature Management and Environmental Protection of Krasnoyarsk Territory".

The study 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 circulation system [2].

III. Results

For a more complete description of the issue under consideration, a result was obtained that leads to the following conclusion that the mortality rate of the population of the city of

Krasnoyarsk from diseases of the circulation system during the from 2013 to 2014 is inferior to the period from 2015 to 2019, as shown in Figure 1. This is confirmed by the fact that the severity of the disease is characterized by coronary heart disease, cerebrovascular diseases, myocardial infarction and oncological diseases [3].

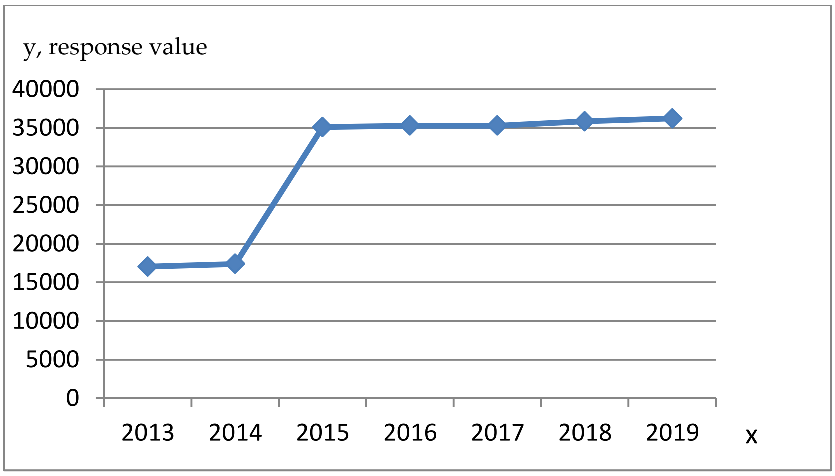

Figure 1: *Mortality of the population of the city of Krasnoyarsk from diseases of the circulatory system*

The probability of deviation of the response marker from the norm for each observation in the data table is calculated using the "sliding window" technology. To do this, each observation in the data table (each value of the exposure marker (x i) is assigned an estimate of the probability of deviation of the response marker from the norm (p i) calculated for the range ("sliding window") [4]:

$$x_i - \delta < x \le x_i + \delta \tag{1}$$

Here δ is the width of the "sliding window", which is determined from the relationship:

$$2\delta = \frac{10x_{max} - x_{min}}{N} \tag{2}$$

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

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

$$p_i = \frac{m_i}{n_i} \tag{3}$$

m_i is the number of studies that deviate from the norm for the range $x_i - \delta < x \le x_i + \delta$; n_i is the total number of studies for range $x_i - \delta < x \le x_i + \delta$.

As a result, an estimate of the probability of the response marker deviation from the norm was obtained using a "sliding window" (Figure 2.).

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

Paired models reflecting the "exposure–response" relationship make it possible to assess the probability of developing specific reactions (diseases and death) from exposure to a chemical.

The parameters of the pair model reflecting the relationship "exposure — response probability" are estimated by constructing a logistic regression model [4]:

$$p = \frac{1}{1+e^{-(b_0+b_1x)}} \tag{4}$$

where, p is the probability of deviation from the norm;
x — exposure level;
b_0 , b_1 — mathematical model parameters.

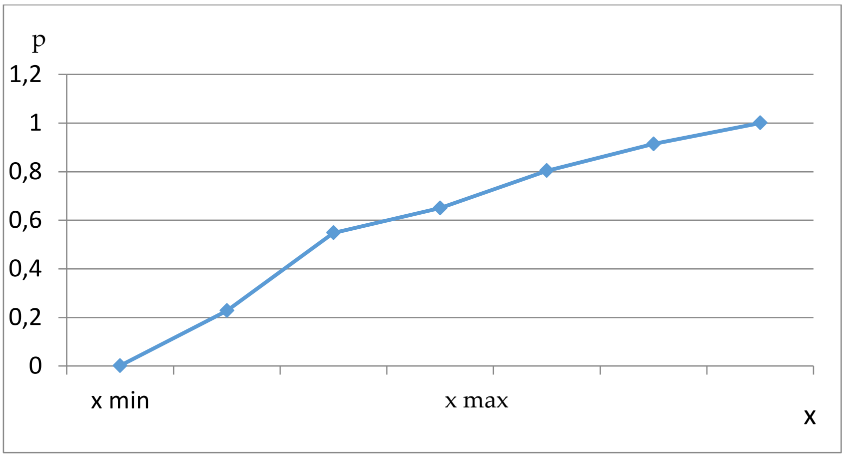

Figure 2: *Estimating the probability of a marker deviation from the norm*

To build the model, the values of data exposure markers (Table 1) and the corresponding probability values are used.

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

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 disorders of the body's system is used, due to the action of a chemical substance during the time determined by the research objectives [4]:

$$\Delta R = g \langle p(x) - p(x_0) \rangle \tag{5}$$

where,
ΔR is an increase in the risk of disorders of the critical system of the body due to the action of the chemical substance during the time determined by the research objectives
g is a coefficient characterizing the severity of violations of the critical system in relation to the performance of body functions. The g coefficient is estimated based on the ratio of mortality and morbidity due to the same cause of dysfunction of an individual org/system; x 0 is the reference level for the marker expositions;
$< x >$, Kelly brackets that take values$<x> = 0$ at $x < 0$ and $<x> = x$ at $x \geq 0$.

The algorithm for calculating x_0 is based on the construction of regression models that reflect the influence of the exposure level on the "odds ratio" (OR) indicator, which characterizes the strength of the relationship between the values of the exposure level and the response. The OR ≥ 1 [4] condition is taken as a criterion for the presence of a connection.

Based on the above algorithms for calculating calculations, the study showed that for each observation, the odds ratio is calculated, which is carried out by conditional division of the sample into two parts: below and above the current level of the exposure marker ([xmin, xi] and [xi, xmax] (figure 3). Accordingly, here xi is the current level of the exposure marker. For both intervals, 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.

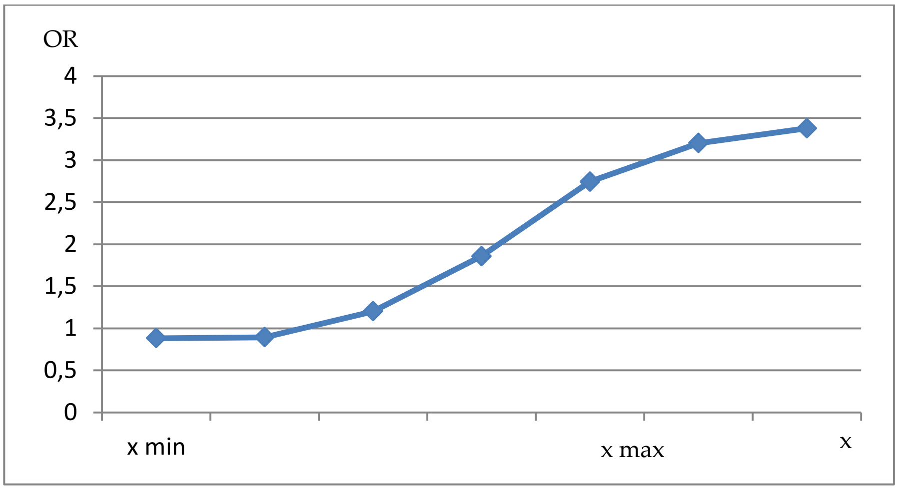

Figure 3: *Increase in the risk of violations of the critical system of the body*

The parameters of the dependence of the odds ratio on the exposure value are estimated by constructing a regression model in the form of an exponential function [4]:

$$OR = e^{a_0 + e^{a_1 x}} \tag{6}$$

where, a_0, a_1 are model parameters determined by regression analysis.

The calculation of the reference level of the exposure factor (x_0) in relation to the type of response is carried out based on the condition $OR = 1$, using the formula:

$$x_0 = \frac{a_0}{a_1} \tag{7}$$

The proposed approach makes it possible to calculate the risk at any given point in time by predicting the accumulation of risk of effects, taking into account the duration of exposure and age. On this basis, it is possible to predict life expectancy and reduce it under the influence of risk factors. To describe the dependencies of the occurrence of adverse effects on human health due to malnutrition, the threshold logistic relationship between the increase in the risk of disease was used and the value of the indicator [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]:

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

RT&A, Special Issue № 4 (70)
Volume 17, November 2022

Based on the data obtained (Table 2), paired models have been compiled, which use the following assessment scale of the given risk index:

— the value $\widetilde{R_t}$ is less than 0.05, which can be assessed as a risk that is negligible (acceptable, allowable), not different from the usual, daily risks;

— the value $\widetilde{R_t}$ is in the range of more than 0.05-0.35, which can be assessed as a moderate risk. Measures are recommended for the organization of continuous monitoring of the structure of nutrition;

— the value $\widetilde{R_t}$ 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 $\widetilde{R_t}$ exceeds 0.6, which is assessed as a very high risk. Measures are recommended to immediately stop non-normative consumption of nutrients and trace elements.

Table 2: *Paired Exposure-Effect Models*

Target organs	Pollutants															
	Carbon monoxide				Sulphur 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
DS	10^{-2}	10^{-4}	10^{-4}	10^{-4}	10^{-2}	10^{-4}	10^{-6}	10^{-5}	-	-	-	-	10^{-2}	10^{-4}	10^{-6}	10^{-5}
CCC	10^{-2}	10^{-2}	10^{-2}	10^{-3}	-	-	-	-	-	-	-	-	10^{-2}	10^{-2}	10^{-6}	10^{-6}
SC	-	-	-	-	10^{-2}	10^{-3}	10^{-2}	10^{-2}	-	-	-	-	-	-	-	-

Notes: *DS-respiratory system; CCC-cardiovascular system, SC-circulatory system.*

Coefficients that take into account the evolution of risk due to natural causes (α_i) are determined based on background morbidity and mortality rates for classes of diseases that reflect functional disorders of critical organs and systems. Health indicators characteristic of the most prosperous regions in terms of pollution of environmental objects are chosen as background levels.

The empirical values of the coefficients take into account both the severity of the clinical course and outcomes of diseases, and the degree of disruption of the activity of the functional systems of the body.

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

The evolutionary model allows you to calculate risk at any given point in time. The prediction of the risk of health disorder in the model is carried out through the calculated risk value at the current time. At the initial point in time, the risk value is assumed to be 0.01. Based on the known change in chemical exposure over time, it is possible to determine a long-term outlook for the period of life expectancy.

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

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

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

$$R_{t+1}^{CK} = R_t^{CK} + (0{,}051 \cdot R_t^{CK} + 0{,}72 \cdot \langle e^{-0{,}000189} - e^{-0{,}000166 \cdot x} \rangle \cdot C \quad (10)$$

where, R_{t+1}^{CK} is the risk of disorders of the body system at time t+1;
R_t^{CK} is the risk of disorders of the body's system at time t;
C is the time empirical coefficient taken in accordance with Table 3.

IV. Discussion

In the structure of morbidity the leading place in Krasnoyarsk is taken by respiratory diseases - 376.1 (the region - 334.7 cases per thousand population, the Siberian Federal District - 392.5 per 1000 population, in the Russian Federation - 403.2), in the second disease of the circulation system - 326.5. The incidence of cancer is 35.4 per thousand of the population. This trend can be seen in most territories. Based on the calculations carried out, it can be concluded that the risk of developing the respiratory system exceeds the risk of the circulation system from sulfur dioxide.It is appropriate to pay attention that in 2017, respiratory diseases are in the first place in terms of prevalence from sulfur dioxide. In 2017, in the Krasnoyarsk Territory, compared to 2016, the incidence of respiratory diseases in cases per 100 employees increased by 4.1%. In the period 2018-2019, as in previous years, acute respiratory infections of the upper respiratory tract accounted for the main share of cases in the structure of respiratory diseases — 70.1... 73.7%; bronchitis and emphysema — 4.9... 6.0%; acute pharyngitis and tonsillitis — 4.0... 5.9%; pneumonia — 2.5... 3.7% and others.

The study made it possible to determine that, in general, the effect on the respiratory system of the population Krasnoyarsk from pollution is more significant than the effect on the circulation system. This is confirmed by the fact that the increase in mortality from respiratory diseases is especially clearly associated with an increase in suspended particles in the atmospheric air with a diameter of less than 10 microns, which can cause many adverse health effects depending on their chemical composition and dispersion [7]. Further calculations can serve as the basis for organizing in-depth studies of the influence of environmental factors on the health of medical and preventive measures. Based on the results of studies, it is possible to identify an additional risk of morbidity and mortality due to diseases of almost all classes and ages.

The research materials were published with the support of the Krasnoyarsk Regional State Autonomous Institution "Krasnoyarsk Regional Fund for Support of Scientific and Scientific and Technical Activities" (application code: 2022052308698).

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