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Research article

PREDICTING GROWTH POTENTIAL IN LIFE EXPECTANCY AT BIRTH OF THE POPULATION IN THE RUSSIAN FEDERATION BASED ON SCENARIO CHANGES IN SOCIO-HYGIENIC DETERMINANTS USING AN ARTIFICIAL NEURAL NETWORK

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The article presents the results produced by predicting growth potential in life expectancy at birth (LEB) of the RF population. The predictions are based on scenario changes in social and hygienic determinants (SHD) identified by using an artificial neural network (ANN). This research is vital given the existing social strategies aimed at improving the medical and demographic situation in the Russian Federation. These strategies stipulate achieving targets set within the major national and federal projects. We identified an optimal ANN structure based on a four-layer perceptron with two inner layers containing eight and three neurons accordingly. This structure is able to produce results at the highest determination coefficient (R^2= 0.78). Differences between actual LEB levels and predicted ones obtained by using the suggested model did not exceed 1.1 % (or 0.8 years). We established that average LEB in the RF would reach 75.06 years (by 2024) provided that the demographic situation in the country recovers in the nearest future, LEB level reaches its values detected in 2018–2019, and SHD values grow to their preset levels according to the target scenario. Therefore, the detected growth potential amounts to 3.0 years (1095 days) against 2018. "Lifestyle-related determinants" produce the greatest effects on the growth potential in LEB by 2024 (461 days). We also identified effects produced by such SHD groups as "Sanitary-epidemiological welfare on a given territory" (212 days), "Social and demographic indicators" (196 days), "Economic indicators" (131 days), "Indicators related to public healthcare" (70 days). An indicator that shows "A share of population doing physical exercises or sports" is the most significant determinant producing the greatest effects on potential changes in LEB. If it grows up to 55.0 %, a potential growth in LEB amounts to 243.5 days. If we do not consider COVID-related processes and rely only on the trends that are being observed now when predicting changes in the demographic situation by 2030, we can expect a possible additional growth in LEB that equals 286 days. The developed algorithm for determining growth potential in population LEB can be used as an instrument for determining and ranking priority health risk factors.

Keywords: *life expectancy at birth, socio-hygienic determinants, artificial neural networks, factor analysis, prediction of a medical and demographic situation, growth potential, national projects, lifestyle, sanitary-epidemiological welfare.*

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The basic provisions of "The unified action plan on achieving national goals of the Russian Federation development for the period up to 2024"[1] highlight that these goals can be achieved by implementing "inter-project" activities. Their achievement requires a complex (systemic) approach to implementing all the actions mentioned in the document. An increase in life expectancy at birth (hereinafter LEB) is "the most significant indicator showing people's quality of life". It is declared a most significant condition for providing natural population growth and is considered especially vital in the post-COVID economy in the country that is also facing the most severe economic sanctions. A priority (key) trend in improving the medical and demographic situation in the country involves "… a substantial reduction in mortality rates in several age groups, including working population and people older than employable age …". This reduction can be achieved by developing preventive activities as per basic causes of death for the RF population (circulatory diseases, malignant neoplasms, and external causes). Simultaneously, experts admit "…this issue cannot be resolved solely with medical means …" and, moreover, it requires "…providing sanitary-epidemiological wellbeing of the population …". Given that, it seems only reasonable "… to support activities aimed at increasing a share of citizens who pursue healthy lifestyle …". Key instruments in implementing this trend include "Healthcare", "Demography" and "Ecology" National Projects as well as several state programs such as "Healthcare development", "Development of sports and physical culture", "Environmental protection" and others. It is obvious that the current project activities accomplished by the state authorities are truly complex (systemic); they all are aimed at improving social strategies and the medical and demographic situation in the country.

It seems relevant to choose LEB as an indicator of a predicted medical and demographic situation when we strive to estimate improvements in basic spheres of people's life activities. LEB is relatively simple to calculate, has a direct correlation with sex- and age-specific mortality due to all causes and is comparable between different countries since it is widely used in multiple studies that focus on estimating people's quality of life [1–4]. Besides, challenges related to increasing LEB are often considered in reports made by many international organizations [5–9].

We can find several approaches to estimating influence exerted by environmental factors on LEB, population mortality taken into account, in scientific literature. They include creating conventional mortality tables [10, 11]; estimates of eliminated reserves [12]; component analysis of mortality [13, 14]; assessment of contribution made by mortality to LEB [15]. In addition, it is quite common to use econometric analysis of influence exerted by a limited number of factors (more often economic ones). The method usually involves building correlation-regression models of relationships between LEB and environmental factors together with determining the hierarchy of the RF regions and their clusterization. The procedure is equally suitable for inter-country estimates [16–20].

Since amounts of heterogeneous analyzed data on relevant indicators that characterize a research object (public health) are only growing, some other methods are considered promising alongside the aforementioned ones. These methods include multidimensional statistical analysis procedures (multiple regressions, factor analysis, neural networks, etc.) and their combinations. Thus, Yu.A. Grigor'ev and O.I. Baran applied a set of statistical procedures for data analysis in their work (principal component method, regression analysis, and factor analysis) bearing in mind lag influ-

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[1] Edinyi plan po dostizheniyu natsional'nykh tselei razvitiya Rossiiskoi Federatsii na period do 2024 goda i na planovyi period do 2030 goda (utv. rasporyazheniem Pravitel'stva RF ot 01.10.2021 № 2765-r (s izm. ot 24.12.2021)) [The unified action plan on achieving national goals of the Russian Federation development for the period up to 2024 and plans for the period up to 2030 (approved by the RF Government Order dated October 01, 2021 No. 2765-r (with alterations made on December 24, 2021))]. *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_398015/ (April 05, 2022) (in Russian).

ences exerted by a factor on population mortality [21].

The Global Burden of Disease is the most remarkable project in this sphere performed by western researchers. This study is accomplished regularly by a consortium that includes researchers from various countries. It concentrates on estimating mortality in dynamics and, above all, aims to determine reasons for negative trends that occur due to effects produced by priority risk factors. The overall data array analyzed so far includes more than 1 billion units of observation. Such a huge volume of statistical data has been analyzed by using innovative technologies of Bayesian statistical modeling and required substantial computational capacities. An analytical instrument called CODEm (the Cause of Death Ensemble model) was applied to solve the task; this ensemble model was created by using several mathematical and statistical procedures with the best predictive validity and biological plausibility of mortality being dependent on analyzed covariates [22].

Some researchers believe that public health should be viewed as a complex adaptive system with multiple dynamic non-linear interactions between its subsystems and determinants of different origin. They also note that interactions between these determinants are contextual during a certain period and they should be analyzed at multiple levels and in large scales. The resulting managerial decisions should only be complex [23, 24].

Yu.P. Lisitsyn, RAS Academician, stated that public (population) health was a complex, developing and dynamic system that required a systemic approach and analysis in any study accomplished in the field[2]. The necessity to apply an interdisciplinary approach to issues of public health (a nation's viability) was also stressed by B.T. Velichkovskiy, RAMS Academician, who stated a need in such an integral science as social human biology [25]. He thought socioeconomic factors creating "a social stress" to be as important as other factors, including hygienic ones. He also pointed out that establishing a relationship between socioeconomic factors and health disorders was among key information and analytical components in the social and hygienic monitoring and believed studies in this field to be vital for hygiene as a science [26, 27].

At present, there are a growing number of studies, biomedical ones included, that are based on using artificial neural networks or ANNs. This method is shown to have greater predictive capacities more often than logistic regression models [28–31]. ANNs are widely used in medicine in multiple spheres including diagnosing, selecting a treatment tactics, patient routing, preparing and accomplishing biomedical research and some others [32–38].

At the same time, we can clearly see that methods for predicting life expectancy at birth that consider multiple and variable impacts exerted on it by environmental factors and lifestyle are not presented sufficiently in domestic and foreign research articles dealing with medical and demographical issues and reasons for them. Verified assessments within "environmental factors – life expectancy at birth", "environmental factors – mortality – life expectancy at birth" systems have not been given much attention in scientific literature either. It is also vital to adjust and supplement well-known risk factors influencing public health and to clarify intensity of their influence.

Therefore, we can state the present research is vital given the current state policy being oriented at improving the medical and demographic situation in the country and aiming to achieve certain levels of relevant indicators (LEB). Another important factor is developing biomedical research with its focus on examining multiple influences exerted by environmental factors on population health that involves using multidimensional statistical procedures, artificial neural networks included.

Our research goal was to make quantitative predictions of influence exerted by a set of social and hygienic determinants on life expec-

[2] Lisitsyn Yu.P. Obshchestvennoe zdorov'e i zdravookhranenie: uchebnik [Public health and healthcare: manual], the 2nd edition. Moscow, GEOTAR-Media, 2010, 512 p. (in Russian).

tancy at birth for the RF population by using a neural network model.

Materials and methods. We analyzed domestic and foreign research works on the subject (influence exerted by environmental factors and lifestyle on public health). As a result, we created a pool of contemporary models that describe cause-effect relationships between multiple environmental factors and public health.

We used relevant scientific data on cause-effect relationships between environmental factors and public health as grounds for creating a list of 148 indicators based on official state statistical data collected in 2010–2018 in all the RF regions. These data were taken from statistical reports and collections issued by Rospotrebnadzor[3], the RF Public Healthcare Ministry[4], and the Federal Statistic Service[5]. We created a data matrix as per groups of the analyzed indicators that included the following: sanitary-epidemiological welfare (53 indicators), lifestyle (30 indicators), economy (14 indicators), public healthcare (9 indicators), a social and demographic situation (34 indicators), weather and climate (8 indicators). These groups were identified conventionally and were applied to estimate effects produced by relevant factor groups with a possibility to make comparisons between them.

The task we set was to predict LEB together with establishing quantitative effects produced by a set of social and hygienic determinants (hereinafter SHD) on LEB and its growth potential. To do that, we created a mathematical model that reflected a system of cause-effect relationships between the analyzed indicators that characterized SHD and LEB. This mathematical model included a sub-model for factor transformation of a system of independent variables into common factors and an artificial neural network (hereinafter ANN).

A factor transformation sub-model was built by using factor analysis and applied to reduce dimensionality of initial data that were fed into an input layer in ANN.

Factor transformation that resulted from examining the system of cause-effect relationships between SHD-characterizing indicators and weather and climate made it possible to switch from the system of interrelated indicators (148 SHD) to pairwise independent common factors (the created model contains 33 such factors).

The factor transformation sub-model is a system of linear algebraic equations that are given as follows in their matrix form (1):

$$Y = A\tilde{X}, \qquad (1)$$

Where $\tilde{X} = \{\tilde{x}_1, \tilde{x}_2, ..., \tilde{x}_I\}^T$ is the column-vector of standardized values determined for independent variables, $I = 148$;

$Y = \{y_1, y_2, ..., y_J\}^T$ is the column-vector of common factors, $J = 33$;

$A = \begin{bmatrix} a_{11} & a_{12} & ... & a_{1J} \\ a_{21} & a_{22} & ... & a_{2J} \\ ... & ... & ... & ... \\ a_{I1} & a_{I2} & ... & a_{IJ} \end{bmatrix}$ is a matrix of factor marks within factor analysis.

The expression (1) is given as follows in its component form (2):

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[3] Ob utverzhdenii statisticheskogo instrumentariya dlya organizatsii Federal'noi sluzhboi po nadzoru v sfere zashchity prav potrebitelei i blagopoluchiya cheloveka federal'nogo statisticheskogo nablyudeniya za sanitarnym sostoyaniem sub"ekta Rossiiskoi Federatsii: Prikaz Rosstata ot 29.12.2017 № 885 (utratil silu s otcheta za 2019 god na osnovanii prikaza Rosstata ot 24 dekabrya 2019 goda № 800) [On approval of statistical tools to organize federal statistical observation of a sanitary situation in an RF region by the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing: The Order by the Rosstat issued on December 29, 2017 No. 885 (became invalid after the 2019 report was issued according to the Order by Rosstat issued on December 24, 2019 No. 800)]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/556189703 (April 07, 2022) (in Russian).

[4] Mediko-demograficheskie pokazateli Rossiiskoi Federatsii v 2018 godu: stat. spravochnik [Medical and Demographic indicators in the Russian Federation in 2018: statistical reference book]. *The RF Public Healthcare Ministry*. Moscow, 2019, 253 p. (in Russian).

[5] Regiony Rossii. Sotsial'no-ekonomicheskie pokazateli. 2018: stat. sb. [Russian regions. Socioeconomic indicators. 2018: statistical data collection]. *Rosstat*. Moscow, 2018, 1162 p. (in Russian).

$$y_j = \sum_{i=1}^{I} a_{ij} \tilde{x}_i \quad (2)$$

The system of independent variables was standardized as per the following relationship (3):

$$\tilde{x}_i = \frac{x_i - \bar{x}_i}{\sigma_i}, \quad (3)$$

where x_i is a value of the *i*-th variable;

$\bar{x}_i$, σ_i are mean and standard deviations of the *i*-th variable as per sampling data.

Our ANN was trained based on using the initial data matrix. When doing it, we determined its optimal structure that was based on a four-layer perceptron with two internal layers containing eight and three neurons accordingly with the determination coefficients being equal to 0.78 (Figure 1).

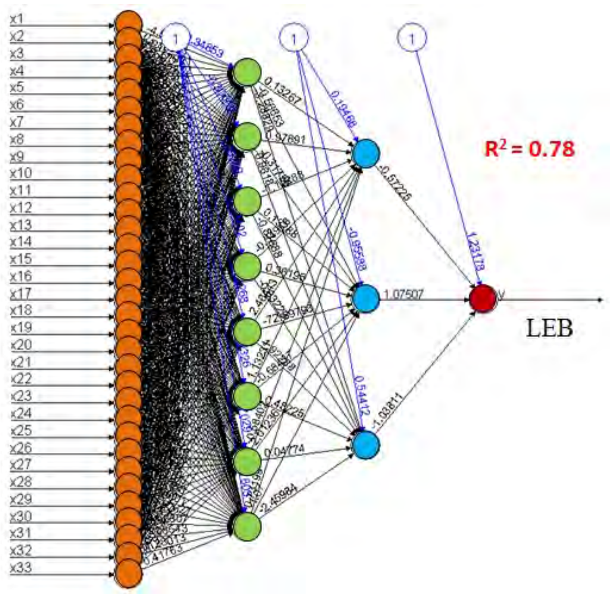

Figure 1. The structure of four-layer perceptron with two internal layers containing eight and three neurons accordingly

Predictive LEB levels were calculated by accomplishing a sequential series of mathematical operations.

Values of common factors that were fed into ANN input layer were standardized as per the formula (4) (after completing factor transformation of values determined for independent variables):

$$\tilde{y}_j = \frac{y_j - y_j^{\min}}{y_j^{\max} - y_j^{\min}}, \quad (4)$$

where $\tilde{y}_j$ is a standardized value of the *j*-the common factor;

$y_j^{\min}$, $y_j^{\max}$ are minimum and maximum values of the *j*-the common factor obtained as per the results produced by factor transformation of the initial system of indicators.

Calculation of input signals for the first internal neuron layer that consisted of eight neurons was performed as per the formula (5):

$$F_{in1k} = b_{0k} + \sum_{j=1}^{33} b_{jk} \tilde{y}_j, k = \overline{1,8}, \quad (5)$$

where F_{in1k} is input signals for the *k*-th neuron in the first internal layer;

b_{0k}, b_{jk} are coefficients of the neural network model for the first neuron layer.

Calculation of output signals for the first internal neuron layer was performed as per the formula (6):

$$F_{out1k} = \frac{1}{1 + e^{-F_{in1k}}}, k = \overline{1,8}, \quad (6)$$

where F_{out1k} is output signals for the *k*-th neuron in the first internal layer.

Calculation of input signals for the second internal neuron layer that consisted of three neurons was performed as per the formula (7):

$$F_{in2l} = c_{0l} + \sum_{k=1}^{8} c_{kl} F_{out1k}, l = \overline{1,3}, \quad (7)$$

where F_{in2l} is input signals for the *l*-th neuron in the second internal layer;

c_{0l}, c_{kl} are coefficients of the neural network model for the second neuron layer.

Calculation of output signals for the second internal neuron layer was performed as per the formula (8):

$$F_{out2l} = \frac{1}{1 + e^{-F_{in2l}}}, l = \overline{1,3}, \quad (8)$$

where F_{out2l} is output signals for the *l*-th neuron in the second internal layer.

Model standardized values of life expectancy at birth were calculated as per the formula (9):

$$\tilde{z} = d_0 + \sum_{l=1}^{3} d_l F_{out2l}, \qquad (9)$$

where $\tilde{z}$ is the model standardized LEB value;

d_0, d_l are coefficients of the neural network model for calculating standardized LEB values (the output layer values).

The model LEB value was calculated as per the formula (10):

$$z = LEB = \tilde{z}(z_{\max} - z_{\min}) + z_{\min}, \quad (10)$$

where $z = LEB$ – model LEB.

To make quantitative predictions of influence exerted by SHD on LEB for the RF population based on the applied ANN, we used a stepwise algorithm that included the following stages.

– Stage 1. Creation of a baseline and target scenario for changes in SHD-characterizing indicators.

– Stage 2. Calculation of predictive LEB values using the ANN according to the baseline and target scenario.

– Stage 3. Calculation of LEB growth potential for the RF population.

SHD values (independent variables) within the baseline scenario were set according to the available data on actual values of the analyzed indicators in 2018 taken from official statistical sources. SHD values within the target scenario were set in accordance with the targets fixed in the national and federal projects and calculated (predictive) values as per linear / logarithmic trends. A target value of an indicator between a linear or logarithmic trend was selected by using the highest value of the determination coefficient (R^2) as a criterion for this selection.

Thus, within the present study, we fixed target SHD values for 10 indicators at the levels outlined for them in the national and federal projects; 103 indicators were changed in accordance with the trends outlined for them by 2024; changes in 21 indicators amounted to 10.0 %[6] against the baseline scenario considering biological sense of their influence on LEB; values of the remaining 14 indicators were set at the baseline scenario levels since any adequate and correct estimates of changes in them were impossible to achieve.

In addition, we estimated whether it was possible to achieve target LEB levels fixed in "The unified action plan on achieving national goals of the Russian Federation development for the period up to 2024 and plans for the period up to 2030"[1] and obtained trend changes in the analyzed indicators that could be expected by 2030.

Growth potential of LEB for the RF population was calculated as per a difference in predicted LEB estimates within the baseline and target scenarios (11):

$$\Delta LEB = z^{Trg} - z^{Bsl}, \qquad (11)$$

where ΔLEB is LEB growth potential;

z^{Trg} is a predictive LEB value within the target scenario;

z^{Bsl} is a predictive LEB value within the baseline scenario.

To statistically analyze the obtained data and perform necessary computations, we used mathematical computational software for statistical data analysis (Statistica 10, RStudio, MS Excel 2010). The results were visualized using geoinformation systems (ArcGis 9.3.1).

Results and discussion. We comparatively assessed actual and model LEB levels to test whether the data obtained by using the developed methodical approach were correct. Thus, according to the baseline scenario, the LEB level calculated by using the developed mathematical model that employed baseline values of 148 determinants in 2018 equaled 72.1 years whereas the actual LEB level in Russia amounted to 72.9 years in 2018. The difference between the actual and model LEB values amounts to 0.8 years or 1.1 % in 2018. This similarity between the LEB calculated within the baseline scenario and the actual

[6] This approach was used due to structural interrelations between certain indicators.

Table 1

Growth potential for life expectancy at birth as per groups of indicators describing the environment and lifestyle based on the scenario modeling by 2024

SHD group	Target scenario for one group, years	LEB growth potential, years (days)	Rank
Lifestyle	73.32	1.26 (461.2)	1
Sanitary-epidemiological welfare on a given territory	72.64	0.58 (211.9)	2
Sociodemographic indicators	72.6	0.54 (196.3)	3
Economic indicators	72.42	0.36 (131.2)	4
Public healthcare	72.25	0.19 (70.0)	5

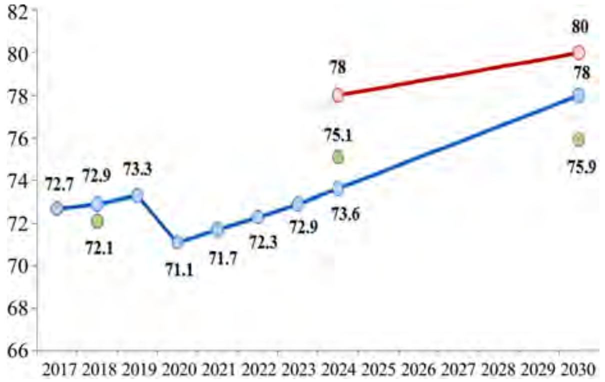

Figure 2. Target and predicted changes in LEB level for the RF population by 2024 and 2030: the red line shows target LEB levels in conformity with the RF President Order No. 204 dated May 07, 2018[7]; the blue line shows target LEB levels according to The unified action plan on achieving national goals of the Russian Federation development for the period up to 2024 and plans for the period up to 2030[8]; green dots show model LEB values according to the ANN

registered LEB level indicates that estimates produced by the developed mathematical model are quite correct.

We estimated scenario changes in the whole set of analyzed SHD values that would occur by 2024 in accordance with the approaches described in "Materials and methods" section of the work. Our estimation revealed that the model LEB value would be equal to 75.1 years; therefore, a predicted LEB growth potential in the RF amounted to 3.0 years (1095 days) over 2018–2024.

Then, we estimated LEB growth potential depending on a change in each conventional group of indicators (when indicators from only one group changed in accordance with the outlined approaches whereas the other determinants retained their baseline values). This estimation revealed that different groups had different predicted values of LEB growth potential by 2024. The highest values were determined for "Lifestyle" indicators (+1.3 years or 461.2 days) (Table 1). They were followed by "Sanitary-epidemiological welfare on a given territory" (+0.58 years or 211.9 days), "Sociodemographic indicators" (+0.54 years or 196.3 days), "Economic indicators" (+0.36 years or 131.2 days), "Public healthcare" (0.19 years or 70.0 days).

Therefore, if the overall demographic situation and LEB recover in the Russian Federation up to their levels detected in 2018–2019, implementation of the National and Federal Projects as well as complex action plans will make it possible to increase LEB by 3 years and its level will reach 75.1 years. At the same time, if we predict changes in the demographic situation by 2030 given the trends detected now and without considering COVID-19-induced processes, we can see a possible additional growth in LEB that is equal to 0.8 years (286 days) (Figure 2).

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[7] O natsional'nykh tselyakh i strategicheskikh zadachakh razvitiya Rossiiskoi Federatsii na period do 2024 goda: Ukaz Prezidenta № 204 ot 07.05.2018 [On national goals and strategic tasks in the development of the Russian Federation for the period up to 2024: The RF President Order No. 204 dated May 07, 2018]. Available at: https://digital.tatarstan.ru/rus/file/pub/pub_1960762.pdf (May 11, 2022) (in Russian).

[8] Edinyi plan po dostizheniyu natsional'nykh tselei razvitiya Rossiiskoi Federatsii na period do 2024 goda i na planovyi period do 2030 goda (utv. rasporyazheniem Pravitel'stva RF ot 01.10.2021 № 2765-r (s izm. ot 24.12.2021)) [The unified action plan on achieving national goals of the Russian Federation development for the period up to 2024 and plans for the period up to 2030 (approved by the RF Government Order dated October 01, 2021 No. 2765-r (with alterations made on December 24, 2021))]. *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_398015/ (April 05, 2022) (in Russian).

The latter means it is necessary to retain the occurring trends by achieving the outlined targets. At the same time, if we want to achieve LEB equal to 78 years by 2030, we have to provide an additional 2.1-year growth in it. It can be comparable with additional implementation of such major projects as "Clean Air", "Clean Water", "Demography" etc. Certain substantial reserves for LEB growth can be found due to target activities aimed at creating stimuli for population to pursue healthy lifestyle. These activities should be structured as per their significance. A growth can also be secured due to changes in some negative trends that are being detected now (working conditions, a number of divorces, demographic load coefficients etc.).

A detailed study with its focus on specific conventional groups of indicators made it possible to estimate influence exerted on LEB by each separate indicator from the whole list of the analyzed determinants. Thus, "A share of population doing sports or physical exercises" produced the most significant effect among all the indicators from the group that described population lifestyles and among all the indicators as well. If this share reaches 55 %, which is its target level according to the "Sport is the standard of living" [9] Federal Project, a growth potential in LEB is equal to 243.5 days. LEB is predicted to grow if there is an increase in "A total number of sport facilities per 100 thousand people"; the effect produced on LEB is +18.9 days. The next important indicator in this group is "Consumption of fruit and vegetables". An increase in this consumption up to its recommended standards[10] can result in a potential growth in LEB by 53 and 39 days accordingly. We also established that LEB would grow by 19.5 days in case ethanol consumption[11] per an adult reduced by 24 % according to data provided by retail outlets dealing with alcohol sales. An isolated 24 % reduction in alcohol retail sales also led to LEB growth, which, if taken as per specific alcohol beverages, would amount to 17 days for beer; 12 days, for vodka; 11 days, for wines; 10 days, for sparkling wines.

Indicators that described working conditions for working population produced the greatest effects on changes in LEB levels in the group of indicators related to sanitary-epidemiological welfare on a given territory. If a specific share of workers who have to work under working conditions deviating from hygienic standards as per certain standardized workplace factors goes down in accordance with the detected trends, we will see the following changes in LEB levels. A 1.8-time decrease in workplaces with working conditions not conforming to the standards as per the biological factor will lead to a growth in LEB that is equal to 37.9 days; a 2.5-time decrease (lighting), a 20.2-day growth in LEB; a 3.3-time decrease (work intensity), a 17.5-day growth in LEB; and a 1.2-time decrease (microclimate), a 8.3-day growth in LEB.

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[9] Pasport federal'nogo proekta «Sozdanie dlya vsekh kategorii grazhdan i grupp naseleniya uslovii dlya zanyatii fizicheskoi kul'turoi i sportom, massovym sportom, v tom chisle povyshenie urovnya obespechennosti naseleniya ob"ektami sporta, a takzhe podgotovka sportivnogo rezerva» – kratkoe naimenovanie: Sport – norma zhizni (utv. proektnym komitetom po natsional'nomu proektu «Demografiya», protokol ot 29.04.2019) [The profile of the Federal Project "Creation of the necessary conditions for doing sports or physical exercises, including an increase in a number of sport objects provided to the population as well as training of sports reserve" the short title being "Sport is the standard of living" (approved by the Project Committee responsible for the "Demography" National project, the meeting report issued on April 29, 2019)]. *Zakony, kodeksy, normativnye i sudebnye akty*. Available at: https://legalacts.ru/doc/pasport-federalnogo-proekta-sozdanie-dlja-vsekh-kategorii-i-grupp_2/ (May 13, 2021) (in Russian).

[10] Ob utverzhdenii Rekomendatsii po ratsional'nym normam potrebleniya pishchevykh produktov, otvechayushchikh sovremennym trebovaniyam zdorovogo pitaniya: Prikaz Ministerstva zdravookhraneniya RF ot 19 avgusta 2016 g. № 614 [On Approval of the Recommendations on rational consumption of food products that conform to the up-to-date standards of healthy diet: The Order by the RF Public Healthcare Ministry issued on August 19, 2016 No. 614]. *GARANT: informational and legal portal*. Available at: https://www.garant.ru/products/ipo/prime/doc/71385784/ (May 13, 2021) (in Russian).

[11] Pasport federal'nogo proekta «Formirovanie sistemy motivatsii grazhdan k zdorovomu obrazu zhizni, vklyuchaya zdorovoe pitanie i otkaz ot vrednykh privychek» (utv. Minzdravom Rossii, protokol ot 14.12.2018 № 3) [The profile of the Federal Project "Creation of stimuli for citizens to pursue healthy lifestyle including healthy diets and giving up bad habits" (approved by the RF Public Healthcare Ministry, the meeting report dated December 14, 2018 No. 3)]. *The RF Ministry of Labor*. Available at: https://mintrud.gov.ru/ministry/programms/demography/4 (May 13, 2021) (in Russian).

Quality of soils that conforms to hygienic standards is another sanitary-epidemiological factor associated with changes in LEB. Given the existing descending trends in a share of soil samples deviating from the hygienic standards as per sanitary-chemical indicators, we can predict certain growth in LEB. Thus, if a share of soil samples that deviate from the standards as per sanitary chemical-parameters goes down by 2.7 times by 2024, LEB is expected to grow by 7 days; as per heavy metal contents (by 2.3 times), by 11.6 days; as per microbiological indicators (by 1.8 times), by 5.5 days accordingly. LEB is expected to grow if the total emissions of contaminants into ambient air decrease by 22.0 % (the target set within the "Clean Air" Federal Project)[12] from all sources, stationary ones in particular. The greatest contribution here (3.6 days) is made by a calculated indicator that describes how environmentally friendly (clean) an economy is in a given region, that is, a quantity of emissions per a gross regional product (kg/million rubles). A significant growth in LEB is expected if food products become safer. Should a share of food products that do not conform to the hygienic standards as per microbiological indicators decrease by 1.2 times and reach zero regarding non-conformity as per sanitary-chemical indicators, an expected growth in LEB can be up to 15 days. A 15.6 % reduction in a share of non-centralized water supply sources (wells, catchments and springs) that do not conform to the sanitary-epidemiological requirements will result in LEB growing by 8.9 days.

As for sociodemographic indicators, "A number of registered crimes per 100 thousand people" turned out to be the most significant one. If it went down from 1428.5 to 1074 crimes per 100 thousand people, an expected growth in LEB would amount to 24 days. A growing share of people with higher education regardless of their employment status (employed, up to 35.4 %; unemployed, up to 26.4 %) would lead to a potential growth in LEB by 9.4 and 20.6 days accordingly. An increase in a number of working hours on average per one employed person from 38.1 hours (in 2018) up to the upper limit of a standardized working week (40 hours) that is stipulated by the RF Labor Code[13] would produce a certain effect on LEB, namely, a growth in it by 19 days. Overall improvement of housing that involves equipping it with water supply, sewage and central heating by 2–4 % against its level detected in 2018 can lead to a growth in LEB, by 16.5, 13.1 and 8.6 days accordingly. "A share of expenses on social policy funded from consolidated budgets" is another indicator producing a positive effect on LEB. An expected growth in it from 20.3 % to 21.7 % will increase LEB by 10 days. A reduction in social inequality (Gini coefficient) from 41.3 % to 40.3 % can result in LEB growing by 1.8 days.

When it comes down to economic indicators, incomes per capita and consumer expenses turned out to be the most significant among them. Their increase up to 45 thousand rubles per month and 35.5 thousand rubles per month can lead to a potential growth in LEB by 16.4 and 82.5 days accordingly. Greater incomes are likely to be associated with wider opportunities to improve one's lifestyle, to make it healthier. A growth in consumer expenses can result from not only purely economic reasons (inflation) but also from buying products or services of higher quality that give an opportunity to maintain or even improve one's health. We did not manage to confirm a

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[12] Pasport natsional'nogo proekta «Ekologiya» (utv. prezidiumom Soveta pri Prezidente RF po strategicheskomu razvitiyu i natsional'nym proektam, protokol ot 24.12.2018 № 16) [The profile of the "Ecology" National Project (approved by the RF Presidential Council on the strategic development and national projects, the meeting report issued on December 24, 2018 No. 16)]. *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_316096/45da8841765f8eb5fcccef6cdb801897e354873b/ (May 13, 20211) (in Russian).

[13] Trudovoi kodeks Rossiiskoi Federatsii ot 30.12.2001 № 197-FZ (prinyat Gosdumoi 21.12.2001). Stat'ya 91. Ponyatie rabochego vremeni. Normal'naya prodolzhitel'nost' rabochego vremeni [The Labor Code of the Russian Federation issued on December 30, 2001 No. 197-FZ (passed by the RF State Duma on December 21, 2001). Clause 91. The concept of working time. The standard working week in Russia]. *GARANT: informational and legal portal*. Available at: https://base.garant.ru/12125268/ (May 11, 2022) (in Russian).

relationship between a growth in a gross regional product and an increase in LEB for population that is usually established by many researchers. In most studies, such a relationship is established by using linear models (pair or multiple regressions) that can oversimplify all the obtained dependences and interpret them too mechanistically. In addition, such a relationship is often established by using data collected at a national level or even in various countries and over longer observation periods. The present study relies on using a model based on artificial neural networks and on data collected at a meso-level (regional one) over ten years. This could both influence differences in the results and detect peculiarities and regularities typical for regions or the country as well as for the existing situation as a whole that is changing rather dynamically.

As for indicators describing the public healthcare system in the country, we found out two most significant indicators, "A number of doctors with all specialties" and "Loads on health workers", an indicator that is functionally related to the first one. An increase in the first indicator in accordance with the targets stipulated within the "Public healthcare" National Project[14] will result in LEB growth by 26.2 days and a relevant decrease in the second one will make LEB grow by 21.9 days. Besides, we established that a decrease in "A share of expenses on public healthcare funded from consolidated budgets" would result in a 4.4-day decrease in LEB on average in the RF. An isolated increase in "Capacities of out-patient polyclinics" could lead to a 2.9-day growth in LEB.

We should note that the present study has certain limitations. The mathematical model applied within its framework describes a complex system of non-linear cause-effect relationships between the analyzed determinants and LEB. This results in disrupted additivity of the computation results as per different scenarios; that is, an aggregated value of LEB growth potential calculated separately as per scenario changes in groups of indicators does not coincide with the results produced by the complex scenario changes in all the indicators. Consequently, it becomes difficult to determine a correct structure of contributions made by effects produced on LEB by specific determinants.

The results produced by predictive estimates of LEB growth potential in the RF as a whole are consistent with estimating contributions made by heterogeneous factors into public health supplementing and extending the results produced by previous studies in the sphere. Thus, lifestyle-related determinants as well as indicators of sanitary-epidemiological welfare turned out to be the most significant factors inducing a potential LEB growth. Still, the described model applied to estimate LEB growth potential has certain limitations such as the domain of the model. An adequate predictive estimation of LEB growth potential that is based on the created model is possible only at the macro- and meso-levels (the RF and its regions). The model can be used on data obtained at other levels (administrative districts within a region, or a country level) only after necessary retraining and, possibly, adjusting a list of analyzed SHD.

Conclusions. We created a mathematical model based on artificial neural networks that employed scenarios involving complete achievement of social and hygienic target indicators stipulated in the National and Federal Projects. All this allowed us to predict LEB growth potential by 2024, which amounted to 3.0 years (1095 days). The differences between a LEB level calculated with the baseline scenario and the actual LEB level in 2018 did not exceed 1.1 %. This indicated that our predictive estimates of LEB growth potential were highly precise. We conventionally decomposed the whole set of the analyzed de-

[14] Pasport natsional'nogo proekta «Zdravookhranenie» (utv. prezidiumom Soveta pri Prezidente Rossiiskoi Federatsii po strategicheskomu razvitiyu i natsional'nym proektam, protokol ot 24 dekabrya 2018 g. № 16) [The Profile of the "Public healthcare" National Project (approved by the RF Presidential Council on the strategic development and national projects, the meeting report issued on December 24, 2018 No. 16)]. *GARANT: informational and legal portal*. Available at: https://base.garant.ru/72185920/ (May 13, 2021) (in Russian).

terminants into separate groups and then analyzed them as per individual scenarios describing changes in them by 2024 with subsequent ranking of LEB growth potential values. The results were consistent with the existing paradigm of priority influence exerted by lifestyle-related factors, ecological and sociodemographic factors on public health. The greatest scenario changes in LEB growth potential were detected for "Lifestyle" (+1.26 years or 461.2 days), "Sanitary-epidemiological welfare on a given territory" (+0.58 years or 211.9 days), and "Sociodemographic indicators" (+0.54 years or 196.3 days).

The created algorithm for determining LEB growth potential for population can be used as an instrument for correct determination of priority factors / groups of factors (social and hygienic determinants) that produce their effects on the integral health indicator (LEB) on a given territory. It is advisable to use this instrument when making managerial decisions on how to improve a medical and demographic situation. Besides, the suggested estimation model corresponds to the up-to-date concept of public health as a complex system that requires a multisided approach to studying and analyzing it as well as interpreting research results. The developed model that describes multiple non-linear interrelations between social and hygienic determinants and life expectancy at birth can be used to achieve the following:

– determining manageable (by executive authorities) priority social and hygienic determinants (hereinafter SHD) that produce the greatest effects on LEB;

– making medical and demographic predictions whether it is possible to achieve target LEB levels considering scenario changes in SHD and specific socioeconomic factors, sanitary-epidemiological situation, and weather and climatic conditions on a given territory (in a specific RF region);

– improving the social and hygienic monitoring system and statistical observation at the regional and federal levels by creating optimal lists of monitored indicators, improving procedures for analyzing and assessing data on public health;

– developing preventive activities that make it possible to either decrease or prevent effects produced by a specific SHD of a group of such determinants on public health;

– providing objective data to people participating in developing and making managerial decisions, including those on prevention activities, aimed at preserving and improving public health, LEB growth, providing sanitary-epidemiological welfare and socio-economic wellbeing.

The results produced by the present study are quite suitable for being implemented into practical activities accomplished by experts of the sanitary-epidemiological service and research institutions dealing with public healthcare issues as well as by municipal authorities. To facilitate the process, a PC software package has been developed. It is entitled "Socio-economic and sanitary-hygienic indicators and an associated growth potential of life expectancy at birth for the RF population" (it was registered in the Software Register on March 28, 2022, the registration certificate No. 2022614959). The software gives an opportunity to perform computational experiments with the trained ANN using only numeric values determined within the baseline and target scenarios.

In future, we plan to continue examining aggregated, share and mutual influence exerted by socio-hygienic determinants on public health in the Russian Federation (mortality and morbidity as per specific causes) including analysis of data obtained at micro- (municipal districts) and macro-levels (different countries) as per sex- and age-specific differences.

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Research article

THE ALGORITHMS FOR DRAWING UP ANNUAL PLANS OF INSPECTIONS PERFORMED BY ROSPOTREBNADZOR'S REGIONAL ORGANIZATIONS WITHIN THE FRAMEWORK OF RISK-BASED MODEL

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The existing model of control and surveillance activities is based on a procedure that involves assigning activities performed by juridical persons or private entrepreneurs and (or) production facilities used by them in these activities into a specific risk category or a specific hazard class (category). The goal of the present work was to develop and improve algorithms for drawing up annual plans of inspections performed by Rospotrebnadzor's territorial organizations within the framework of the risk-based model.

For the first time, we have formulated conceptual and mathematical statement of the problem of planning control and surveillance activities performed by Rospotrebnadzor. This allowed us, among other things, to consider history of violations (integrity of a given subject) over a specific period and availability of objects for inspections. The latter is described with several parameters that include both regional peculiarities (a distance between objects, quality of road networks) and "complexity" of checking a particular object. When analyzing the mathematical statement, we identified certain model parameters that had the greatest influence on a solution to the problem, that is, the most sensitive parameters that should be regulated with special care if we want to make control and surveillance activities more effective.

We have created planning algorithms with preset parameter values (scenario forecasting programs) and tested them at the regional level. We have developed three criteria for comparing these algorithms: coverage of a number of subjects that are to be inspected; coverage of a number of objects that are to be inspected; coverage by the total risk. The testing results indicate that the combined algorithm has higher coverage rates since in this case not all objects are inspected when a given subject is being checked. Consequently, this allows reducing overall labor costs required to perform an inspection.

The suggested approaches give an opportunity to achieve more effective distribution and use of resources allocated by Rospotrebnadzor for scheduled inspections.

Keywords: *planning algorithms, control and surveillance activities, economic entities, scheduled inspections, risk-based surveillance, hazard class, working hours fund, mathematical model.*

The risk-based approach is being actively implemented in the Russian Federation in various spheres [1–6], for example, state control in sea and river ports, state surveillance over industrial safety, customs administration, etc. Belarus and Kazakhstan have accumulated certain experience in implementing the risk-based approach into control and surveillance activities. The work [7] dwells on analyzing Russian practices of risk-based regulation and gives suggestions on how to develop its instruments. The authors pay special attention to risk-based regulation of the financial sector and risk regulation in the environmental protection and emergencies. The work [8] concentrates on applying risk-based procedures in tax administration. The authors of the work [9] describe both foreign and Russian experience in effective use of the risk-based approach when inspecting technical devices at oil and gas extraction facilities. A risk is assessed by creating a risk matrix (this matrix is based on a probability of an event and its "severity") that facilitates making

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effective and well-structured decisions. The paper [10] describes a methodical approach to risk-based surveillance over activities performed by lending institutions. The concept of the risk-based approach and its practical implementation are widely used in internal audit [11, 12]. The authors of the work [13] suggest a planning procedure for the risk-based approach as per key performance indicators. Use of the risk-based approaches in planning of control activities by surveillance bodies of the EMERCOM of Russia is presented in the work [14]. The paper [15] describes an optimal planning procedure for prevention within the HSE management system. A special procedure was developed for optimal planning of preventive activities; this procedure is based on minimization of any residual occupational risk taking into account preset technical and economic limitations. The work [16] dwells on contemporary procedures for planning activities aimed at strengthening security of critical facilities. These procedures rely on using program-target approaches. Besides, planning and organization of the public healthcare system in a situation when resources are limited are described in detail in the work [17]. Therefore, we can see that the risk-based approach is being widely used in multiple spheres.

The legislation in the RF stipulates rules for assigning activities performed by juridical persons and private entrepreneurs and (or) production facilities used by them in these activities into a certain risk category or into a certain hazard class (category). These rules are fixed in two documents: the RF Government Order issued on August 17, 2016 No. 806 "On application of the risk-based approach when organizing specific control (surveillance) activities and making alterations into some orders of the RF Government"[1] and the Methodical Guidelines MR 5.1.0116-17 "The risk-based model of control and surveillance activities in the sphere of providing sanitary-epidemiological welfare. Classification of economic entities, types of activity and objects under surveillance as per potential health risks for organizing scheduled control and surveillance activities" [2]. The existing model of control and surveillance activities is based on a procedure that involves assigning activities performed by juridical persons or private entrepreneurs and (or) production facilities used by them in these activities into a specific risk category or a specific hazard class (category). This category is determined as per potential health risk for people influenced by these economic activities [18].

In our previous works, we suggested an algorithm for planning control and surveillance activities. It was based on a procedure that involved stepwise adding of economic entities into a schedule, starting from those belonging to the 1st hazard category and up to depletion of all the allocated resources according to working time fund [19, 20]. It hardly seems optimal to use only one attribute (hazard class) when drawing up schedules of control and surveillance activities since this cannot provide sufficient coverage of economic activities performed by economic entities and production facilities used in these activities that should be inspected. Given that, use of any additional attributes when planning control and surveillance activities can make them more effective. Absence of any violations during a specific period (in case an economic entity is law-abiding) can be a potential additional attribute. It can be measured both as per a whole set of possible violations and as per isolated facts of violations (for example, specific measured indicators or chemicals). The second way to make planning of activities more effective is to reduce time allocated for one inspection, for example, by selecting priority objects and an optimal program of laboratory support.

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[1] O primenenii risk-orientirovannogo podkhoda pri organizatsii otdel'nykh vidov gosudarstvennogo kontrolya (nadzora) i vnesenii izmenenii v nekotorye akty Pravitel'stva Rossiiskoi Federatsii: Postanovlenie Pravitel'stva RF ot 17.08.2016 № 806 [On application of the risk-based approach when organizing specific control (surveillance) activities and making alterations into some orders of the RF Government: The RF Government Order issued on August 17, 2016 No. 806]. *GARANT: information and legal support*. Available at: https://base.garant.ru/71473944/ (February 25, 2022) (in Russian).

[2] MR 5.1.0116-17. Risk-orientirovannaya model' kontrol'no-nadzornoi deyatel'nosti v sfere obespecheniya sanitarno-epidemiologicheskogo blagopoluchiya. Klassifikatsiya khozyaistvuyushchikh sub"ektov, vidov deyatel'nosti i ob"ektov nadzora po potentsial'nomu risku prichineniya vreda zdorov'yu cheloveka dlya organizatsii planovykh kontrol'no-nadzornykh meropriyatii (utv. i vved. v deistvie Rukovoditelem Federal'noi sluzhby po nadzoru v sfere zashchity prav potrebitelei i blagopoluchiya cheloveka, Glavnym gosudarstvennym sanitarnym vrachom Rossiiskoi Federatsii A.Yu. Popovoi 11.08.2017 [The risk-based model of control and surveillance activities in the sphere of providing sanitary-epidemiological welfare. Classification of economic entities, types of activity and objects under surveillance as per potential health risks for organizing scheduled control and surveillance activities (approved and enacted by A.Yu. Popova, the Head of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing and the RF Chief Sanitary Inspector on August 11, 2017)]. *KODEKS: electronic fund for legal and reference documentation.* Available at: https://docs.cntd.ru/document/555601296 (February 25, 2022) (in Russian).

Given all that, it is necessary to develop more effective planning of control and surveillance activities bearing in mind both its theoretical and applied aspects including:

– developing algorithms for drawing up annual schedules of inspections that implement a differentiated approach to planning. This approach should consider a hazard class of activities performed by juridical persons and private entrepreneurs and (or) production facilities used in these activities;

– comparative analysis of the suggested algorithms in order to reveal the most rational decisions on activity planning.

The goal of the present work was to develop and improve algorithms for drawing up annual schedules of inspections performed by Rospotrebnadzor's territorial organizations in RF regions within the framework of the risk-based model. To achieve this goal, we solved the following tasks:

- we determined parameters of interaction between Rospotrebnadzor and economic entities within control and surveillance activities;
- we formulated conceptual and mathematical statement of the problem of planning control and surveillance activities performed by Rospotrebnadzor within scheduled inspections;
- we identified model parameters and examined a system of equations suggested within the mathematical statement of the problem to detect sensitivity to changes in parameters;
- we developed planning algorithms with preset parameter values (scenario forecasting programs) and tested them at the regional level within the risk-based model.

Materials and methods. We used system analysis, mathematical modeling, statistical and regression analysis in our study.

Overall, Rospotrebnadzor has a complicated hierarchical structure. In this work, we concentrated on control and surveillance activities performed by Rospotrebnadzor's territorial organizations and their branches. To determine parameters of Rospotrebnadzor facilities, it is advisable to consider several following characteristics of the surveillance service. They are a number of workers who participate in scheduled control and surveillance activities according to an organizational chart as per specific divisions (surveillance sectors); laboratory facilities (a number of workers, a number of tests as per factors). Economic entities are identified as per the following parameters: a potential health risk as per types of economic activities, production facilities; a share (frequency) of detected violations as per economic activities or production facilities; a hazard category of an economic entity; a hazard category as per an economic activity; a hazard category as per production facilities; periodicity of inspections; the date of the latest inspection.

Our basic hypothesis was that inspections performed by Rospotrebnadzor required certain resources (material costs and time). Material costs are financial resources spent on labor (salaries paid to workers who perform control and surveillance activities) and costs spent on an inspection itself (documentary and laboratory support). Resources spent on each inspection are taken from the total resource fund allocated for a given year. When developing planning algorithms, it is advisable to ensure that resources are spent evenly (meaning that financial loads are also even) in real time. We should note that time resources are given in actual values; therefore, it is necessary to correlate them with a real time scale for planning inspections within a calendar year. It seems advisable to introduce two time axes: a continuous one showing actual labor costs over time and a real calendar. They should be interrelated with a transformation operator. In this case, several economic entities can be included into a schedule. This transformation is also necessary due to certain requirements fixed in regulatory documents. These requirements concern duration of an inspection, which is usually measured in real time.

Within the suggested approaches, we considered some rules for classifying economic entities, their activities and production facilities; rules for transition from a risk category to periodicity of inspections; rules for regulating parameters of an inspection; rules for using facilities available to Rospotrebnadzor's territorial divisions. As a result, we formulated a conceptual and mathematical basis for describing the analyzed processes. To avoid overloading the text with multiple details, we provide only the basic mathematical relationships used in the suggested algorithms.

The following formula (1) determines the total fund of working time allocated for control and surveillance activities within scheduled inspections at the beginning of a given year:

$$H_0 = \delta \cdot N \cdot (h_f \cdot Y_f + h_{nf} \cdot Y_{nf}), \qquad (1)$$

where H_0 is the total fund of working time allocated for scheduled inspections at the beginning of a year, person-hours;

δ is a share of working time spent by Rospotrebnadzor personnel on scheduled inspections;

N is a number of Rospotrebnadzor personnel who take part in control and surveillance activities;

h_f is a number of hours in a full workday;

Y_f is a number of full workdays in a calendar year (minus vacation);

h_{nf} is a number of hours in a shortened workday (for example, a workday before a public holiday);

Y_{nf} is a number of shortened workdays in a calendar year.

Real time T and the time variable t, which means time spent on scheduled inspections, are bound with the following transformation:

$$T = \frac{365 \cdot 24}{\delta(h_f \cdot Y_f + h_{nf} \cdot Y_{nf})} t, \qquad (2)$$

where t is the variable used to express working hours spent by personnel on scheduled inspections; T is the real time variable.

A baseline version of the function that expresses labor costs spent on an inspection involves multiplicative influence exerted by various factors on duration of an inspection:

$$h_{jl} = h_{jl\max} f(r_{jl}) \cdot f(v, K_{jl}) \cdot f(p_{jvl}), \qquad (3)$$

where h_{jl} are labor costs spent on an inspection performed at the l-th object belonging to the j-th economic entity, person-hours;

$h_{jl\max}$ are the maximum possible labor costs spent on the inspection performed at the l-th object belonging to the j-th economic entity at $f(r_{jl}) \cdot f(v, K_{jl}) \cdot f(p_{jvl})$ =1, person-hours;

$f(r_{jl})$ is the continuous function of the availability factor of the l-th object belonging to the j-th economic entity;

$f(v, K_{jl})$ is the discrete function of an economic activity and a hazard class of a given object with its values varying from 0 to 1;

$f(p_{jvl})$ is the continuous function of the frequency of detected violations as per the v-th economic activity with its values varying from 0 to 11.

The following formula shows the relationship between Rospotrebnadzor's resources (the left part) with labor costs that are necessary to perform inspections (the right part):

$$Nt = \sum_j h_j(t), \qquad (4)$$

where N is a number of Rospotrebnadzor personnel who are involved in control and surveillance activities;

$h_j(t)$ are labor costs on the inspection at the j-th economic entity that have been spent by the moment of time t during the inspection at the j-th economic entity, person-hours.

Labor costs spent on the inspection at the j-th economic entity are determined by a number of inspected objects and labor costs spent on checking each of them:

$$h_j = \sum_{l=1}^{L} a_{jl} h_{jl}, \qquad (5)$$

where h_j are labor costs spent on the inspection at j-th economic entity, person-hours;

L is a number of objects belonging to the inspected economic entity, which should be checked;

a_{jl} are weighing factors (from 0 to 1).

We can take $a_{jl} = 1$ for the principal inspected object included into an inspection schedule. As for the other objects, we take $a_{jl}(v) < 1$ depending on an activity. Therefore, this coefficient taken for the principal inspected object covers labor costs both on drawing up relevant documents regarding an inspection at an economic entity (making orders and experts' inquiries; sending notifications to economic entities; issuing inspection reports, orders, statements, records about an administrative offence etc) and on time spent at this object. The coefficients $a_{jl}(v) < 1$ for the remaining inspected objects cover additional labor costs that occur during an inspection at these objects including those performed at the principal one (the main production grounds) and at the others (beyond them).

At present, some clues for determining labor costs can be found in the methodical guidelines "Sample standards for activities performed by organizations and institutions of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing in situations when their budgeting is to be result-oriented". These guidelines were approved by the Rospotrebnadzor's Order issued on October 10, 2008

No. 368[3]. Besides, there are standard calculated labor costs on accomplishing scheduled inspections at economic entities and their objects; they have been established based on regional practices. These documents do not provide any information on a hazard class of activities performed by inspected economic entities and all their production facilities (objects). Given that, all the aforementioned standards are taken as typical for a certain economic entity that falls within an average risk category (the 3rd hazard class as per its economic activity). Besides, the available data were extrapolated when used as reference points as per economic activities and hazard classes. The coefficients a_{jl} were obtained for all the first (principal) objects located at each address by using a relationship between an additional time spent at another address where actual activities were being performed and the overall labor costs spent at checking the first (principal) object located at the main address. All the labor costs on drawing up documentation were also assigned to this main address.

When identifying ranges within which model parameters varied and examining sensitivity of model solutions to changes in these parameters, we spotted out the most sensitive ones. They were a coefficient per frequency of inspections in case violations are absent and extrapolated values of the labor costs function.

The planning algorithms are certain rules for creating a schedule of inspections that are to be accomplished at economic entities and their production facilities and that focus on economic activities performed there within the rick-based model. We suggest three planning algorithms: a basic, alternative, and a combined one. Forecasting scenarios include variants with realistic, minimal, and maximum values of the model parameters.

The basic planning algorithm corresponds to the existing legislation. It is based on an assumption that an inspection should cover an economic entity with all its objects where an economic activity that should be checked is being performed. The algorithm contains the following stages:

1. The register of the operating economic entities and their activities is analyzed with the aim to spot out juridical persons and private entrepreneurs that are to be inspected within the planned period of time according to requirements fixed in the valid regulatory documents;

2. A structured list of economic entities and their activities is created. These economic entities and their activities are selected from the overall list of those that are subject to surveillance within the planned period according to levels of risks they may cause. Bearing in mind that certain economic activities have great hygienic significance, the structured list should primarily include the economic activities that are enlisted in the RF Government Order No. 944 issued on November 23, 2009[4];

3. The first economic entity in the list is included into the inspection schedule with all its objects and economic activities that should be checked; all the necessary labor costs on the inspection are calculated as per the relationship (3);

4. The next step is to determine a number of experts to be involved in an inspection performed at a certain economic entity;

5. Then, we calculate an actual time spent on an inspection, or t (from the formula 4), and calendar time T when an inspection at a given economic entity is complete (2).We should note that the maximum time of inspection completion should be inserted in schedules according to the legislation. This provides flexibility of control and surveillance activities;

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[3] Ob utverzhdenii metodicheskikh rekomendatsii «Primernye normativy deyatel'nosti organov i organizatsii federal'noi sluzhby po nadzoru v sfere zashchity prav potrebitelei i blagopoluchiya cheloveka v usloviyakh byudzhetirovaniya, orientirovannogo na rezul'tat»: Prikaz Rospotrebnadzora ot 10.10.2008 № 368 [On Approval of the methodical guidelines "Sample standards for activities performed by organizations and institutions of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing in situations when their budgeting is to be result-oriented": The Rospotrebnadzor's Order issued on October 10, 2008 No. 368]. *GARANT: information and legal support*. Available at: https://base.garant.ru/4187404/ (March 01, 2022) (in Russian).

[4] Ob utverzhdenii perechnya vidov deyatel'nosti v sfere zdravookhraneniya, sfere obrazovaniya, sotsial'noi sfere, v oblasti proizvodstva, ispol'zovaniya i obrashcheniya dragotsennykh metallov i dragotsennykh kamnei, osushchestvlyaemykh yuridicheskimi litsami i individual'nymi predprinimatelyami, v otnoshenii kotorykh planovye proverki provodyatsya s ustanovlennoi periodichnost'yu: postanovlenie Pravitel'stva RF № 944 ot 23.11.2009 [On Approval of the list of economic activities in public healthcare, education, social sphere, production, use and distribution of precious stones and precious metals, which are performed by juridical persons and private entrepreneurs who are subject to scheduled inspections performed according to the established periodicity: The RF Government Order No. 944 issued on November 23, 2009]. *GARANT: information and legal support*. Available at: https://base.garant.ru/12171128/ (March 01, 2022) (in Russian).

6. In case there are available experts who are not involved in any inspection, another economic entity is included into the schedule with the same inspection date. The step continues until there are no more available experts;

7. In case there are not enough available experts to check an economic entity that is the next in the schedule, this entity is given a priority and will be included in the schedule just as a number of available experts is enough to inspect it. The first economic entity in the list for which a required number of experts is available at the present day is the first to be included into the schedule;

8. Experts become available just as an inspection is near its completion (over a time calculated as per the algorithm and not that stated in the schedule according to maximum periods) and the next entity is included into the schedule. The priority is given to economic entities from the priority lists.

The alternative algorithm is based not on analyzing the register of the operating economic entities but on making out a list of their production facilities. It involves inspecting only those objects that are subject to surveillance according to the existing legislation:

1. The register is analyzed with the aim to spot out objects that are subject to surveillance in accordance with the requirements fixed in the valid regulatory documents;

2. A structured list of objects is created where these objects are ranked as per their relevant risks. The priority is given to objects with activities enlisted in the RF Government Order No. 944 issued on November 23, 2009[4];

3. An economic entity that owns the object included as No. 1 in the list is the first to be included into the schedule. Only objects included into the scheduled at the first stage are to be inspected and all the necessary labor costs are calculated in accordance with the relationship (3).

The stages 4–8 are similar to those included into the basic algorithm.

The third algorithm is based on a combined approach. The first two stages in the combined algorithm are similar to those in the basic one. However, only those objects that are included into the list created according to the alternative algorithm are to be inspected and all the labor costs are calculated at the third stage only for inspections performed at these objects. The remaining stages are similar to those included into the basic algorithm.

We selected three criteria to compare these algorithms: coverage of a number of subjects that are to be inspected; coverage of a number of objects that are to be inspected; coverage by the total risk. All these criteria have values form 0 to 1. Coverage of a number of subjects that are to be inspected is calculated as a ratio of a number of subjects included into the schedule to the total number of subjects that are to be inspected within a given calendar year. Coverage of a number of objects that are to be inspected is calculated as a ratio of a number of objects included into the schedule to the total number of objects that are to be inspected within a given calendar year. Coverage by the total risk is calculated as a ratio of a potential health risk caused by economic activities of subjects included into the schedule to a potential health risk caused by economic activities of all the subjects that are to be inspected.

Realistic forecasting scenarios involve setting baseline values of all the coefficients determined at the stage when the model parameters are identified. In forecasting scenarios with the maximum values of parameters, we set the coefficient a_{jl} for the first, second, and next objects at each address at a value being by 1.5 times higher than in the realistic scenario. In a forecasting scenario with the minimum values, we set the coefficient a_{jl} for the first, second and the next objects at each address at a value being by 1.5 times lower than in the realistic scenario. Considering variability of the parameter a_{jl} seems important since the suggested alternative and combined approaches to planning are based on using hazard classes of objects.

Therefore, we considered nine different scenarios for drawing up an inspection schedule: minimum basic, realistic basic and maximum basic; minimum alternative, realistic alternative and maximum alternative; minimum combined, realistic combined and maximum combined. The calculation results are tables with dates of scheduled inspections and necessary labor costs on each inspection.

Results. The suggested approaches were tested using data on a model RF region. The total number of experts involved in control and surveillance activities equaled 272. A parameter showing a share of working time spent by Rospotrebnadzor experts on scheduled inspections was $\delta = 0.32$. In 2019, a number of full workdays amounted to 241 and there were six workdays shortened by 1 hour. Therefore, according to the formula (1), the total working time fund allocated for control and surveillance activities amounted to:

$$H_0 = 0.32 \cdot 272 \cdot (241 \cdot 8 + 6 \cdot 7) =$$
$$= 171{,}468.8 \text{ person} - \text{hours} \qquad (6)$$

The register of the economic entities, their activities and production facilities in the selected region contains data on 17,049 types of economic activities performed by economic entities; 35,301 production facilities and other objects. Out of them, 1359 belong to the extremely high risk category; 3868, the high risk category; 6871, the significant risk category; 10,031, the average risk category; 9135, the moderate risk category; and 3767, the low risk category. The total health risk equals 1.346 as per the total number of objects; objects belonging to the 1st category (with extremely high risk) account for 83.9 % in this total risk and objects from the 2nd category (high risk) account for another 11.1 % in it.

According to the rules that stipulate transition from a risk category to periodicity of inspections, we set inspection periodicity coefficients for each activity and each production facility (object). Lists of subjects and objects that were to be inspected within a given calendar year were created for all three algorithms (stages 1–2 in them). It was done based on the periodicity coefficients using the random variable generator that conformed to uniformed distribution.

A list created within the basic algorithm included 4205 economic entities, 4710 economic activities performed by them, and 9966 production facilities (objects), or 28.2 % of all the objects in the register. One thousand two hundred and eleven of them belonged to the 1st category (89.1 %) and 1901 objects were from the 2nd category (49.1 %). The total health risk caused by all the objects included in the list amounted to 1.149 thus accounting for 85.3 % of the total health risks as per the overall number of objects included in the register. Labor costs necessary to inspect all the objects belonging to economic entities included in the schedule amounted to 374,684.1 person-hours within the realistic basic scenario; 401,091.7 person-hours, within the maximum basic scenario; and 357,079.1 person-hours, within the minimum realistic scenario. We can see that the resources allocated by Rospotrebnadzor territorial organizations in the model regions are not sufficient within any basic scenario and cannot cover all the production facilities (the formula (6)) that are to be inspected.

We provide a fragment of a table that contains results produced by calculating necessary labor costs according to the basic algorithm for each economic entity ranked as per potential health risks within three possible scenarios, realistic, maximum, and minimum one (stage 3 in the algorithm) (Table 1). At a first approximation, a number of experts involved in inspecting an economic entity N is equal to four in any algorithm (stage 4). The calculation results show that in case a number of objects to be inspected is great, labor costs can be much bigger even when risk levels are similar and economic entities have the same hazard class.

Table 2 provides an example calculation of a real time spent on an inspection, t (from the formula (4)), and a calendar time T when an inspection of an economic entity is complete. The calculations are made within the basic realistic scenario (stages from 5 to 8 in the algorithm).

We can clearly see that the legislation-based date when an inspection should be completed is much earlier than the date of an actual completion that is calculated as per necessary labor costs. It is especially true for those entities that are in the beginning of the list with labor costs being typically higher for them. Obviously, actual inspections accomplished at economic entities that belong to extremely high and high risk categories and have many production facilities (objects) where they perform their activity will require more experts if we wish to complete them in due time fixed in the existing legislation.

As a result, the realistic basic scenario predicts that 1068 economic entities will be covered by inspections during a calendar year (25.4 % of the necessary quantity); 4877 production facilities (objects) or 48.9 % of all the objects that should be inspected; coverage by risk amounts to 1.143 (99.5 % of the total risk caused by economic activities of all the economic entities that should be inspected). Coverage of the objects from the 1st and 2nd category amounts to 100 % (1211 objects) and 86.6 % (1647 objects) accordingly. The maximum basic scenario predicts that inspections will be accomplished at 856 economic entities during

Table 1

Calculation of necessary labor costs as per the basic algorithm for each economic entity (a fragment)

Entity No.	Total risk	Labor costs within the realistic scenario, person-hours	Labor costs within the maximum scenario, person-hours	Labor costs within the minimal scenario, person-hours	A number of objects
1	2.09E-01	922.5	1311.3	663.3	28
2	1.14E-01	548.1	749.7	413.7	15
3	1.89E-01	173.7	188.1	164.1	4
4	7.60E-02	323.1	382.5	303.9	12
5	6.99E-02	349.2	356.4	344.4	5
6	4.47E-02	231.3	274.5	202.5	27
7	3.51E-02	188.1	209.7	173.7	9
8	2.19E-02	375.3	490.5	298.5	13
9	2.28E-02	303.3	382.5	250.5	10
10	1.63E-02	260.1	317.7	221.7	7
11	1.55E-02	173.7	188.1	164.1	3
12	1.31E-02	144.9	144.9	144.9	2
13	2.65E-02	231.3	274.5	202.5	5
14	2.30E-02	620.1	857.7	469.2	48
15	1.03E-02	349.2	356.4	344.4	2
16	9.12E-03	173.7	188.1	164.1	2
17	1.16E-02	1547.1	2187.9	1119.9	115
18	9.80E-03	385.2	410.4	368.4	23
19	6.50E-03	349.2	356.4	344.4	2
20	5.32E-03	144.9	144.9	144.9	1

Table 2

Calculation a real time spent on an inspection, *t* (from the formula (4)), and a calendar time *T* when an inspection of an economic entity is complete within the basic realistic scenario (a fragment)

Entity No.	*t*, hours	*T*, hours	The date when an inspection started	The date when an inspection was completed	The date of an actual completion calculated as per labor costs
1	230.63	3204.75	Jan 01, 2019	Jan 21, 2019	May 14, 2019
2	137.03	1904.09	Jan 01, 2019	Jan 21, 2019	Mar 21, 2019
3	43.43	603.43	Jan 01, 2019	Jan 21, 2019	Jan 26, 2019
4	80.78	1122.44	Jan 01, 2019	Jan 21, 2019	Feb 16, 2019
5	87.30	1213.12	Jan 01, 2019	Jan 21, 2019	Feb 20, 2019
6	57.83	803.53	Jan 01, 2019	Jan 21, 2019	Feb 03, 2019
7	47.03	653.46	Jan 01, 2019	Jan 21, 2019	Jan 28, 2019
8	93.83	1303.79	Jan 01, 2019	Jan 21, 2019	Feb 24, 2019
9	75.83	1053.66	Jan 01, 2019	Jan 21, 2019	Feb 13, 2019
10	65.03	903.58	Jan 01, 2019	Jan 21, 2019	Feb 07, 2019
…	…	…	…	…	…
101	60.45	840.01	Feb 18, 2019	Mar 10, 2019	Mar 25, 2019
102	36.56	508.07	Feb 18, 2019	Mar 10, 2019	Mar 11, 2019
103	55.74	774.52	Feb 20, 2019	Mar 12, 2019	Mar 24, 2019
104	26.49	368.07	Feb 20, 2019	Mar 12, 2019	Mar 07, 2019
105	26.49	368.07	Feb 20, 2019	Mar 12, 2019	Mar 07, 2019
106	26.49	368.07	Feb 20, 2019	Mar 12, 2019	Mar 07, 2019
107	146.74	2039.06	Feb 20, 2019	Mar 12, 2019	May 16, 2019
108	23.89	331.94	Feb 21, 2019	Mar 13, 2019	Mar 07, 2019
109	46.31	643.56	Feb 22, 2019	Mar 14, 2019	Mar 21, 2019
110	33.53	465.86	Feb 24, 2019	Mar 16, 2019	Mar 15, 2019

a calendar year (20.4 % of the necessary quantity); 3911 production facilities (objects) or 39.2 % of all the objects that should be inspected; coverage by risk amounts to 1.141 (99.3 % of the total risk caused by economic activities of all the economic entities that should be inspected). However, within this scenario, only 76.1 % of the objects from the 1st and 2nd category will be inspected. The minimum basic scenario predicts inspections to be accomplished at 1254 economic entities during a calendar year (29.8 % of the necessary quantity); 5551 production facilities (objects) will be inspected (55.7 % of the total number of objects that should be inspected); 1.144 risk will be covered (99.6 % of the total risk caused by economic activities of economic entities that should be inspected). Within this scenario, inspections cover 99.9 % of all the objects from the 1st and 2nd categories.

The alternative algorithm allowed creating a list with 4882 economic entities and 10,764 production facilities (objects) (30.5 % of all the objects in the register). One thousand one hundred and sixteen of them belonged to the 1st category (82.1 %) and 1839 belonged to the 2nd category (47.5 %). The total health risk caused by all the objects in the list amounted to 1.157, which accounted for 85.3 % of the total number of objects in the regional register. According to the realistic alternative scenario, labor costs that were necessary to inspect all objects belonging to economic entities included in the list amounted to 388,655.5 person-hours; the minimum alternative scenario, 401,091.7 person-hours; the maximum alternative scenario, 410,862.7 person-hours. Obviously, resources allocated by Rospotrebnadzor on scheduled inspections are not sufficient to cover all the production facilities (objects) that should be inspected within any alternative scenario (the formula (6)).

As a result, the alternative realistic scenario predicts that 1027 economic entities will be covered by inspections during a calendar year (21 % of the necessary quantity); 5035 production facilities (objects) or 47.2 % of all the objects that should be inspected; 1.148 risk (99.2 % of the total risk caused by economic activities of all the economic entities that should be inspected). Coverage of the objects from the 1st and 2nd category amounts to 100 % (1116 objects) and 93.2 % (17,157 objects) accordingly. The maximum alternative scenario predicts that inspections will be accomplished at 880 economic entities during a calendar year (18 % of the necessary quantity); 4061 production facilities (objects), which accounts for 38 % of all the objects that should be inspected; 1.146 risk (99.1 % of the total risk caused by economic activities of all the economic entities that should be inspected. However, within this scenario, only 82.5 % of the objects from the 1st and 2nd category will be inspected. The minimum alternative scenario predicts inspections to be accomplished at 1151 economic entities during a calendar year (23.6 % of the necessary quantity); 5260 production facilities (objects) will be inspected (49.3 % of the total number of objects that should be inspected); 1.149 risk will be covered (99.4 % of the total risk caused by economic activities of economic entities that should be inspected). Within this scenario, inspections cover 97.4 % of all the objects from the 1st and 2nd categories.

The combined algorithm assumes that if an economic entity that should be inspected in this calendar year has only one production facility, this facility should be inspected regardless of being included in the list created within the alternative algorithm or not. According to the combined algorithm, the list included 3961 economic entities and 7134 production facilities (objects) (20.2 % of all the objects in the register), 1033 of them belonging to the 1st category (76.0 %) and 1205 to the 2nd category (31.1 %). The total health risk caused by all the objects in the list amounts to 1.112, which accounts for 82.4 % of the total health risk caused by all the objects in the register. According to the realistic combined scenario, labor costs that were necessary to inspect all objects belonging to economic entities included in the list amounted to 306,550 person-hours; the maximum combined scenario, 322,266.3 person-hours; the minimum combined scenario, 296,105.5 person-hours. We can again clearly see that resources allocated by Rospotrebnadzor on scheduled inspections in the model regions are again insufficient to cover all the listed objects in all three scenarios (the formula (6)). Still, these necessary labor costs calculated according to the combined algorithms are approximately by 25 % lower than the costs calculated by using the basic or alternative algorithm.

As a result, the realistic combined scenario predicts 1337 economic entities (33.8 % of the necessary quantity) and 3950 production facilities (objects (55.4 % of all the objects that should be inspected) to be covered with inspections during a calendar year. A covered risk amounts to 1.108 (99.7 % of the total risk caused by all economic entities that should be inspected). The maximum combined scenario predicts inspections to be accomplished at 1145 economic entities (28.9 % of the necessary quantity) during a calendar year. Three thousand three hundred and twelve objects will be inspected (46.4 % of the total number of objects that should be checked) and 1.107 risk will be covered (99.6 % of the total risk caused by all economic entities that should be inspected). The minimum combined scenario predicts that inspections will cover 1474 economic entities (37.2 % of the necessary quantity); 4125 production facilities (objects) (57.8 % of all the objects that should be inspected); 1.109 risk (99.7 % of the total risk caused by all the economic entities that should be inspected). Inspections will cover 83.0 % of the objects from the 1st and 2nd categories within the maximum combined scenario. This coverage amounts to 99.9 % within two other maximum scenarios, basic and alternative one.

Therefore, the alternative algorithm produced coverage rates that were quite similar to those calculated with the basic algorithm. The combined algorithm produces greater coverage rates since not every object is checked when an economic entity is being inspected. Only the most hazardous objects are covered by an inspection thereby reducing labor costs spent on it.

Discussion. We described parameters of interactions between Rospotrebnadzor and economic entities within control and surveillance activities. This allowed us to spot out major characteristics that give an opportunity to describe how Rospotrebnadzor resources are spent in terms of labor costs. One of our primary hypotheses is that the total working time fund allocated for control and surveillance activities is spent evenly. When an inspection schedule is created, it is advisable to distribute loads evenly so that personnel work in ergonomic conditions without any unnecessary deadline pressures.

The relationships, which we introduced with the mathematical statement of the task, allowed us to consider a history of violations (integrity and law abidance of an economic entity) during a given period; parameters related to availability of objects for an inspection including both regional peculiarities (a distance between objects, quality of a road network) and "complexity" of checking a specific object. Differentiation of production facilities (objects) that belong to an economic entity gives grounds for planning volumes and contents of surveillance activities.

We identified the model parameters at a first approximation. These parameters can be used to estimate and substantiate the necessity and sufficiency of resources involved in performing control and surveillance activities. We determined which model parameters had the greatest influence on the solution, that is, the most sensitive parameters that should be regulated with special care if we want to make control and surveillance activities performed by Rospotrebnadzor more effective.

The results produced by testing the suggested algorithms prove their relevance and efficiency. However, conclusions on the suggested algorithms being effective require more profound examination of the results. This might include examining results produced by a more complicated model, for example, a model that allows for territorial distribution of Rospotrebnadzor organizations within a given region. Besides, we should additionally discuss whether it is advisable to check all the production facilities of an economic entity (within the existing legislation) bearing in mind that a hazard class of some objects belonging to this entity may be lower than a hazard class of specific economic activities performed by it.

Conclusion. This study has provided further development of theoretical and applied aspects of the risk-based model for control and surveillance activities performed by Rospotrebnadzor. We have also developed a scientific basis for describing interactions between Rospotrebnadzor and economic entities. Among other things, we have suggested new approaches to improving planning of Rospotrebnadzor activities involved in inspecting economic entities and their production facilities.

We have produced new statements (conceptual and mathematical) that give an opportunity to provide a formal description of an inspection process within the risk-based model. We have determined certain parameters of the described processes together with identifying the major parameters and indicators that should be considered within the suggested model. We have created three planning algorithms, which can be considered rules for drawing up an inspection schedule. This schedule comprises inspections of economic activities performed by economic entities and productions facilities used by them in the process within the risk-based model. We have selected three criteria to compare the algorithms: coverage of a number of subjects that are to be inspected; coverage of a number of objects that are to be inspected; coverage by the total risk.

The suggested approaches have been tested at a regional level. The testing results indicate that the combined algorithm produces greater coverage rates. The developed approaches give an opportunity to create planning algorithms with preset (predicted) values of parameters and to assess whether the algorithms are effective using the suggested comparison criteria. Ultimately, this will allow more effective distribution and use of Rospotrebnadzor resources allocated for scheduled inspections.

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Research article

METHODICAL APPROACHES TO ASSESSING SUBJECTIVE HEALTH RISK PERCEPTION BY POPULATION UNDER EXPOSURE TO AMBIENT AIR POLLUTION

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There is a growing demand by the civil society for relevant information on the environment quality and related health risks. The state should be able to satisfy this demand and this makes the present research truly vital. It concentrates on correlating expert and non-expert opinions expressed when perceiving risk quantification.

Our goal was to answer two following questions: 1) How does an average unprofessional person quantify a probability and severity when he or she hears certain verbal expressions that denominate them? 2) How can we possibly identify the assessment of health risks associated with environmental pollution factors given by the population in general or specific social groups?

To find answers to these questions, we applied quantitative methods for data collection and analysis. The first stage involved collecting data on subjective correlation of a verbal probability scale with its numeric expression among people living in industrial cities. The second stage focused on testing the methodology for studying assessments of health risks associated with ambient air pollution given by the population/social groups. This methodology relied on the results obtained at the previous stage.

We established that only 70 % of people actually correlated words with figures. We determined that experts tended to rate probabilities approximately by 10 % higher than "average people" did when it came down to such words as "Virtually certain" and "Very likely". Such words as "Likely", "Similarly likely" and "Unlikely" were also rated differently but with a smaller gap between the opinions. The study also provides a method for determining the public assessment of health risks associated with ambient air pollution. The research results give an opportunity to solve a practical task related to informing the population about health risks and to overcome a so-called language barrier between experts and ordinary people. For example, messages aimed for decision-makers can be adapted considering all the identified perception peculiarities.

Keywords: *risk perception, risk assessment, risk rate, probability assessment, subjective risk assessment, probability of risk realization, health risk, informing.*

Most contradictions that are associated with informing people about health risks and their assessment as well as with establishing a relevant level of social acceptability arise due to ambiguity of risk perception and language used to describe this risk within various groups. These groups involved into a risk situation are experts, decision-makers, economic entity, mass media, and population at large. Experts use a language of science when they consider probabilistic nature of coming adverse events; supervisors at different levels rely on socioeconomic and political senses[1]. Mass media retranslate information coming from other sub-

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jects and process it trying to attract their audience with striking headings [1]. People more often appeal to the emotional component in risks, fears and anxieties; they do not understand expert language [2, 3] and, as a rule, do not trust decision-makers and mass media [4]. This induces growing social tensions and leads to further mismatch between opinions and managerial decisions [5]. As it was noted in the WHO report on health and the environment, *"In general, people do not understand probability. Public reaction to risk often appears to be at odds with scientific estimates. … the suggestion that a hazard poses an annual risk of death of 'one chance in x' may cause anything from panic to virtual indifference"* [6]. The necessity to consider perception and needs of various subjects within the risk space has been discussed for the last 20 years and substantial work has been done in the field. Thus, the Climate Change 2001: Synthesis Report by the Intergovernmental Panel on Climate Change (IPCC) suggested using certain words and expressions to discuss uncertainties and probabilities. The authors created the following definitions for authenticity: virtually certain (a probability that the result is authentic exceeds 99 %); very likely (a probability is 90–99 %); likely (a probability is 66–90 %); about as likely as not (33–66 %); unlikely (10–33 %); very unlikely (1–10 %); and exceptionally unlikely (a probability is less than 1 %) [7]. This gradation relies on collective judgment made by the authors about authenticity of a conclusion and the judgment is based on data produced by observations, modeling results and theories analyzed by them.

In 2004, the IPCC suggested testing uncertainty descriptors on target audiences prior to using them [8], and this might be affected by the scale being tested by other researchers. For example, A.G. Patt and D.P. Schrag performed their experiment on students attending natural sciences faculties and concluded that their respondents understood the suggested verbal scale a bit differently. Nevertheless, the authors noted the procedure had a lot of potential [9].

Research goals and tasks. Our major goal was to answer two questions. The first one was how an average unprofessional person quantified a probability and severity when he or she heard certain verbal expressions that denominated them. An answer to this question solves a task related to informing people about health risks. This task is associated with certain difficulties people meet when they try to perceive numeric data. If we determine what words correlate with these or those quantitative (numeric) ranges, any messages about risks aimed for a broad audience can be formulated in such a way so that they are understood correctly by it. In other words, this makes it possible to join expert language and language used by "ordinary people". The second question was how to identify the assessment of health risks associated with environmental pollution factors given by the population in general or specific social groups. Finding an answer to this question provides an instrument for identifying public risk assessment that is considered by management when population health risks are regulated.

Materials and methods. The study consisted of two stages. At the first stage, we collected data on subjective correlations between the verbal likelihood scale and its numeric expression. The data were collected by performing formalized questionings among people living in industrial cities. Overall, three questioning were performed over several years (2014[2], 2016[3] and 2020[4]). Each questioning suggested the respondents answer seven questions: "How

[2] The formalized questioning of Perm region population aged 18 years and older "Risk communications within the environmental risks sphere" (the grant provided by the RHSF No. 14-16-59011) was performed by the experts from Federal Scientific Center for Medical and Preventive Health Risk Management Technologies in 2014, a phone survey, quota sampling (*n* = 1041).

[3] The formalized questioning of workers employed at PJSC Uralkalii (town of Berezniki) was performed by the experts from Federal Scientific Center for Medical and Preventive Health Risk Management Technologies in 2016, handout questionnaires filled in at workplaces, target sampling (*n* = 119).

[4] The formalized questioning of people living in large industrial cities in Russia was performed by the experts from Federal Scientific Center for Medical and Preventive Health Risk Management Technologies in 2020 by handout and on-line questioning, opportunity sampling (*n* = 163).

do you estimate a probability of an event in %, if this event is …". Each question had various endings corresponding to the verbal likelihood scale suggested in the IPCC Report (virtually certain; very likely; likely; about as likely as not; unlikely; very unlikely; exceptionally unlikely) (*n* = 1324). These data represent opinions of working age population aged from 18 to 60 years living on territories with high anthropogenic loads.

The second stage involved testing the procedure for examining health risk assessments given by population / social groups. The focus was on health risks associated with ambient air pollution and the assessments relied on the results produced at the previous stage. We performed an online survey in Perm and Krasnoyarsk in 2021; the link to it was located on SurveyMonkey, a specialized survey platform for online surveys. The city population was questioned without any limitations imposed on social and demographic features (except age, 18 years and older; convenience sampling). In addition, targeted advertising was placed in virtual social networks "VKontakte" and "Odnoklassniki" to attract their users to participate in the survey (they should be 18 years or older and live in Krasnoyarsk or Perm; opportunity sampling) (*n* = 1334). Then, we applied simple random sampling to "remove" redundant respondents to create a sampling that reflected the actual structure of urban working age population in Russia (*n* = 677).

The procedure involved reducing subjective assessment of health risks associated with ambient air pollution by people living in an industrial city to the standard risk assessment formula:

$$R = P \cdot g,$$

where P is probability, g is gravity.

Likelihood of risk realization (likelihood to fall sick) was established by using two questions. The first one was, "Here you can see a list of diseases, which, as some people think, are associated with ambient air pollution. In your opinion, how likely are ***those*** people from your microdistrict who do not have these diseases to fall sick with them?" The second question was, "In your opinion, how likely are ***you*** to fall sick with these diseases if you do not have them now?" The list included such diseases as bronchial asthma, bronchitis, ischemic heart disease, stroke, chronic obstructive pulmonary disease, and lung cancer. The scale was taken from the procedure: Virtually certain; Very likely; Likely; About as likely as not; Unlikely; Very unlikely; Exceptionally unlikely. To analyze the suggested verbal likelihood scale, we transformed the respondents' answers into percents according to the data obtained at the first stage in the study[5]. These two questions for measuring subjective assessments of how likely a disease was are determined by risk perception being combined with multiple prejudices and opinions; people's inclination to believe they are somehow immune to risk is one of them [10]. A task was to get an insight into the difference between how people assessed likelihood of risk realizations for themselves and for others. This was necessary to make conclusions, first, about this prejudice influencing assessments made by people regarding likelihood of diseases associated with ambient air quality and, second, how great a mismatch was between these assessments.

Gravity of health outcomes associated with the analyzed risks was assessed by using the following question, "How severe do you think the enlisted diseases are?" The scale suggested the following estimates: Severe; Average; Mild. Therefore, to assess a certain risk, respondents first had to assess likelihood of a specific nosology and then they had to assume how grave health outcomes would be if the risk was realized[6].

Next, a risk assessment matrix was created (Table 1)[6, 7] showing shares of popula-

[5] At the first stage, the respondents were suggested to correlate a verbal expression of likelihood and its percent expression according to their conceptions.

[6] State Standard GOST R 58771-2019. The National Standard of the Russian Federation. Risk management. Risk assessment technologies; approved and introduced by the Order of the Federal Agency on Technical Regulation and Metrology on December 17, 2019 No. 1405-st. Moscow, Standartinform, 2020, 86 p. (in Russian).

[7] State Standard GOST R 51901.1-2002. The State Standard of the Russian Federation. Dependability management. Risk analysis of technological systems; approved and introduced by the Order of the RF Gosstandart on June 7, 2002 No. 236-st. Moscow, Gosstandart of Russia, 2002, 23 p. (in Russian).

tion who assessed a risk as high, average, or low.

Obviously, the matrix is created according to the “traffic light” rule and based on how individuals see a certain situation [11, 12]. We can determine an element in the matrix that corresponds to a cross point between likelihood and gravity and determine a risk rate established by different groups of respondents. The matrix included three risk rates (H meant high risk (red color); A, average risk (yellow color); and L, low risk (green color)). Quantitative estimates of an event likelihood that were obtained at the first stage showed numeric ranges of likelihood corresponding to its quantitative characteristics.

All the obtained data were statistically analyzed using SPSS 16.0 software package for Windows.

Results and discussion. Data on how people understand likelihood and how its different levels are reflected in their minds when they hear different verbal expression describing them made it possible to establish that only 70 % of the respondents correlated a text with a number. The remaining 30 % had certain difficulty in doing it since they either omitted a difficult question or put the same values in all their answers.

Overall, 1324 people were questioned at different times. After we deleted incorrect data (396 completely omitted answers), we got the combined data array with 928 observation units in it (70 % of the initial data array). We included those respondents who answered at least one of seven questions assuming that if an answer was given, then this word or expression had its reflection as a number in a person’s mind. Two ± one % of the respondents as per each specific variable failed to cope with the task and omitted the question. We established that transformation of words into numbers was not influenced by any sociodemographic characteristics of the respondents. Statistical significance of differences between the variables as per sex, age, incomes and education was checked in every survey (2014, 2016 and 2020); it was also checked as per combined data produced by all the surveys and in this case a year of a specific survey was added as another parameter. We did not detect any authentic differences.

The gradation suggested by the IPCC was established not to correspond to the senses existing in mass perception of the respondents from Russia. For example, experts believe that words “virtually certain” should correspond to likelihood that exceeds 99 %; still, our analysis revealed that only 14.1 % of the respondents understood this expression in the same way. This concerned also the expression “very likely”, which, according to the IPCC experts, means a likelihood higher than 90 %, but only 8.3 % of the respondents are of the same opinion (Table 2).

The highest percent of opinion matches is observed for the average likelihood (about as likely as not) and low likelihood (unlikely) since 83.8 % and 70.3 % of the respondents’ opinions accordingly matched expert estimates. The category “likely” is perceived similarly by experts and “ordinary people” in 41.6 % of the cases. The highest likelihood (“Virtually certain” and “Very likely”) and the lowest one (“Very unlikely and “Exceptionally unlikely”) are estimated differently; therefore, it is necessary to determine how they are interpreted by population in order to interact with people more effectively when informing them about risks.

Our analysis of mean values[8] revealed that the verbal expression “Virtually certain” was associated with likelihood within the range of 85–88 % in the respondents’ minds; “Very likely”, 77–79 %; “Likely”, 64–66 %; “About as likely as not”, 48–49 %; “Unlikely”, 23–25 %; “Very unlikely”, 13–15 %; and “Exceptionally unlikely”, 5–7 % (Table 3).

We used the mean model due to the data being expressed as per metric scales; “a measure of the central trend for nominal variables can be only the modal value, that is, the most

[8] Quality of the mean value as a model was estimated by analyzing the standard error of the mean and comparing values with general mathematical expectation ((mean value ± 2) · the standard error of the mean).

Table 1

A model matrix showing health risk assessment by population

	Qualitative characteristic of an event likelihood						
	Virtually certain	Very likely	Likely	About as likely as not	Unlikely	Very unlikely	Exceptionally unlikely
	Quantitative characteristic of an event likelihood						
Gravity of outcomes	n–n %	n–n %	n–n %	n–n %	n–n %	n–n %	n–n %
Severe	H	H	H	H	H	A	A
Average	H	H	A	A	A	L	L
Mild	A	A	L	L	L	L	L

Table 2

Expert and ordinary people's opinions on numeric expression and verbal description of likelihood

Verbal expression / word	Numeric expression of a verbal expression / word suggested by the IPCC (%)	A share of respondents with the opinion matching the IPCC gradation (%)
Virtually certain	> 99	14.1
Very likely	> 90	8.3
Likely	> 66	41.6
About as likely as not	33–66	83.8
Unlikely	< 33	70.3
Very unlikely	< 10	25.5
Exceptionally unlikely	< 1	17.9

Table 3

Mean values of a numeric expression for a verbal likelihood description

Verbal expression	Mean value	The standard error of the mean
Virtually certain	86.6	0.57179
Very likely	77.7	0.53538
Likely	65.1	0.63818
About as likely as not	48.6	0.44188
Unlikely	24.2	0.44748
Very unlikely	13.8	0.39453
Exceptionally unlikely	6.0	0.30225

common number in a data set. The modal value does not have any spread" [9]. The median is used as a measure of the central trend for variables given as per the ordinal scale. Therefore, when testing the procedure for establishing group assessments of health risks associated with ambient air pollution, we used ranges of mean values of numeric equivalents determined for verbal likelihood description to analyze the results.

Subjective perception of health risks associated with ambient air pollution was determined through the respondents' ideas about what *diseases could occur* due to this factor and *how grave and likely* those diseases would be (that is, risk assessments made by the respondents).

In the respondents' opinion, ambient air can be a risk factor of bronchial asthma since 78.1 % of them mentioned it. This opinion was

[9] Kryshtanovskii A.O. Analiz sotsiologicheskikh dannykh s pomoshch'yu paketa SPSS: uch. posobie dlya vuzov [Sociological data analysis with SPSS software: the manual for higher education institutions]. Moscow, HSE Publ., 2006, 281 p. (in Russian).

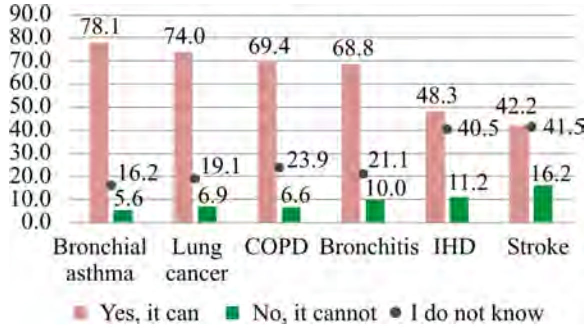

Figure 1. Distribution of the respondents' answers to the question "Do you think these diseases can occur due to ambient air pollution in those people living in your microdistrict who do not have them now?" (a % of the total number of the respondents)

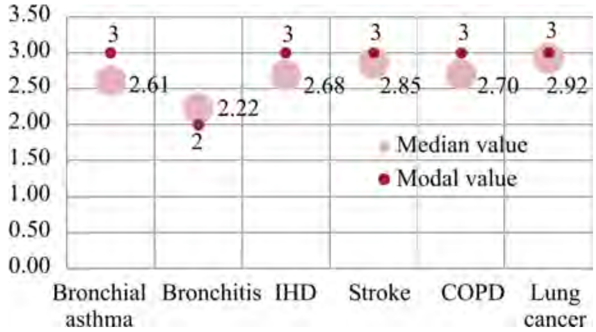

Figure 2. Measuring central trends in subjective assessments of disease severity

more typical for people with higher education[10] and from older age groups[11]. Most respondents think that ambient air pollution creates risks of lung cancer (74.0 %), chronic obstructive pulmonary disease (COPD) (69.4 %), and bronchitis (68.8 %). A bit less than a half of the respondents believe ambient air pollution to cause risks of such diseases as ischemic heart disease (IHD) (48.3 %) and stroke (42.2 %) (Figure 1).

In general, severity of a disease is estimated by experts as a ratio between its prevalence and mortality caused by it. All the diseases are divided into three groups: severe, average and mild. Accordingly, each disease has its severity depending on a group. This is usually called severity of illness index (SOI) and it varies from 0 to 1. Thus, diseases from the "mild" group tend to have average SOI that is equal to 0.0000055 (the range is 0.000001–0.00001); diseases from the "average" group, 0.0042 (the range is 0.000011–0.0085); diseases from the "severe" group, 0.50 (the range is 0.0079–0.099). When SOI equals 1, it means death. Bronchitis, IHD, stroke and bronchial asthma are known to belong to the average group whereas COPD and lung cancer fall within the severe category[12]. The respondents were suggested to subjectively estimate severity of each disease using a three-score scale where 1 means a disease is mild and 3 means it is severe (Figure 2).

Obviously, the research results indicate that most respondents believed practically all the enlisted diseases were severe, bronchitis excluded.

We identified risks of each enlisted disease according to the respondents' opinions using the risk assessment matrix and showed shares of the respondents who determined a specific likelihood and severity of a disease. A calculation example is provided in Table 4.

We can conclude that in general risks of bronchial asthma associated with ambient air pollution were characterized as mild by 11.0 % of the respondents (this zone is colored green in Table 4); risks were assessed as average (the yellow zone) by one third of the respondents (35.3 %); and the remaining 53.6 % of the respondents believed those risks were high (the red zone).

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[10] We detected statistically significant differences in the variable "Do you think ambient air pollution can cause bronchial asthma in those people living in your microdistrict who do not have this disease now?" depending on the respondents' education (the Kruskal – Wallis test; the significance equals 0.015).

[11] We detected statistically significant differences in the variable "Do you think ambient air pollution can cause bronchial asthma in those people living in your microdistrict who do not have this disease now?" depending on the respondents' age (the Kruskal – Wallis test; the significance equals 0.000).

[12] Methodical guidelines MR 2.1.10.0033-11. 2.1.10. Sostoyanie zdorov'ya naseleniya v svyazi s sostoyaniem okruzhayushchei sredy i usloviyami prozhivaniya naseleniya. Otsenka riska, svyazannogo s vozdeistviem faktorov obraza zhizni na zdorov'e naseleniya [Population health under exposure to the existing ecological situation and living conditions. Assessment of health risks associated with effects produced by lifestyle-related factors on population health]. Moscow, Rospotrebnadzor's Federal Center for Hygiene and Epidemiology, 2011, 62 p. (in Russian).

Table 4

Assessing risks of bronchial asthma associated with ambient air pollution in Perm and Krasnoyarsk (% of the total number of the respondents)

	Qualitative characteristic of event likelihood						
	Virtually certain	Very likely	Likely	About as likely as not	Unlikely	Very unlikely	Exceptionally unlikely
Gravity of outcomes	Quantitative characteristic of event likelihood (%)						
	85–88	77–79	64–66	48–49	23–25	13–15	5–7
Severe	6.9	9.3	12.7	13.4	8.3	5.3	5.8
Average	1.2	1.8	7.2	10.5	6.2	4.1	4.3
Mild	0.3	0.0	0.3	0.6	0.4	0.4	0.9

Table 5

Assessing risks of the enlisted diseases associated with ambient air pollution in Perm and Krasnoyarsk (% of the total number of the respondents)

		Bronchial asthma	Bronchitis	IHD	Stroke	COPD	Lung cancer
Assessing risks for oneself	High	53.6	37.2	59.5	69.9	58.8	74.9
	Average	35.3	44.2	30.7	25.8	33.2	23.0
	Low	11.0	18.6	9.7	4.3	8.0	2.1
Assessing risks for others	High	62.3	38.1	63.8	74.6	67.2	85.5
	Average	32.3	46.1	26.6	22.0	26.6	12.7
	Low	5.3	15.8	9.6	3.4	6.2	1.8

Table 5 provides the results produced by assessing risks of all the enlisted diseases associated with exposure to ambient air pollution.

It was foreseeable that the respondents assigned the highest risk (74.9 %) to lung cancer. Interestingly, most respondents also perceived risks of stroke and IHD as high (69.9 % and 59.5 % accordingly). Although less than a half of the respondents believed that these two diseases were associated with ambient air pollution, their outcomes were considered grave by 88.2 % and 71.5 % of the respondents. Quite a high share of the respondents thought these diseases to be likely with their likelihood being 48–66 % (this share exceeded 45.0 %). Obviously, we should question an instrument applied to measure estimates of disease likelihood. Although the question included a special instruction that likelihood should be estimated considering a health risk factor associated with ambient air pollution, we cannot possibly be sure that this instruction was truly taken into account by the respondents when they gave their assumptions on the matter. Stroke and ischemic heart disease are widespread; if initially respondents state that these diseases are not associated with ambient air pollution and then claim that they are highly likely to appear, we can clearly see that the risk factor itself, ambient air pollution in our case, has been lost by the respondents. We checked correlations between the variables to identify any possible correlation of the risk factor and the health outcome with likelihood estimate and failed to confirm this doubt. People who do not associate stroke[13] and IHD[14] with ambient

[13] We established statistically significant differences in the variable "In your opinion, how likely are ***you*** to have stroke?" depending on answers to the question "Do you think ambient air pollution can cause stroke in those people living in your microdistrict who do not have it now?" (the Kruskal – Wallis test; the significance equals 0.000. Cramer's V is 0.308, $p = 0.000$ (a moderate correlation)).

[14] We established statistically significant differences in the variable "In your opinion, how likely are ***you*** to have IHD?" depending on answers to the question "Do you think ambient air pollution can cause IHD in those people living in your microdistrict who do not have it now?" (the Kruskal – Wallis test; the significance equals 0.000. Cramer's V is 0.342, $p = 0.000$ (a moderate correlation)).

air pollution actually tend to estimate their likelihood due to this pollution as low. Therefore, these results can be due to gravity of outcomes ascribed to a given disease.

Risks of bronchitis are most often (62.8 % of the respondents) estimated as low or average due to outcomes of this disease being perceived as mild (10.6 %) or average (59.8 %). Although its likelihood is estimated as high (starting from 64 % and higher in 72.2 % of the cases), the risk, as a whole, is considered permissible.

The risk characteristics outlined above are based on estimating likelihood of falling sick with a certain disease and gravity of its outcomes for the respondents themselves. When the respondents estimated this likelihood and gravity for other people, their estimates tended to be higher. For example, a risk of COPD in estimated by the respondents as high by 8.7 % more frequently for other people than for themselves; COPD, by 8.4 % more frequently; and lung cancer, by 10.6 %. This different subjectively estimated likelihood indicates there is a typical cognitive distortion here associated with risk perception and likelihood estimates. We can call it "an illusion of invulnerability" when a person or a group of people believe that "bad things" more often happen to others and not to them.

The results produced by cluster analysis showed that the analyzed sampling was divided into three clusters. The first one was made of people with their risk estimates being closer to average and they accounted for almost half of the respondents (48.8 %). The second cluster included people who more often estimated risks as high (approximately one third of the respondents or 29.5 %). The third cluster was made of respondents who tended to estimate risks of diseases associated with ambient air pollution as being low (one fifth of the respondents or 21.7 %).

Conclusion. "Non-experts" usually have certain difficulty perceiving numeric expressions of likelihood. Bearing this in mind, we attempted to correlate qualitative likelihood characteristics, that is, its verbal descriptions, with ranges of its numeric values that came to people's minds when they heard certain words or expressions. We found out that only 70 % of people actually correlated words with figures while the remaining 30 % failed to accomplish the task. We determined that some people among those who correlated verbal descriptions of likelihood with their quantitative expressions preset values for them that fell out of the ranges estimated by experts.

Experts tend to estimate likelihood approximately by 10 % higher than "ordinary people" when it comes down to such words as "Virtually certain" and "Very likely". "Likely", "About as likely as not" and "Unlikely" are also estimated in a different way, but the gap between the opinions is smaller in this case. "Very unlikely" and "Exceptionally unlikely" are estimated by experts approximately by 5 % lower than by "ordinary people". Certain differences were also detected regarding estimates of disease severity. According to expert estimates, only two out of six enlisted diseases are severe, namely lung cancer and COPD; the remaining ones have average severity. In contrast, most people tend to think that all the enlisted diseases, except bronchitis, are severe.

Our results make it possible to solve a practical task related to informing people about health risks and to overcome a so-called language barrier between experts and ordinary people. This includes, among other things, messages aimed for decision-makers that can be adapted considering all the detected peculiarities of risk perception. For example, when experts have ready results produced by risk assessment, they can correlate likelihood values exactly with the words that reflect them correctly in "ordinary people's" minds and use these words to create information texts for people or decision makers.

It is necessary to know how people assess risks to make relevant decisions on how to manage them. This necessity calls for identifying what instruments can be used to get this knowledge. In this research, we have considered the procedure for identifying public assessments of health risks associated with ambient air pollution. This procedure includes using such variables as likelihood and severity of outcomes thereby making it possible to create risk assessment matrices. Such matrices make for faster distribution of response strategies and "it is easier for decision-makers to fill in a risk matrix when they operate with specific response strategies and not with abstract generalized risk categories" [14]. If risk managers know how people assess this or that risk, they have better understanding what strategy should be developed considering both experts' opinions and public expectations. Health risk management activities are aimed at a) a factor that creates a risk [15–17], ambient air pollution in our case, and they should reduce its effects on health, in other words, ambient air quality should be improved; b) at influencing risk consumers, that is, communicating with them about this risks [18]. In the first case, managerial decisions are mostly based on expert risk assessments; in the second case, on public ones. When people assess health risks as high and significant, communications should be built on a dialogue-based model. Bearing in mind, that risk perception and its subjective assessment includes two components, emotional and cognitive one [19], these activities should be aimed at increasing people's trust in decision-makers (working with irrational components in an ordinary mind) and at developing the cognitive component, that is, providing people with more knowledge about ambient air quality.

The suggested procedure helps determine approximate proportions regarding distribution of risk assessments in the analyzed group. This pilot research has established that almost half of the respondents tend to estimate health risks associated with ambient air pollution as being average and one third consider them high. The created matrix of public health risk assessment indicates that emergency activities are redundant but certain urgent communications are required since most people tend to estimate the analyzed risks as average or high. Should the risks be estimated only as average, only scheduled communications with people would be necessary without any pressure or speeding up. When people estimate risks as low (and experts are of the same opinion), such a situation does not require any specific risk communications. However, if people estimate risks as low but experts consider them high, additional risk communications should be introduced since subjective health risk assessments underlie choices on risk-associated behavior (self-preservation or self-destruction) [20].

We have developed an approach to identifying assessment of health risks associated with ambient air pollution by a large social group. The approach is universal and can be applied to identify assessment of other health risks.

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Research article

METHODICAL APPROACHES TO RAISING THE RELIABILITY OF HEALTH RISK ASSESSMENT WHEN USING POLYMER MATERIALS IN DRINKING WATER SUPPLY

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Plastic pipes and coatings may contain additives, including metal stabilizers and antioxidants, designed to protect the material during manufacture and use. Some chemical compounds can be released from these plastic pipes and affect quality of drinking water. The article focuses on analyzing various approaches to examining polymer materials with the aim to assess migration of chemicals into drinking water. These approaches usually underlie methodologies of hygienic assessment developed for polymers.

Migration was assessed under the same conditions as per two types of migration processes, a continuous and a sequential one. These two types of migration processes emulate conditions typical for different flows in drinking water pipelines: situations of continuous stagnation in the system and a standard flow when water is renewed regularly in water supply networks. More than 20 organic compounds were identified in tested water samples. Most of them occurred in small concentrations (excluding benzenesulfonic acid butyl amide). Moreover, many of these chemicals are not regulated in drinking water, there no standards or reference concentrations fixed for them or a relevant toxicological assessment. Given that, it is practically impossible to assess health risks caused by exposure to these chemicals according to conventional assessment procedures.

It was also shown that release of chemicals differed considerably under different experimental designs. The results produced by successive migration tests indicated that intensity of migration from polymer materials the pipes were made from tended to change over time whereas the results of continuous migration tests showed that in case of stagnation quality of drinking water could deteriorate rather rapidly due to migration of organic compounds.

Keywords: *water supply, drinking water, hygienic assessment of polymer materials, polymers, migration, polyurethane coatings, chromato-mass spectrometric studies, water risk.*

Polymer pipes and polymer coatings protect inner surfaces of pipelines; they are often used to repair and reconstruct the existing drinking water supply systems, including main and distribution water supply networks since they are cheaper and easier to install in comparison with metallic alternatives. Unfortunately, plastic pipes and coatings can contain various additives such as metal stabilizers, plasticizers and other antioxidants that protect the materials they are made of during manufacturing and utilization. Since a plasticizer molecule or a molecule of any other additive is usually not chemically bound to a polymer chain, it can be released when a polymer is being manufactured or later during its routine use. Migration of plasticizers during a polymer product life span can contaminate the environment and do damage to human health [1–7].

In time, contamination of drinking water with organic compounds is going to become a more pressing issue due to wider use of up-to-date polymer coatings in pipelines. At present, such toxic environmental contaminants as semi-volatile organic compounds

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(SVOC) already occur everywhere [8–10]. The study [11] describes an established considerable correlation between SVOC contents in drinking water and a scale of economy and population in cities in China, which means that the problem is aggravated by the scientific and technical progress in general and developing chemical industry in particular. However, occurrence of semi-volatile chemical compounds in tap water and associated human health risks have not been studied enough [12], despite the fact that these compounds can produce negative effects on human health even in low concentrations. To assess this exposure and calculate associated risks, relevant toxicity tests are required. However, data on toxicity are not available for many compounds and even if they are, it takes specific searching in literature sources to find them.

Field observations can give an opportunity to trace migration of organic compounds into drinking water [13–20]. Migration of pollutants into tap water is potentially influenced by various housing types since they tend to vary in terms of water supply and distribution system, water consumption choices and other hydraulic factors. Contents of organic compounds in tap water turned out to be greatly dependent, among other things, on whether housing was high-rise or landed [18]. Migration of plastic organic compounds falls considerably during the first several months of water supply exploitation. However, a period during which drinking water is stagnated in pipes also has great influence on contents of organic compounds. Organic compounds migrate from materials into drinking water in higher quantities as a stagnation period becomes longer. The authors of the work [19] considered it necessary to create an instruction for users stating the necessity to drain certain amount of water prior to drinking it.

Although, a conventional way to reduce pollutant concentration in drinking water is to replace it with fresh one, there are still disputes on the issue and the issue itself has not been given proper attention in scientific literature. All this makes it difficult to predict what volume of water will be necessary to reduce the secondary organic pollution.

Results described in the work [20] indicate that it is likely to take several days of continuous flushing to remove pollutants in quantities sufficient to reduce their levels below the hygienic standards.

At present, mathematical molecular dynamic simulation of diffusion can be used to calculate theoretical migration of additives for various surface-to-volume ratios and concentrations of compounds introduced into a polymer on the surface of the material. Precise data on coefficients showing diffusion of additives in a polymer make it possible to predict migration into drinking water over a certain period [21–23]. It was shown in several previous domestic studies that migration decreased over time as per an exponential curve[1]. It was established that chemical compounds were washed out most intensively from polymer materials during the first days of a contact with water; later on, levels of toxicant release decreased.

Studies on chemical migration and calculation of diffusion coefficients for additives in a polymer give a possibility to predict probable secondary pollution in drinking water. Analysis of the results gives grounds for developing various approaches to hygienic assessment of polymer materials. It is a rather serious methodical issue since correct assessment of exposure to a hazardous matter in water is important for interpreting its results and for further health risk assessment as a vital method of hygienic assessment. The matter is that multiple different factors can change composition, concentration, and, consequently, toxicity of a mixture of migrating compounds and can ultimately influence the precision of prediction techniques.

[1] Sheftel V.O., Dyshinevich N.E., Sova R.E. Toksikologiya polimernykh materialov [Toxicology of polymer materials]. Kiev, Zdorov'ya, 1988, 210 p. (in Russian).

These factors complicate assessment of health and environmental risks caused by these compounds. Besides, any studies on assessment of risks created by a mixture of compounds will unavoidably face insufficient toxicological data and gaps in knowledge about synergic effects produced by a mixture of pollutants [24].

Similar conclusions were made by the authors who assessed water risks [25]. They concluded that most compounds never occur in concentrations that individually create an appreciable human health risk. However, they noted that several detected substances might still impose certain health hazards, for example, vinyl chloride, trichloroethylene, bromodichloromethane, phenol, 2-chlorobenzylamine, and some others. For part of the selected substances, toxicological risk assessment for drinking water could not be performed since no data on their toxicity were available. In case the necessary data were absent, the authors suggested using "Threshold of Toxicological Concern" (TTC) to assess screening level risks.

Turning back to correct assessment of exposure to a matter in water, we should note that in such countries as Great Britain, Germany and some others, hygienic assessment of polymer materials is performed after water change. This assessment involves analyzing water extracts from two- or three-day contacts between a material and drinking water. That is, the assessment is based on analyzing a subsequent migration process that simulates a normal (standard) water flow with regular water renewal in water supply networks.

In Russia, according to the methodical guidelines MU 2.1.4.2898-11 "Sanitary-epidemiological examinations (tests) of materials, reagents and equipment used for water treatment and preparation"[2], hygienic assessment on materials used in drinking water supply is based on examining a continuous migration process that simulates a continuous stagnation of water in a water supply network.

Therefore, **our research goal** was to examine and compare different approaches to hygienic assessment of polymer materials with its focus on chemical migration into drinking water. Migration was estimated under similar conditions as per two types of migration processes, a continuous and subsequent one. These two types emulate conditions typical for different flows in drinking water pipelines: continuous stagnation in the system and a normal flow when water is regularly renewed in drinking water supply networks.

Materials and methods. The study involved examining a two-component polyurethane coating manufactured in a European country. According to the covering technical documentation, this material is allowed for use in drinking water supply in a country of origin. According to a manufacturer's manual, this coating is used in main pipelines with a pipe diameter varying from 100 to 610 mm.

The samples prepared for analysis were smooth and solid but still elastic grey plates, 0.3 cm thick, without any smell.

We ran two series of tests to confirm our previous assumptions [26, 27]. The first series concentrated on a continuous migration process. The two-component polyurethane coating was assessed bearing in mind the Unified Requirements (The EAEU Unified sanitary-epidemiological and hygienic requirements to

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[2] MU 2.1.4.2898-11. Pit'evaya voda i vodosnabzhenie naselennykh mest. Sanitarno-epidemiologicheskie issledovaniya (ispytaniya) materialov, reagentov i oborudovaniya, ispol'zuemykh dlya vodoochistki i vodopodgotovki / utv. Rukovoditelem Federal'noi sluzhby po nadzoru v sfere zashchity prav potrebitelei i blagopoluchiya cheloveka, Glavnym gosudarstvennym sanitarnym vrachom Rossiiskoi Federatsii; vved. v deistvie 12.07.2011 (vzamen MU 2.1.4.783-99) [Drinking water and drinking water supply in settlements. Sanitary-epidemiological examinations (tests) of materials, reagents and equipment used for water treatment and preparation, approved by the Head of the Federal Service for Surveillance over Consumer Rights Protection and Human Well-being, the RF Chief Sanitary Inspector; introduced on July 12, 2011 (as a replacement to the MU 2.1.4.783-99)]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200089967 (February 11, 2022) (in Russian).

goods that are subject to sanitary-epidemiological surveillance (control)”[3] (2010)). We also examined certain indicators that were not mandatory in the assessment of polymer materials used in drinking water supply. The samples were preliminarily prepared in accordance with the methodical guidelines MU 2.1.4.2898-11 “Sanitary-epidemiological examinations (tests) of materials, reagents and equipment used for water treatment and preparation”[2].

The second series involved using a procedure accepted by the DWI (Drinking Water Inspectorate, Great Britain) as a model one to examine a continuous migration process. The samples were washed with running water for one hour and then were submerged into water for testing. The following periods of contacts with water (ST) were applied: ST1, 1 hour; ST2, 23 hours; ST3, 24 hours; ST4, 24 hours; ST5, 72 hours; ST6, 72 hours. After each period of a contact with water (ST) was over, a sample was taken out and placed into fresh water (distillate) for the next period. The samples from ST2, ST3 and ST6 were analyzed.

A ratio between volume of a material and volume of contacting water was 1 cm^2 to 1 cm^3. Tap water from a distribution network in Moscow and distilled water were used as initial water to prepare water extracts (test samples). The water extracts were kept under 20 ^{o}C. The same water types were applied as reference samples in order to perform proper hygienic assessment. Test samples (water extracts) and reference samples used in the first series of the study were taken on the 1st, 3rd, 5th, 15th and 30th day of the experiment.

The water extracts were analyzed to determine their organoleptic properties and to examine migration of organic compounds and metals. Organoleptic properties of water extracts (smell, taste, color and turbidity) were examined with physical and chemical methods; we also determined water pH and permanganate oxidation.

Tests aimed at identifying and quantifying hardly volatile organic compounds in water were performed by using chromatography-mass-spectrometry. This method allows reliable identification and quantification of a wide range of organic compounds C1-C40 in water with unknown pollution structure with the sensitivity at the level of hygienic standards or even below them. The examination was performed on Focus GC chromatography-mass-spectrometer with DSQ II (USA) in conformity with the existing methodical documents on control over organic compounds. We also identified several substances that were mandatory within this hygienic assessment according to the Unified sanitary requirements. These substances were formaldehyde, acetaldehyde, methanol and ethylene glycol.

Non-organic compounds were analyzed in the water extracts according to the State Standard GOST 31870-2012[4] by using atomic spectroscopy.

Results and discussion. In the first series of tests, the examined material practically did not make any changes into smell or taste of a water extract. Turbidity and color of Moscow tap water did not grow considerably after contacts with it. We also did not detect any differences between water pH of the test and reference samples.

Having analyzed data on probable migration of organic compounds from the examined material, we revealed that permanganate oxidation grew in the test water extract practically in the same way as in the reference samples and did not exceed hygienic standards.

[3] Edinye sanitarno-epidemiologicheskie i gigienicheskie trebovaniya k produktsii (tovaram), podlezhashchei sanitarno-epidemiologicheskomu nadzoru (kontrolyu) (s izmeneniyami na 22.02.2022) / utv. Resheniem Komissii tamozhennogo soyuza ot 28.05.2010 № 299 [The EAEU Unified sanitary-epidemiological and hygienic requirements to goods that are subject to sanitary-epidemiological surveillance (control) (last edited on February 22, 2022), approved by the Decision of the Customs Union Commission on May 28, 2010 No. 299]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/902249109 (March 13, 2022) (in Russian).

[4] GOST 31870-2012. Drinking water. Determination of elements content by atomic spectrometry methods: inter-state standard, approved by the Inter-state Council on Standardization, metrology and certification (the meeting report issued on November 15, 2012 No. 42); became valid on January 01, 2014. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200097409 (March 13, 2022) (in Russian).

To analyze migration of organic compounds, distilled water under 20 °C was used as initial water to prepare water samples. Tests aimed at identifying and quantifying organic compounds in water were performed by using chromatography-mass-spectrometry on the 1st, 2rd and 5th day of the experiment. We identified up to 27 organic compounds in the water extracts from the samples of the examined two-component polyurethane coating (Table 1).

Table 1

Organic compounds identified in water extracts from the analyzed polyurethane-based material (under 20 °C) when a continuous migration process was examined

№	Compound	Gross formula	CAS	Concentration, mg/dm³		
				1st day	3rd day	5th day
1	Tetradecane	$C_{14}H_{30}$		0.003	-	0.004
2	Hexadecane	$C_{16}H_{34}$		0.002	0.004	0.004
	spirits					
3	Hexadecanol	$C_{16}H_{34}O$	36653-82-4	0.003	-	0.003
4	Heptadecanol	$C_{17}H_{36}O$		0.006	-	-
	phenols					
5	4,4-isopropylidene diphenol	$C_{15}H_{16}O_2$	80-05-7	0.003	0.006	-
6	2,6-Di-tert-butyl-4-ethylphenol	$C_{16}H_{26}O$	4130-42-1	0.004	-	-
7	Para-tert-butylphenol	$C_{10}H_{14}O$	98-54-4	0.005	0.002	
8	2,4-Di-tert-butylphenol	$C_{14}H_{22}O$	96-76-4	-	0.003	
	simple ethers					
9	2,5,8,11- Tetraoxadodecane *	$C_8H_{18}O_4$	112-49-2	0.056	0.016	-
10	Pentaoxapentadecane	$C_{10}H_{22}O_5$	-			0.023
	ketones					
11	Benzophenone	$C_{13}H_{10}O$	119-61-9	0.004	0.004	0.008
	carboxylic acids					
12	Tetradecane	$C_{14}H_{28}O$	544-63-8	-	0.005	0.004
13	Hexadecane	$C_{16}H_{32}O$	57-10-3	0.011	0.019	0.016
	complex ethers					
14	Dimethylethyl methyl propanol ether of 2-methylpropanoic acid	$C_{16}H_{30}O_4$	74381-40-1	0.005	0.014	0.011
15	Diisobutyl ether of adipic acid	$C_{14}H_{26}O_4$	141-04-8	0.030	0.025	0.014
16	Dimetoxy tetraethylene glycol*	$C_{10}H_{22}O_5$	143-24-8	0.018	0.64	**0.149**
17	Methyl ether of tetrapropylene glycol *	$C_{13}H_{28}O_5$	20324-34-9	0.012	-	-
18	Dimethyl ether of hexaethylene glycol*	$C_{14}H_{30}O_7$	1072-40-8	0.035	0.050	**0.227**
19	Acetyl tributyl citrate	$C_{20}H_{34}O_8$	77-90-7	-	-	0.022
	phthalates					
20	Dimethyl phthalate	$C_{10}H_{10}O_4$	131-11-3	0.001	0.003	-
21	Diisobutyl phthalate	$C_{14}H_{26}O_4$	84-69-5	0.032	0.026	0.033
22	Dibutyl phthalate	$C_{14}H_{26}O_4$	84-69-2	0.021	0.019	0.078
23	Monobutyl phthalate	$C_{12}H_{14}O_4$	131-70-4	0.063	0.023	0.084
	Nitrogen-containing compounds					
24	Acridine	$C_{13}H_9N$	260-94-6	0.006	0.003	0.014
25	1,2,3,4,5,6,7,8-Octahydroacridine	$C_{13}H_{17}N$	1658-088-8	0.003	0.003	0.003
26	4-Piperidinyl-1-methyl-4(2-methyl-2-propenyl)*	$C_{10}H_{19}NO$	-	0.034	-	-
	Nitrogen-, sulfur containing compounds					
27	N-Butylbenzenesulfonamide	$C_{10}H_{15}NO_2S$	3622-84-2	0.044	0.075	**0.123**

Note: * means identification is conventional.

Some of the identified compounds were detected in insignificant concentrations; most of them do not have maximum permissible levels in drinking water established for them by regulatory documents. These compounds are mostly oxygen-containing ones, including ketones, ethers and phthalates. The following compounds were detected in the highest concentrations: dimethyl ether of hexaethylene glycol, 0.227 mg/l, and dimetoxy tetraethylene glycol, 0.149 mg/l. These compounds were identified conventionally and there are no established MPCs for them in drinking water (ethylene glycol MPC is 1 mg/l). Besides, nitrogen-containing compounds were identified in insignificant concentrations; we also identified a nitrogen- and sulfur-containing compound, namely N-Butylbenzenesulfonamide (CAS No. 3622-84-2) in a concentration higher than its maximum permissible one, 0.123 mg/l (4.1 MPC). N-Butylbenzenesulfonamide is standardized as per a sanitary-toxicological harmfulness factor and assigned into the 2nd hazard category.

Non-organic compounds were analyzed in a water extract on the 30th day in the experiment (an extract from the analyzed material on distilled water under 20 ^{o}C). The analysis revealed that toxic elements belonging to I and II hazard category such as lead, nickel, cobalt and lithium practically did not migrate into water.

We also analyzed such organic pollutants as acetaldehyde and formaldehyde in water extracts. Acetaldehyde migrated in quantities equal to 0.75 MPC and the other identified pollutants occurred in water in even smaller quantities.

As for metals, only chromium and cadmium were detected in water extracts and their concentrations were insignificant, 0.0005 mg/l (0.005 MPC) and 0.00003 mg/l (0.03 MPC) accordingly.

We identified 21 organic compounds (Table 2) in water extracts from the samples of the analyzed polyurethane coating in the second series of tests (when a subsequent migration process was analyzed). All the compounds were detected in insignificant quantities. Their migration was estimated as stable or declining. N-Butylbenzenesulfonamide was detected in concentrations equal to 0.023 mg/l, 0.006 mg/l, and 0.005 mg/l, that is, lower than MPC fixed for this compound and this indicated the migration was declining.

We also determined several substances that were mandatory within this hygienic assessment according to the Unified sanitary requirements. These substances were formaldehyde, acetaldehyde, methanol and ethylene glycol. Acetaldehyde migrated in quantities equal to 0.25 MPC (in ST2 and ST3 periods), all the other analyzed compounds were detected in even lower concentrations.

The analysis of non-organic compounds in water extracts showed that toxic elements belonging to the I and II hazard category and metals that could affect organoleptic properties of water practically did not migrate from the analyzed material.

Conclusion. A potential increase in human health risks caused by drinking tap water that is polluted with organic compounds migrating from plastic is a major challenge in hygienic assessment of polymer materials.

On one hand, a trend to replace metal pipelines with polymer ones in quite justified since the latter are cheaper, easier to install, not prone to corrosion, etc.

On the other hand, it is practically impossible to avoid migration of organic compounds from plastics into drinking water given the contemporary development of chemical industry. There are ongoing studies on developing new plasticizers, searching for new compounds that can secure good mechanic properties of a material with simultaneous limited or even zero migration, resistance to extraction and low volatility[5]. Still, at present, as it is also obviously confirmed by our research results, it

[5] R 1.2.3156-13. Otsenka toksichnosti i opasnosti khimicheskikh veshchestv i ikh smesei dlya zdorov'ya cheloveka: rukovodstvo / utv. vrio Glavnogo gosudarstvennogo sanitarnogo vracha Rossiiskoi Federatsii ot 27 dekabrya 2013 g. [Assessment of toxicity and hazards of chemicals and their mixtures for human health: guide, approved by the (acting as) RF Chief Sanitary Inspector on December 27, 2013]. Moscow, The Federal Center for Hygiene and Epidemiology, 2014, 639 p. (in Russian).

Table 2

Organic compounds identified in water extracts from the analyzed polyurethane-based material (under 20 °C) when a subsequent migration process was examined

№	Compound	Gross formula	CAS	Concentration, mg/dm³		
				ST2	ST3	ST6
1	Tetradecane	$C_{14}H_{30}$		0.003	-	0.002
2	Hexadecane	$C_{16}H_{34}$		0.002	0.004	0.002
	spirits					
3	Hexadecanol	$C_{16}H_{34}O$	36653-82-4	0.003	-	0.003
4	Heptadecanol	$C_{17}H_{36}O$		0.006	-	-
	phenols					
5	4,4-isopropylidene diphenol	$C_{15}H_{16}O_2$	80-05-7	0.003	0.006	-
6	2,6-Di-tert-butyl-4-ethylphenol	$C_{16}H_{26}O$	4130-42-1	0.004	-	-
	simple ethers					
7	2,5,8,11- Tetraoxadodecane*	$C_8H_{18}O_4$	112-49-2	0.056	0.016	-
	ketones					
8	Benzophenone	$C_{13}H_{10}O$	119-61-9	0.004	0.004	-
	carboxylic acids					
9	Tetradecane	$C_{14}H_{28}O$	544-63-8	-	0.005	0.004
10	Hexadecane	$C_{16}H_{32}O$	57-10-3	0.011	0.019	0.016
	complex ethers					
11	Dimethylethyl methyl propanol ether of 2-methylpropanoic acid	$C_{16}H_{30}O_4$	74381-40-1	0.005	0.014	0.011
12	Diisobutyl ether of adipic acid	$C_{14}H_{26}O_4$	141-04-8	0.030	0.025	0.014
13	Dimetoxy tetraethylene glycol*	$C_{10}H_{22}O_5$	143-24-8	0.018	0.016	0.018
14	Methyl ether of tetrapropylene glycol *	$C_{13}H_{28}O_5$	20324-34-9	0.012	-	-
	phthalates					
15	Dimethyl phthalate	$C_{10}H_{10}O_4$	131-11-3	0.001	0.003	-
16	Diisobutyl phthalate	$C_{14}H_{26}O_4$	84-69-5	0.032	0.026	0.033
17	Dibutyl phthalate	$C_{14}H_{26}O_4$	84-69-2	0.021	0.019	0.016
18	Monobutyl phthalate	$C_{12}H_{14}O_4$	131-70-4	0.063	0.023	-
	nitrogen-containing compounds					
19	1,2,3,4,5,6,7,8-Octahydroacridine	$C_{13}H_{17}N$	1658-088-8	0.003	0.003	0.003
20	4-Piperidinyl-1-methyl-4(2-methyl-2-propenyl)*	$C_{10}H_{19}NO$	-	0.034	-	-
	Nitrogen-, sulfur containing compounds					
21	N-Butylbenzenesulfonamide	$C_{10}H_{15}NO_2S$	3622-84-2	0.023	0.006	0.005

is necessary to pay attention to health effects produced by migrating organic compounds.

We assessed a two-component polyurethane coating that was already allowed for use in drinking water supply in the country of its origin. The assessment results indicate that chemical concentrations in the tested water differ considerably in different experimental designs. When a subsequent migration process was analyzed, contents of organic compounds indicated that intensity of their migration tended to decrease over time whereas the results produced by analyzing a continuous migration process according to the methodical guidelines MU 2.1.4.2898-11[2] indicated that quality of drinking water could deteriorate rapidly due to ongoing migration during long-term stagnation.

More than 20 organic compounds were identified in the analyzed water samples. Most of them occurred in insignificant concentrations (excluding N-Butylbenzenesulfonamide). We should note that many of them do not have hygienic standards or reference concentrations in drinking water established for them in regulatory documents and a relevant toxicological assessment is also absent [28]. Given that, it is practically impossible to perform conventional assessment of human health risks caused by exposure to these compounds. Further research is necessary to specify risk parameters and toxicity for specific pollutants as well as to examine how these detected chemicals interact with each other.

Our research confirms the necessity to perform hygienic assessment of materials in conditions close to their actual use in drinking water supply. It concerns estimating an area of contact between a material and test water, analyzing a continuous or subsequent migration process, and applying a set of indicators that are subject to mandatory control. All this again highlights the necessity to actualize and test all the assessment procedures applied to materials that are planned for use in drinking water supply, depending, among other things, on a type of a material and its functional purpose.

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Competing interests. The authors declare no competing interests.

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Research article

SUBSTANTIATING OPTIMAL PARAMETERS OF RISK FACTORS EXISTING IN THE EDUCATIONAL ENVIRONMENT FOR SCHOOLCHILDREN AS PER INDICATORS OF PHYSICAL, MENTAL AND SOMATIC HEALTH

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Schoolchildren are simultaneously exposed to several risk factors associated with the educational process, nutrition in school, ambient air quality, water quality, socioeconomic conditions etc. Their intensity and combinations largely determine indicators of children's physical, somatic and mental health. Our research goal was to quantify influence exerted by a set of risk factors existing in the educational environment on key indicators of schoolchildren's health. We examined 661 children who attended four secondary education institutions of different types. The educational processes in each institution were estimated to check their conformity with sanitary-epidemiological requirements and hygienic standards. Psychological testing included tests aimed at assessing attention, cognitive functions, memory and stress. Laboratory tests involved using liquid and gas chromatography and spectrophotometry. Nutrition provided by schools was estimated to check whether it conformed to the standards stipulated in the Sanitary Rules and Norms SanPiN 2.3/2.4.3590-20. Socioeconomic factors influencing the examined children were assessed as per results produced by a social survey. All the data were statistically analyzed with conventional statistical procedures and mathematical analysis. Influence exerted by risk factors on body composition, incidence and results of psychological testing was assessed by using single-factor logistic regression modeling of "dose – likelihood of a response (effect)" relationships. Significance of the created models was estimated as per Fischer's test.

We established parameters of risk factors that would ensure absence of any negative effects on schoolchildren's health under simultaneous exposure. The article provides the results produced by comparative analysis of the educational environment in different types of schools and its conformity with established optimal parameters as well as existing standards. We have also developed certain recommendations on how to create a health-preserving environment for a contemporary schoolchild, both in school and beyond classes.

Keywords: *children's population, factors of the educational process, blood contamination, socio-economic state, nutrition, body composition, incidence structure, psychological testing.*

Modern educational programs that are implemented in secondary schools produce certain harmful effects on schoolchildren who have to study under combined exposure to several risk factors. These risk factors occur within a school environment due to peculiarities of educational processes. Among such peculiarities, we can mention intensified intellectual loads, a growing number of lessons per day or per week, greater digitalization of educational processes that is usually combined with limited physical activity of children. In addition, meals provided at school do not conform to the health standards and a school environment can often fail to meet the requirements fixed in the sanitary legislation. All this impairs adaptation capabilities of a child's growing body and induces somatic pathologies in schoolchildren[1] [1–4].

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Analysis of results produced by dynamic periodical examinations of schoolchildren indicates that chronic pathologies are becoming more and more frequent among them as they grow older and move to the next level in school education. Growing prevalence has been detected for chronic pathologies of the digestive organs, endocrine, nervous and cardiovascular system; besides, anxiety is established to be also growing in older schoolchildren against their younger counterparts [5–9]. According to some authors, a number of morphofunctional disorders per one schoolchild as well as the polymorbidity index of chronic diseases have grown by 1.6–2.4 times over the last 30 years [10, 11].

Contemporary secondary education relies, among other things, on creating specialized schools (gymnasiums, lyceums, schools with advanced studies of various subjects, and military schools). These specialized schools strive to make education they provide more effective; to do that, they develop a wide range of educational programs and technologies [12–14]. At present, several basic risk factors produce negative effects on schoolchildren's health within the contemporary innovative educational process. They are educational loads exceeding the levels established by the hygienic standards; violated rules for safe use of modern technical teaching aids; combined mandatory and optional education without considering simultaneous loads on a student; excessive emotional overloads [3, 15]. If we analyze how educational processes are organized in different specialized schools, we can clearly see that schoolchildren who attend them have to face much more significant educational loads against their counterparts from ordinary secondary schools. This allows us to include schoolchildren from specialized schools into a risk group prone to development of school-induced pathologies [16].

Nutrition is a most significant factor influencing health of a growing body. According to some authors, diseases that result from improper nutrition can become apparent not only in childhood but also at later stages in ontogenesis [17]. The results produced by examining actual meals provided to schoolchildren in urban schools have revealed that more than a half of them do not get enough animal food products (milk, sour milk products, butter, eggs, meat or fish), vegetables and fruit. Potatoes are the most widely spread food for 60.0 % of children; 40.0 % of schoolchildren are given macaroni and cereals in excessive quantities and 60.0 % get more confectionary than they should [18, 19]. Given that, it becomes more and more significant to provide schoolchildren with qualitative meals at school. To be more exact, these meals should conform to children's age-specific physiological needs as per contents of macro- and micronutrients in them as well as their total caloric contents [20–25].

Since any educational institution is included into an ecosystem of a city or a rural settlement, a significant contribution made on children's health belongs to chemical environmental factors detected inside school premises, in ambient air and consumed water. Several studies have detected that contents of formaldehyde, phenol, styrene, ethylbenzene and benzene in air inside secondary schools exceed the hygienic standards; children who attend these schools have these chemicals in their biological media in concentrations being up to 3 times higher than maximum permissible levels [26]. Chronic inhalation and oral introduction of technogenic chemical pollutants creates persistent chemical contamination of schoolchildren's biological media with overall resorptive and organotropic negative effects developing in future [8, 27–29].

Although children spend a significant part of their time at school, we cannot underestimate a role played by socioeconomic factors existing in a child's family as well as by a child's activities beyond classes [30–32]. V.R. Kuchma with colleagues established that 59.8 % of schoolgirls and 43.1 % of schoolboys did not have enough physical activity to meet the requirements fixed for their age by the World Health Organization. Thirty percent of schoolchildren did physical exercises only during their physical training lessons and 57.6 % of schoolchildren spent less than 2 hours a day outdoors [33]. At the same time, a rapidly developing contemporary information-interactive space is engaging more and more children to be its active users. According to the data provided by the Foundation for Internet Development, on average 91.0 % of Russian children who are aged 10–17 years use the Internet and more than 90.0 % have their own mobile phones [33].

At present, not enough attention has been paid to influence exerted by a set of factors related to the educational process (how this process is organized, meals provided at school, a school environment) on schoolchildren's health and there are no sufficient data on so called "no-effect" safe levels of risk factors related to the educational process. At present, a vital task the hygiene as a science has to tackle is to establish peculiarities of effects produced by the educational process on health of children attending different types of secondary schools.

Our research goal was to substantiate optimal parameters of risk factors that would not produce any negative effects on physical, somatic and mental health of children attending secondary schools.

Materials and methods. Our task was to examine peculiarities of influence exerted by the educational process (how this process is organized, meals provided at school, sanitary-hygienic indicators of an outer and intra-school environment) on schoolchildren's health. To do that, we performed a clinical-functional and laboratory examination of 661 children who attended five different schools where the educational process was organized in four different ways. The first type was a secondary school with an additional educational program with more profound studies of natural sciences (physics and mathematics). The second type was a secondary school with an additional educational program that focused on general development (more profound studies of humanitarian sciences). The third type was a secondary school with an additional educational program focusing on sports and physical training (more profound military training). The fourth type was a secondary school without any additional educational program; it was located in a regional center and children who attended it were from families with a higher socioeconomic status. The fifth type was also a secondary school without any additional programs but it was located in a smaller town and children attending it were from families with a lower socioeconomic status. Overall, we examined 282 junior schoolchildren, 224 middle schoolchildren and 155 teenagers from senior school.

Indicators related to the educational process were assessed by analyzing their conformity with the sanitary-epidemiological requirements and hygienic standards established by the existing legislation[2]. Intensity of the educational process was examined in accordance with the recommendations created by the Russian Society for Development of School and University Medicine and Health[3].

Nutrition at school was estimated by analyzing daily menus and calculating a chemical structure of a typical meal (proteins, fats, carbohydrates, vitamins B1, B2, C, A, minerals Ca, P, Mg, Fe), energy value and ratios of basic nutrients in it. The results were then compared with the requirements fixed in the Sanitary Rules SanPiN 2.3/2.4.3590-20[4]. We analyzed data on schoolchildren's weekly ration and compara-

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[2] SP 2.4.3648-20. Sanitarno-epidemiologicheskie trebovaniya k organizatsiyam vospitaniya i obucheniya, otdykha i ozdorovleniya detei i molodezhi (utv. postanovleniem Glavnogo gosudarstvennogo sanitarnogo vracha RF ot 28.09.2020 № 28; vvedeny v deistvie 01.01.2021) [Sanitary Rules SP 2.4.3648-20. Sanitary-epidemiological requirements to organizing education, leisure and health improvement of children and youth (approved by the Order of the RF Chief Sanitary Inspector dated September 28, 2020 No. 28; became valid on January 01, 2021)]. *Rospotrebnadzor*. Available at: https://www.rospotrebnadzor.ru/files/news/SP2.4.3648-20_deti.pdf (March 05, 2022) (in Russian); SanPiN 1.2.3685-21. Gigienicheskie normativy i trebovaniya k obespecheniyu bezopasnosti i (ili) bezvrednosti dlya cheloveka faktorov sredy obitaniya (utv. postanovleniem Glavnogo gosudarstvennogo sanitarnogo vracha RF ot 28 yanvarya 2021 goda № 2; vvedeny v deistvie 01.03.2021) [Sanitary Rules and Standards SanPiN 1.2.3685-21. Hygienic standards and requirements to providing safety and (or) harmlessness of environmental factors for people (approved by the Order of the RF Chief Sanitary Inspector dated January 28, 2021 No. 2; became valid on March 01, 2021)]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/573500115 (March 05, 2022) (in Russian).

[3] Rukovodstvo po gigiene detei i podrostkov, meditsinskomu obespecheniyu obuchayushchikhsya v obrazovatel'nykh organizatsiyakh. Model' organizatsii, federal'nye rekomendatsii okazaniya meditsinskoi pomoshchi obuchayushchimsya [The guide on children and adolescents hygiene, medical support provided for students and schoolchildren. Organizational model and federal recommendations on how to provide healthcare for students and schoolchildren]. In: V.R. Kuchma, Corresponding Member of the RAS ed. Moscow, Scientific Center of Children's Health of the RF Public Healthcare Ministry, 2016, 610 p. (in Russian).

[4] SanPiN 2.3/2.4.3590-20. Sanitarno-epidemiologicheskie trebovaniya k organizatsii obshchestvennogo pitaniya naseleniya (utv. postanovleniem Glavnogo gosudarstvennogo sanitarnogo vracha RF ot 27 oktyabrya 2020 g. № 32; vvedeny v deistvie 27.10.2020) [Sanitary Rules and Standards SanPiN 2.3/2.4.3590-20. Sanitary-epidemiological requirements to organizing catering provided for population (approved by the Order of the RF Chief Sanitary Inspector dated October 27, 2020 No. 32; became valid on October 27, 2020)]. *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_367564/47eed3976d21a946bdffdc2bd5b9535a2f8930c3/ (February 08, 2022) (in Russian).

tively assessed whether an actual average daily ration provided to them conformed to the ration recommended by the SanPiN 2.3/2.4.3590-20[4].

We performed hygienic assessment of ambient air quality on the territories where the analyzed schools were located, quality of air inside school premises and quality of drinking water provided in these schools. The assessment was based on the results produced by field observations. Ambient air samples and air samples inside school premises were taken according to the State Standards GOST 17.2.3.01-86[5] and GOST R ISO 16000-1-2007[6]. Tap water samples were taken at nutrition units at schools in accordance with the State Standard GOST 31862-2012[7]. Hygienic assessment of drinking water quality was performed in conformity with the hygienic standard HS 2.2.5.1315-03[8]. Laboratory tests aimed at assessing ambient air quality, air quality inside school premises and drinking water quality involved using unified conventional procedures including high-performance liquid chromatography (formaldehyde), gas chromatography (aromatic hydrocarbons, chloroform), spectrophotometry (phenol) and mass-spectrometry (lead, manganese, chromium, and nickel). The tests were performed in accordance with the valid regulatory and methodical documents: MUK 4.1.1045-01, MUK 4.1.662–97, RD 52.04.186- 89, RD 52.04.186–89, PND F 14.1:2:3.171-00[9].

Biomedical examinations were accomplished in full conformity with the ethical principles stated in the Declaration of Helsinki (1975) and the RF National Standard GOST R 52379–2005

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[5] State Standard GOST 17.2.3.01-86. Nature protection. Atmosphere. Air quality control regulations for populated areas (introduced by the Order of the USSR State Committee on Standards on November 10, 1986 No. 3395; became valid on January 01, 1987). *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200012789 (February 08, 2022) (in Russian).

[6] GOST R ISO 16000-1-2007. Indoor air. Part 1. Sampling. General (approved and introduced by the Order of the Federal Agency on Technical Regulation and Metrology on March 15, 2007 No.30-st). *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200049806/titles (February 08, 2022) (in Russian).

[7] GOST 31862-2012. Voda pit'evaya. Otbor prob (Primenenie v kachestve natsional'nogo standarta RF prekrashcheno) [Drinking water. Sampling (no longer applied as the RF National Standard)]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200097517/titles/7D60K4 (September 19, 2021) (in Russian).

[8] HS 2.1.5.1315-03. Predel'no dopustimye kontsentratsii (PDK) khimicheskikh veshchestv v vode vodnykh ob"ektov khozyaistvenno-pit'evogo i kul'turno-bytovogo vodopol'zovaniya (utv. Glavnym gosudarstvennym sanitarnym vrachom RF, Pervym zamestitelem Ministra zdravookhraneniya RF G.G. Onishchenko 27.04.2003 (utratilo silu s 1 marta 2021 goda na osnovanii postanovleniya Glavnogo gosudarstvennogo sanitarnogo vracha RF ot 28 yanvarya 2021 goda № 2)) [Maximum permissible concentrations (MPC) of chemicals in water taken from water objects of drinking wand communal water supply (approved by G.G. Onishchnko, the RF Chief Sanitary Inspector and the First Deputy to the RF Public Healthcare Minister on April 27, 2003 (no longer valid since March 01, 2021 according to the Order by the RF Chief Sanitary Inspector dated January 28, 2021 No. 2))]. *KODEKS: electronic fund for legal and reference documentation.* Available at: https://docs.cntd.ru/document/901862249 (February 16, 2021) (in Russian).

[9] MUK 4.1.1045-01. Metody kontrolya. Khimicheskie faktory. VEZhKh opredelenie formal'degida i predel'nykh al'degidov (C_2–C_{10}) v vozdukhe (utv. Glavnym gosudarstvennym sanitarnym vrachom RF, Pervym zamestitelem Ministra zdravookhraneniya RF G.G. Onishchenko 5 iyunya 2001 g.; data vvedeniya 1 oktyabrya 2001 g.) [Control procedures. Chemical factors. HPLC applied to determine formaldehyde and saturated aldehydess (C_2–C_{10}) in ambient air (approved by G.G. Onishchenko, the RF Chief Sanitary Inspector and the First Deputy to the RF Public Healthcare Minister on June 5 2001; became valid on October 1, 2001)]. *MEGANORM: regulatory documents.* Available at: https://meganorm.ru/Data2/1/4294814/4294814986.pdf (February 16, 2021) (in Russian); MUK 4.1.662-97. Metody kontrolya. Khimicheskie faktory. Metodicheskie ukazaniya po opredeleniyu massovoi kontsentratsii stirola v atmosfernom vozdukhe metodom gazovoi khromatografii (utv. Pervym zamestitelem Predsedatelya Goskomsanepidnadzora Rossii, zamestitelem Glavnogo gosudarstvennogo sanitarnogo vracha RF 31.10.1996) [Control procedures. Chemical factors. Methodical guidelines on determining mass concentrations of styrene in ambient air with gas chromatography (approved by the First Deputy to the Head of the Russian State Sanitary Epidemiological Surveillance, deputy to the RF Chief Sanitary Inspector on October 31, 1996)]. *MEGANORM: regulatory documents.* Available at: https://meganorm.ru/Index2/1/4293814/4293814194.htm (February 16, 2021) (in Russian); RD 52.04.186-89. Rukovodstvo po kontrolyu zagryazneniya atmosfery (Chasti II, III. Prilozheniya k chasti I) (otmenen v chasti) [Guide on control over ambient air pollution (Parts II and III. Supplements to Part I) (Part I is no longer valid)]. *KODEKS: electronic fund for legal and reference documentation.* Available at: https://docs.cntd.ru/document/1200037440/titles (February 16, 2021) (in Russian); PND F 14.1:2:3.171-00. Kolichestvennyi khimicheskii analiz vod. Metodika vypolneniya izmerenii massovoi kontsentratsii khloristogo metila, vinilkhlorida, vinilidenkhlorida, metilenkhlorida, khloroforma, chetyrekhkhloristogo ugleroda, 1,2-dikhloretana, benzola, trikhloretilena, 1.1.2-trikhloretana, toluola, orto-ksilola, summarnogo soderzhaniya, meta- i paraksilolov v stochnykh, prirodnykh poverkhnostnykh i podzemnykh vodakh gazokhromatograficheskim metodom (utv. direktorom FGU «Tsentr ekologicheskogo kontrolya i analiza» G.M. Tsvetkovym 6 avgusta 2002 g.) [Quantitative chemical analysis of waters. The procedure for measuring mass concentrations of methyl chloride, vynil chloride, vynilene chloride, methylene chloride, chloroform, carbon tetrachloride, 1,2-dichloroethane, benzene, trichloroethylene, 1.1.2-trichloroethane, toluene, orto-xylene, total contents, meta- and paraxylenes in sewage, natural surface and underground waters with gas chromatography (approved by G.M. Tsvetkov, Director of the Center for Ecological Control and Analysis on August 6, 2002)]. *MEGANORM: regulatory documents.* Available at: https://meganorm.ru/Data2/1/4293739/4293739708.htm (February 16, 2021) (in Russian).

"Good Clinical Practice" (ICH E6 GCP)[10]. Legal representatives of all the examined children gave their written informative voluntary consent to children's participation in the research in conformity with the federal legislation.

Socioeconomic risk factors were assessed by analyzing results of a social survey. The survey was accomplished by handing out questionnaires and concentrated on examining a child's family, parents' education, whether parents had a full-time or a part-time job or were unemployed, income per one family member, living conditions, whether a child had his or her own room etc. The social survey also involved analyzing how children spent their free time (time spent outdoors on walking or doing sports, on using gadgets or watching TV, on some creative activities or going to sport clubs). Attention was paid to optional education in case of having any (studies with a tutor, going to optional education institutions) and to breaks between different types of educational activities, time spent on doing homework etc. Children's physical activity was estimated by analyzing how regularly they did sports and how much time they spent outdoors either playing or doing exercises, how frequently they walked on foot for longer than 20 minutes etc.

All the participating children were examined by a pediatrician, allergologist, neurologist, gastroenterologist, ENT doctor and a cardiologist. Children's physical development and their somatic health were assessed by accomplishing anthropometric studies, BIA, ECG, heart rate variability examination, US of the abdominal cavity organs, conventional general clinical, biochemical and immunological analyses. Psychological testing was performed by using Vienna Test system for computerized psychological assessments and "NS-Psychotest" software for psychophysiological testing. The tests involved assessing a time needed to react to a stimulus, motor function velocity, attention level (RT-test), cognitive functions (STROOP-test), visual-spatial short-term working memory (CORSI-test), and a psychological stress level (Luscher test).

A complete clinical diagnosis was put for each child based on the results produced by the aforementioned clinical-functional and laboratory examinations.

Concentrations of technogenic chemicals (formaldehyde, phenol, ethylbenzene, benzene, toluene, chloroform, lead, nickel, chromium and manganese) were determined in children's blood as per conventional procedures in accordance with the valid regulatory and methodical documents MUK 4.1.2111-06; MUK 4.1.2115-06; MUK 4.1.765-99; MUK 4.1.2108-06; MUK 4.1.3230-14; MUK 4.1.3161-14[11]. The examina-

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[10] GOST R 52379-2005. Good Clinical Practice (GCP) (approved by the Order of the Federal Agency Technical Regulation and Metrology on September 27, 2005 No. 232-st). *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200041147/titles (March 18, 2021) (in Russian).

[11] Opredelenie vrednykh veshchestv v biologicheskikh sredakh: sbornik metodicheskikh ukazanii MUK 4.1.2102–4.1.2116-06 (utv. i vved. v deistvie Rukovoditelem Rospotrebnadzora, Glavnym gosudarstvennym sanitarnym vrachom RF 9 avgusta 2006 g.) [Determination of harmful chemicals in biological media: the collection of methodical guidelines MUK 4.1.2102–4.1.2116-06 (approved and introduced by G.G. Onishchenko, the Head of Rospotrebnadzor, the RF Chief Sanitary Inspector on August 09, 2006)]. Moscow, The Federal Center for Hygiene and Epidemiology of Rospotrebnadzor, 2008, 183 p. (in Russian); MUK 4.1.765-99. Gazokhromatograficheskii metod kolichestvennogo opredeleniya aromaticheskikh (benzol, toluol, etilbenzol, o-, m-, p-ksilol) uglevodorodov v biosredakh (krov') (utv. Glavnym gosudarstvennym sanitarnym vrachom RF G.G. Onishchenko 6 iyulya 1999 g.) [Gas chromatography applied to quantify aromatic (benzene, toluene, ethylbenzene, o-, m-, p-xylene) hydrocarbons in biological media (blood) (approved by G.G. Onishchenko, RF Chief Sanitary Inspector on July 06, 1999)]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200039012/titles (March 15, 2021) (in Russian); MUK 4.1.2108-06. Opredelenie massovoi kontsentratsii fenola v biosredakh (krov') gazokhromatograficheskim metodom / utv. Rukovoditelem Rospotrebnadzora, Glavnym gosudarstvennym sanitarnym vrachom RF G.G. Onishchenko 9 avgusta 2006 g. [Determination of mass concentration of phenol in biological media (blood) with gas chromatography (approved by G.G. Onishchenko, the Head of Rospotrebnadzor, the RF Chief Sanitary Inspector on August 09, 2006)]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200065240 (March 15, 2021) (in Russian); MUK 4.1.3230-14. Izmerenie massovykh kontsentratsii khimicheskikh elementov v biosredakh (krov', mocha) metodom mass-spektrometrii s induktivno svyazannoi plazmoi (utv. Rukovoditelem Rospotrebnadzora, Glavnym gosudarstvennym sanitarnym vrachom RF A.Yu. Popovoi 19 dekabrya 2014 g.) [Determination of chemical mass concentrations in biological media (blood, urine) with mass spectrometry with inductively coupled plasma (approved by A.Yu. Popova, the Head of Rospotrebnadzor, the RF Chief Sanitary Inspector on December 19, 2014)]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/495856222 (March 15, 2021) (in Russian); MUK 4.1.3161-14. Izmerenie massovykh kontsentratsii svintsa, kadmiya, mysh'yaka v krovi metodom mass-spektrometrii s induktivno svyazannoi plazmoi (utv. vrio rukovoditelya Rospotrebnadzora, Glavnogo gosudarstvennogo sanitarnogo vracha RF A.Yu. Popovoi 24 fevralya 2014 g.) [Determination of mass concentrations of lead, cadmium and arsenic in blood with mass spectrometry with inductively coupled plasma (approved by A.Yu. Popova, acting as the Head of Rospotrebnadzor, the RF Chief Sanitary Inspector on February 24, 2014)]. *MEGANORM: regulatory documents*. Available at: https://meganorm.ru/Data2/1/4293766/4293766470.htm (March 15, 2021) (in Russian).

tions were performed at the Department for Chemical and Analytical Research Techniques of the Federal Scientific Center for Medical and Preventive Health Risk Management Technologies (headed by the T.S. Ulanova, Doctor of Biological Sciences). Reference or regional background concentrations were applied as assessment criteria to estimate the results produced by chemical-analytical examinations of children's biological samples (blood).

The results were statistically analyzed by using conventional statistical procedures and mathematical analysis in Statistica 6.0 and statistical functions built into Microsoft Excel, 2010. Influence exerted by the educational process (how it is organized, meals provided at school and an intra-school environment) and by socioeconomic factors on children's anthropometric parameters, body composition, somatic and mental health was estimated by using one-factor logistic regression models of "dose – likelihood of a response (effect)" relationships. The model significance was estimated as per Fischer's test (F) with giving a constant value (b_0), regression coefficient (b_1), and Nagelkerke determination coefficient (R^2). Any differences were considered statistically significant at $p \le 0.05$. Overall, the logistic regression model was formulated as follows:

$$p = \frac{1}{1 + e^{-(b_0 + b_1 x)}},$$

where p is a probability that a response will deviate from the standard; x is exposure level; b_0, b_1 are parameters of the mathematical model.

"Optimal" values (x_0) of factors related to the educational process that ensured no negative effects produced on the body were estimated through creating regression models. These models showed how exposure levels influenced "odds ratio" (OR), an indicator characterizing how strong a correlation is between an exposure level and a response. The condition $OR \ge 1$ was taken as a criterion confirming a correlation existed.

We calculated odds ratios for each factor value. The calculations were performed by conventional division of the sampling into two parts: below and above the current level of an exposure marker. For both intervals, a value was calculated that characterized a likelihood of a response marker deviating from the standard: p_i^- and p_i^+ accordingly as a ratio of a number of observations deviating from the standard to the total number of observations. Odds ratio was determined for each observation as per the following relationship:

$$OR_i = \frac{p_i^+}{1 - p_i^+} \Big/ \frac{p_i^-}{1 - p_i^-},$$

where i is an index showing the number of an observation.

Parameters describing dependence between odds ratio and an exposure value were estimated by creating a regression model in the form of an exponential function:

$$OR = e^{a_0 - a_1 x},$$

where a_0, a_1 are model parameters.

An optimal level of an exposure factor (x_0) with respect to a type of a response was calculated considering the condition OR=1 as per the following relationship:

$$x_0 = \frac{a_0}{a_1}.$$

Results and discussion. We assessed how the educational process was organized in the analyzed schools. The assessment revealed that in the first-type school a number of students in a class, an overall number of lessons per day and per week, and a period when technical teaching aids were used during a lesson exceeded the hygienic standards stipulated in the SanPiN 1.2.3685-21 and SR 2.4.3648-20[2] for schoolchildren of all ages. The educational process (duration of breaks both between lessons and between mandatory and optional classes, interchanges between difficult and easy subjects during a school day and distribution of educational loads over a week) was the most intense in this school in comparison with the other analyzed ones.

In the second-type school, only primary schoolchildren had daily and weekly loads that were higher than their maximum permissible levels. However, a number of schoolchildren in one class did not conform to the hygienic standards in primary, middle and senior school whereas the educational process was quite close to conformity with the SR 2.4.3648-20[2].

In the third-type school, only senior schoolchildren had weekly loads that exceeded the maximum permissible levels and the educational process at any level was quite close to meeting the hygienic requirements.

In the fourth- and fifth-type schools, overall number of lessons a day and a week and a period when technical teaching aids were used during a lesson corresponded to the requirements fixed in the SanPiN 1.2.3685-21 and SR 2.4.3648-20[2]; however, the educationnal process was organized improperly at all levels (primary, middle and senior school).

Therefore, we detected several factors related to the educational process that were common for most analyzed schools. These factors created certain health risks for schoolchildren. They included a number of children in a class; too short breaks, either between lessons or between mandatory and optional classes; improper interchange between difficult and easy subjects during a day; and improper distribution of educational loads over a week. We should note that the educational process estimated as per all the violations of the requirements to its organization fixed in the SanPiN 1.2.3685-21 and SR 2.4.3648-20[2] is more intense in schools that have additional education programs with their focus on various subjects than in schools that offer only standard education programs.

Our examinations focusing on nutrition provided by schools revealed that menus in all the analyzed schools were made with improper ratios between macronutrients (fat and carbohydrate contents were by 1.5–1.8 times higher than necessary) and decreased contents of vital micronutrients (vitamins B_1, B_2, C, A, iron, calcium, magnesium, and phosphor, from 5.0 to 45 % lower than necessary). Total caloric contents of a ration did not conform to the recommended values either[4] (95–120 % of the necessary level). We should note that those violations, both as per their absolute values and their frequency, were more typical for schools with additional educational programs. In addition, our research established that a daily ration usually consumed by schoolchildren (both at school and at home, with home meals accounting for 76.0–92.2 % in it) did not satisfy their age–specific physiological needs[4]. Schoolchildren who attended the analyzed schools had by 1.7–2.0 times more sausage, by 1.4–1.5 times more macaroni and by 7.8–8.0 more confectionary than recommended whereas their consumption of vegetables, fruit, fish and cereals was by 1.6–3.8 times lower. A daily ration that was the closest to the recommended one[4] was detected in the third–type school where schoolchildren were provided with three meals a day.

Our sanitary–hygienic assessment of ambient air on the territories where the analyzed schools were located established the following. Concentrations of benzene (0.0025 ± 0.0004–0.0190 ± 0.0027 mg/m^3; MPC$_{av.d.}$ = 0.1 mg/m^3), ethylbenzene (< 0.002–0.0083 ± 0.0009 mg/m^3; MPC$_{av.d.}$ = 0.02 mg/m^3), nickel (0.000009 ± 0.000002–0.000015 ± 0.0000035 mg/m^3; MPC$_{av.d.}$ = 0.01 mg/m^3), lead (0.000006 ± 0.000001–0.000020 ± 0.000004 mg/m^3; MPC$_{av.d.}$ = 0.01 mg/m^3), manganese (0.00004 ± 0.0000008–0.000183 ± 0.000038 mg/m^3; MPC$_{av.d.}$ = 0.001 mg/m^3) and chromium (0.000013 ± 0.0000087–0.000024 ± 0.000004 mg/m^3; MPC$_{av.d.}$ = 0.015 mg/m^3) corresponded to the requirements fixed in the SanPiN 2.1.6.1032-01[12] and HS 2.1.6.1338–03[13], whereas concentrations of phenol (0.0068 ± 0.0024–0.0075 ± 0.0019 mg/m^3; MPC$_{av.d.}$ = 0.006 mg/m^3) and toluene (0.0827 ± 0.0116 mg/m^3; MPC$_{av.d.}$ = 0.05 mg/m^3) were by 1.1–1.7 times higher than MPC$_{av.d.}$ Most frequently, air inside school premises contained elevated concentrations of formaldehyde (0.0124 ± 0.0025–0.02136 ± 0.0044 mg/m^3; MPC$_{av.d.}$ = 0.01 mg/m^3), phenol (0.0062 ± 0.0016–0.0064 ± 0.0016 mg/m^3; MPC$_{av.d.}$ = 0.006 mg/m^3) and toluene (0.0721 ± 0.0145–0.0737 ± 0.0103 mg/m^3;

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[12] SanPiN 2.1.6.1032-01. Hygienic Requirements for Atmospheric Air Protection in Populated Areas (approved by the RF Chief Sanitary Inspector on May 17, 2001). *MEGANORM: regulatory documents*. Available at: https://meganorm.ru/Index2/1/4294847/4294847621.htm (March 18, 2021) (in Russian).

[13] HS 2.1.6.1338-03. Predel'no dopustimye kontsentratsii (PDK) zagryaznyayushchikh veshchestv v atmosfernom vozdukhe naselennykh mest: Gigienicheskie normativy (utv. Glavnym gosudarstvennym sanitarnym vrachom RF, Pervym zamestitelem Ministra zdravookhraneniya 21 maya 2003 g.) [Maximum permissible concentrations (MPC) of pollutants in ambient air in settlements: Hygienic Standards (approved by the RF Chief Sanitary Inspector and the First Deputy to the RF Public Healthcare Minister on May 21, 2003)]. Moscow, The Russian register of potentially hazardous chemical and biological substances of the RF Public Healthcare Ministry, 2003, 86 p. (in Russian).

$MPC_{av.d.}$ = 0.05 mg/m^3), which were by 1.2–1.5 times higher than $MPC_{av.d.}$ Quality of drinking water in schools did not conform to the requirements fixed in SanPiN 2.1.4.1074-01[14] and HS 2.1.5.1315–03 as per certain sanitary–hygienic indicators, namely, contents of chloroform (0.138 ± 0.01–0.186 ± 0.007 mg/m^3; $MPC_{av.d.}$ = 0.06 mg/m^3) and formaldehyde (0.094 ± 0.002–0.123 ± 0.004 mg/m^3; $MPC_{av.d.}$ = 0.05 mg/m^3). Their concentrations were by 1.9–3.1 times higher than the existing hygienic standards. Biological media of schoolchildren from primary, middle and senior school most frequently contained elevated concentrations of phenol (0.015 ± 0.005–0.084 ± 0.031 μg/ml; the background level is 0.005 ± 0.001 μg/ml), formaldehyde (0.013 ± 0.008–0.0502 ± 0.0073 μg/ml; the background level is 0.01 ± 0.001 μg/ml), benzene (0.0002 ± 0.0001–0.009 ± 0.0003 μg/ml; the background level is 0.0 μg/ml), toluene (0.0003 ± 0.0001–0.0009 ± 0.0001 μg/ml; the background level is 0.0 μg/ml), ethylbenzene (0.0002 ± 0.0001–0.0005 ± 0.0003 μg/ml; the background level is 0.0 μg/ml), chloroform (0.0002 ± 0.0001–0.0003 ± 0.0001 μg/ml; the background level is 0.0 μg/ml), manganese (0.014 ± 0.003–0.015 ± 0.002 μg/ml; the reference level is 0.013 ± 0.004 μg/ml), lead (0.012 ± 0.0035–0.056 ± 0.0075 μg/ml; the reference level is 0.01 ± 0.0067 μg/ml), nickel (0.023 ± 0.009–0.026 ± 0.0055 μg/ml; the reference level is 0.015 ± 0.007 μg/ml) and chromium (0.0039 ± 0.0018–0.0072 ± 0.0008 μg/ml; the reference level is 0.003 ± 0.002 μg/ml).

We comparatively analyzed socioeconomic factors in children's families. The analysis revealed that typically children who attended secondary schools with additional educational programs (the first-, second- and third-type schools) were from families with incomes per one family member being by 1.6–1.7 times higher than in those families where children attended ordinary secondary schools. Schoolchildren from the schools with additional educational programs had by 2.7–3.4 times greater educational loads and spent by 1.1–3.5 times more time on doing physical exercises or sports. In addition, a number of parents with higher education was by 4.0–19.0 times higher in families with children attending schools with additional educational programs than in families with children going to ordinary secondary schools (the fourth- and fifth-type).

Our anthropometric studies established that primary and middle schoolchildren who attended schools with additional educational programs tended to have average weight and height, chest excursion and circumference as well as grip strength that corresponded to age–specific physiological standards. However, a number of children with drastically disharmonic body development grew among senior schoolchildren. We should note that the maximum number of children with their physical development corresponding to the standards was established in the third-type school (the military school). As for ordinary secondary schools (the fourth- and fifth-type), we detected a growing number of children with overweight and obesity already in primary school; a number of children with drastically disharmonic body development grew substantially among senior schoolchildren in these schools.

We analyzed data produced by bioelectrical impedance analysis in dynamics and established certain differences between the analyzed schools. Thus, in the first-type school, primary schoolchildren tended to have higher body mass index and fate mass; then, both these indicators decreased by 1.8–2.5 times by senior school against a 1.3–2.6-time growth of the phase angle, metabolically active cell and bone and muscle mass indicating that metabolic processes intensified in children's bodies and they became more physically active (p = 0.02). We established that children from the second–type school were physically fit and had enough

[14] SanPiN 2.1.4.1074-01. Pit'evaya voda. Gigienicheskie trebovaniya k kachestvu vody tsentralizovannykh sistem pit'evogo vodosnabzheniya. Kontrol' kachestva. Gigienicheskie trebovaniya k obespecheniyu bezopasnosti sistem goryachego vodosnabzheniya (utv. Glavnym gosudarstvennym sanitarnym vrachom RF, Pervym zamestitelem Ministra zdravookhraneniya G.G. Onishchenko 26 sentyabrya 2001 g. (utratilo silu s 1 marta 2021 g.)) [Drinking water. Hygienic requirements to quality of water from centralized water supply systems. Quality control. Hygienic requirements to providing safety of hot water supply systems (approved by G.G. Onishchenko, the Head of Rospotrebnadzor, the RF Chief Sanitary Inspector on September 26, 2001 (no longer valid since March 01, 2021))]. *KODEKS: electronic fund for legal and reference documents.* Available at: https://docs.cntd.ru/document/901798042 (February 26, 2021) (in Russian).

physical activity in primary, middle and senior school. As a result, their metabolic processes had proper intensity and their bone and muscle mass grew by 3.2 times in senior school, which corresponds to the physiological standard ($p = 0.003$). Indicators describing body composition grew most harmonically and were closest to the age–specific physiological standards in schoolchildren from the third–type school. The results produced by biological impedance analysis indicated they were the fittest and had the most physical activity in primary, middle and senior school than their counterparts from any other analyzed school. This was accompanied by 1.2–2.7 times better physical and metabolic activity, greater metabolically active cell mass and bone and muscle mass ($p < 0.001$). We detected a 2.0–2.3 time growth in a number of schoolchildren from the fourth-type and fifth-type schools in senior school with their body mass index and fat mass being by 1.4–1.8 times higher than the physiological standard ($p = 0.02$). Simultaneously, 14.0–31.0 % of school leavers had metabolically active body cell mass, bone and muscle mass that were lower than the physiological standard. We detected only isolated cases of it in primary school in these schools.

Having analyzed morbidity among schoolchildren, we established an authentic growth in diseases of the eye and adnexa among senior schoolchildren in all the analyzed schools. The maximum number of such diseases was typical for schoolchildren from the first-type school (71.6 %). The minimal number of such pathologies was registered in the third–type school (23.0 %). Senior schoolchildren from the second-, fourth- and fifth-type schools had eye pathologies in 51.6–62.0 % of cases. In addition, children in those schools tended to have digestive diseases much more frequently since they were detected in 91.7–100 % of them. We detected an ascending trend for diseases of the nervous system among schoolchildren who attended the first-type school. Although we did not detect any significant differences, we could still trace a growth in a number of endocrine diseases and it was typical for all the analyzed schools, except the first–type one, where we detected an inverse trend.

We assessed influence exerted by the analyzed factors on schoolchildren's body composition. The assessment revealed that phenol and chromium contents in blood ($R^2 = 0.55$–0.71; $p < 0.001$) led to a smaller probability that metabolically active body cell mass would form; at the same time, when iron and vitamins C and B1 are introduced with food in proper quantities, this results in a greater probability that this mass meets the age–specific physiological standards ($R^2 = 0.34$–0.56; $p < 0.001$).

A probability that bone and muscle mass will form in accordance with its physiological standards grows when children are provided with balanced introduction of calcium, magnesium, phosphor and proteins with food ($R^2 = 0.23$–0.86; $p < 0.001$). This probability goes down, especially when it comes down to senior schoolchildren, when nickel and formaldehyde occur in blood in elevated concentrations ($R^2 = 0.30$–0.45; $p < 0.001$) (Figure). Factors related to the educational process have less significant influence on formation of metabolically active body cell mass and bone and muscle mass in primary schoolchildren ($R^2 = 0.23$–0.34; $p < 0.001$) whereas growing educational loads in middle and senior school produce by 2.2–3.9 times greater effects on formation of these body components ($R^2 = 0.75$–0.89, $p < 0.001$). An increase in monotony of educational loads and greater learning intensity result in an authentic decrease in formation of fat-free mass in the body in primary schoolchildren ($R^2 = 0.79$–0.84; $p < 0.001$). In middle school, greater influence is exerted, according to the modeling results, by shorter breaks and lower recovery index values ($R^2 = 0.87$–0.98; $p < 0.001$). Fat-free mass is to a lesser extent influenced by elevated chromium and formaldehyde contents in blood ($R^2 = 0.62$ and 0.11 accordingly, $p < 0.001$). In senior school, magnesium and protein contents in meals provided at school produce authentically greater effects on fat-free mass formation ($R^2 = 0.76$ and 0.34 accordingly, $p < 0.001$). Basic metabolic indicators in primary and middle schoolchildren go down largely due to influence exerted by such factors related to the educational process as growing educational loads, shorter breaks and lower recovery index values ($R^2 = 0.87$–0.98; $p < 0.001$). In senior school, factors related to the educational process exert by 3.2–3.6 times smaller influence ($R^2 = 0.27$; $p < 0.001$). Quality of metabolic processes deteriorates due to elevated chromium concentrations in blood ($R^2 = 0.74$; $p < 0.001$) and to a lesser extent due to formaldehyde concentrations ($R^2 = 0.49$; $p < 0.001$).

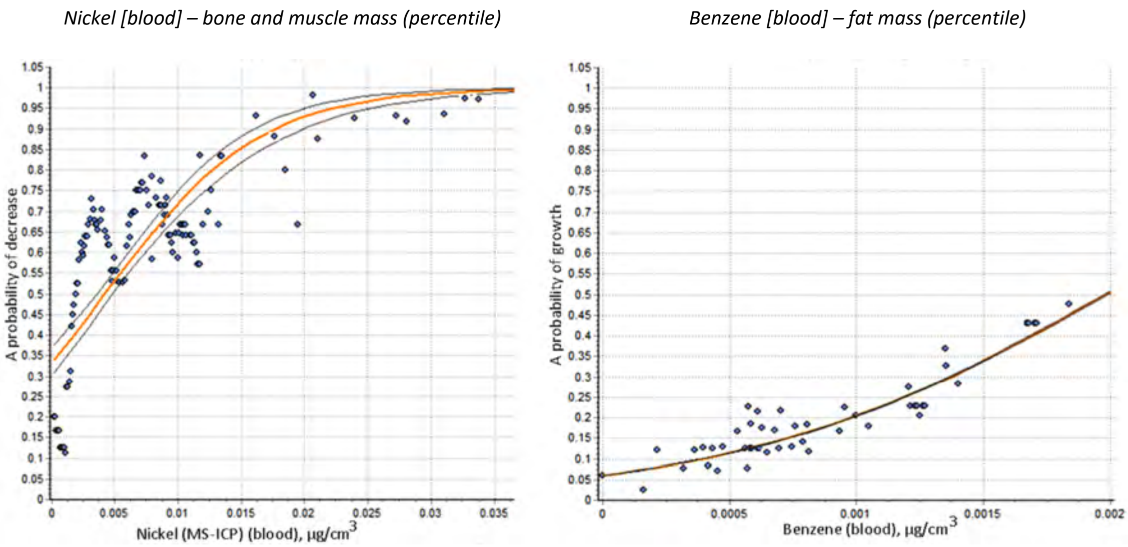

Figure. Influence exerted by nickel and benzene on formation of schoolchildren's bone, muscle and fat mass

Certain factors of the educational process, including lower educational loads and their intellectual components as well as shorter breaks, increase a probability for primary school children that fat mass will accumulate in their bodies and body mass index will grow (R^2 = 0.74–0.87; $p < 0.001$) whereas elevated chromium concentrations in blood reduce a probability of fat mass formation (R^2 = 0.54–0.87; $p < 0.001$). The aforementioned factors related to the educational process produce by 3.7–14.5 times smaller effects in middle school (R^2 = 0.06–0.20; $p < 0.001$). Benzene exerts significant influence on primary school children since its concentration in their blood increases a probability that excessive fat mass will accumulate in their bodies (R^2 = 0.44–0.56; $p < 0.001$) (Figure 1). Influence exerted on fat mass formation in senior schoolchildren by all the factors related to the educational process is insignificant (R^2 = 0.09–0.28; $p < 0.001$). Consumption of proteins, fats and carbohydrates becomes very significant in middle and senior school: (R^2 = 0.15–0.52 and R^2 = 0.20–0.40 accordingly; $p < 0.001$). In primary school, lead and nickel contents in blood deteriorate children's growth (R^2 = 0.42; $p < 0.001$) whereas in middle and senior school macronutrient consumption with food becomes the most important. Height is more likely to correspond to its physiological standards when children are provided with proper quantities of calcium, phosphor, iron, vitamins B1, B2, C in their nutrition (R^2 = 0.23–0.65; $p < 0.001$).

We assessed influence exerted by the analyzed factors on morbidity among schoolchildren. Mathematical modeling revealed that manifestation of cardiovascular diseases was influenced the most significantly by nickel, benzene and lead contents in children's blood (R^2 = 0.70–0.86; $p < 0.001$) as well as by growing daily educational loads (R^2 = 0.67; $p < 0.001$). It was also influenced, though to a lesser extent, by shorter breaks and lower recovery index values (R^2 = 0.26–0.44; $p < 0.001$). In senior school, occurrence of such diseases is influenced by 1.9–2.4 times more greatly by shorter breaks and lower recovery index values (R^2 = 0.83–0.89; $p < 0.001$). Diseases of the nervous system develop more frequently due to caloric contents in school meals being higher than the standards (R^2 = 0.90; $p < 0.001$), as well as due to magnesium and vitamin B1 deficiency (R^2 = 0.53–0.59; $p < 0.001$) and due to lead, formaldehyde and phenol contents in blood (R^2 = 0.47–0.81; $p < 0.001$). These diseases occur most frequently due to such factors related to the educational process as a growing number of lessons a day and growing monotony of learning (R^2 = 0.75–0.80; $p < 0.001$); to a lesser extent, due to excessive daily educational loads and emotional loads (R^2 = 0.23–0.31; $p < 0.001$). Diseases of the genitourinary, digestive and respiratory system are more likely to occur in case of chloroform, nickel, formaldehyde, chromium, lead and phenol contents in blood (R^2 = 0.57–0.86; $p < 0.001$). Diseases of the digestive system can also occur due to factors related to the educational process, including a growing number of lessons a day, growing monotony of learning and excessive daily educational loads (R^2 = 0.57–0.86; p < 0.001); to a lesser extent, due to shorter breaks and lower recovery index values (R^2 = 0.22–0.27; p < 0.001) as well as magnesium deficiency (R^2 = 0.74; p < 0.001). In senior school, digestive diseases become more probable due to protein and vitamin C deficiency (R^2 = 0.55–0.75; p < 0.001) as well as excessive fat contents (R^2 = 0.25; p < 0.001) in school meals. Diseases of the respiratory system might occur, to a lesser extent, due to monotony and intensity of learning, a growing number of lessons a day as well as toluene in biological media (R^2 = 0.21–0.72; p < 0.001). Our further analysis of the created models established a direct correlation between developing diseases of the eye and adnexa and elevated formaldehyde contents in blood (R^2 = 0.24–0.73; p < 0.001), chronic deficiency of vitamins A and C in school meals (R^2 = 0.32–0.87; p < 0.001), growing emotional and intellectual loads as well as a growing number of lessons a day (more than recommended) (R^2 = 0.36–0.63; p < 0.001). We detected a correlation between growing socioeconomic states of primary schoolchildren's families and development of such diseases in them (R^2 = 0.64; p < 0.001). Diseases of skin and subcutaneous tissues are induced by elevated chromium and nickel contents in blood (R^2 = 0.65–0.82; p < 0.001) as well as by some factors related to the educational process, including growing monotony and intensity of learning and daily educational loads (R^2 = 0.76–0.80; p < 0.001). In senior school, effects produced by these factors on development of skin pathologies go down by 1.3–1.5 times (R^2 = 0.52–0.59; p < 0.001). Factors that induce diseases of the musculoskeletal system probably include excessive caloric contents in school meals and vitamin C deficiency (R^2 = 0.74–0.86; p < 0.001); to a lesser extent, carbohydrates deficiency and elevated lead and manganese contents in blood (R^2 = 0.29–0.38; p < 0.001). Such factors related to the educational process as a growing number of lessons a day, growing intensity of learning and its intellectual components produce practically the same effects on primary schoolchildren regarding skin pathologies (R^2 = 0.45–0.58; p < 0.001). In middle school, development of these diseases is by 2.0–1.1 times more influenced by growing educational loads, a growing number of lessons a day, and shorter breaks (R^2 = 0.63–0.89; p < 0.001). Diseases of the endocrine system in primary and middle schoolchildren are largely influenced by excessive carbohydrates consumption as well as deficiency of proteins, vitamins C and B1 in school meals (R^2 = 0.39–0.70; p < 0.001). In senior school, shorter breaks produce by 2.5–3.9 times greater effects (R^2 = 0.86; p < 0.001) (Table 1).

Our next step was to estimate influence exerted by the analyzed factors on the results produced by psychological testing. We revealed that growing monotony of learning, a growing number of lessons a day/week, growing intellectual and emotional loads impaired visual–spatial short–term operating memory (R^2 = 0.16–0.66; p < 0.0001) whereas growing recovery index values were likely to help produce better results of Corsi–testing (R^2 = 0.25; p < 0.0001). Cognitive rigidity decreases authentically due to growing intellectual loads and more intense learning (STROOP–test) (R^2 = 0.48–0.53; p < 0.0001). A reaction time detected by testing (STROOP–test) grows probabilistically when intellectual loads go up, classes become longer and breaks become shorter in primary school (R^2 = 0.19–0.27; p < 0.0001). The same effect occurs in middle school when intellectual loads and a number of lessons a day grow (R^2 = 0.14–0.38; p < 0.0001). In senior school, visual–spatial short–term operating memory deteriorates authentically due to growing educational loads and longer duration of classes (R^2 = 0.17–0.18; p < 0.0001). At the same time, when recovery index goes up and breaks become longer, it results in greater probability to pass Corsi–testing satisfactorily (R^2 = 0.12–0.25; p < 0.0001). Factors related to the educational process exert by 1.3–2.8 times smaller influence on cognitive flexibility and a reaction time during testing (R^2 = 0.08–0.09; p < 0.0001).

Having assessed effects produced by technogenic chemicals on children's mental health, we established that cognitive functions of children in primary, middle and senior school decreased in the same way in case they had elevated concentrations of manganese, lead, nickel (R^2 = 0.29–0.75; p < 0.001) as

Table 1

The models describing correlations between parameters of the educational process and morbidity among primary schoolchildren

Educational loads	Diseases	*b1*	Error	Fischer's test (*F*)	Authenticity of the model (*p*)	Determination coefficient (R^2)	NOL*
Duration of breaks (minutes)	Diseases of the circulatory system	-0.002	1E-08	398.72	< 0.001	0.44	-
Recovery index (arbitrary units)		-3.38	0.10	109.84	< 0.001	0.26	0.32
Daily educational loads (scores)		0.43	0.0004	506.65	< 0.001	0.67	-
Duration of breaks (minutes)	Diseases of the endocrine system	-0.001	5E-08	39.81	< 0.001	0.07	387.2
Recovery index (arbitrary units)		-2.45	0.49	12.32	0.002	0.03	0.29
Intellectual loads (scores)		1.73	0.01	313.05	< 0.001	0.58	-
Number of lessons a day		0.27	0.009	8.68	0.004	0.03	-
Monotony of learning (scores)		0.39	0.0009	162.65	< 0.001	0.42	-
Weekly educational loads (scores)		0.009	1.79E-09	42.15	< 0.001	0.16	-
Emotional loads (scores)		1.62	0.02	110.45	< 0.001	0.33	-
Duration of breaks a week (minutes)	Diseases of the digestive system	-0.001	2E-08	137.05	< 0.001	0.26	273.5
Recovery index (arbitrary units)		-3.15	0.14	70.91	< 0.001	0.22	0.25
Number of lessons a week		0.08	0.0002	34.85	< 0.001	0.10	23.8
Number of lessons a day		1.66	0.008	348.30	< 0.001	0.52	-
Number of lessons a day	Diseases of the nervous system	1.03	0.021	51.4	< 0.001	0.14	-
Monotony of learning (scores)		2.10	0.005	994.79	< 0.001	0.82	-
Weekly educational loads (scores)		0.02	1.4E-05	27.53	< 0.001	0.08	127.2
Emotional loads (scores)		2.30	0.08	66.96	< 0.001	0.23	1.1
Intellectual loads (scores)	Diseases of the eye and adnexa	1.19	0.004	377.43	< 0.001	0.63	-
Number of lessons a week		0.06	0.0005	9.20	0.003	0.03	25.0
Number of lessons a day		2.19	0.02	270.32	< 0.001	0.46	-
Number of lessons a week	Diseases of the respiratory organs	0.18	0.0004	85.34	< 0.001	0.21	23.6
Number of lessons a day		2.91	0.01	822.93	< 0.001	0.72	-
Duration of classes (minutes)	Diseases of the musculoskeletal system	0.001	6E-08	22.53	< 0.001	0.07	-
Intellectual loads (scores)		2.28	0.03	182.18	< 0.001	0.45	-
Number of lessons a week		0.09	0.0002	48.52	< 0.001	0.13	23.7
Number of lessons a day		1.56	0.006	430.62	< 0.001	0.58	-

Note: * NOL means no-effect level.

well as phenol and chloroform (R^2 = 0.10–0.16; p < 0.001) in their blood. Effects produced by phenol and chloroform become much more significant in senior school (R^2 = 0.56–0.85; p < 0.001). Elevated concentrations of nickel in primary schoolchildren (R^2 = 0.25; p < 0.001), phenol and chloroform in middle schoolchildren (R^2 = 0.27–0.59; p < 0.001), manganese and nickel in senior schoolchildren (R^2 = 0.58; p < 0.001) could impair visual–spatial short–term operating memory. Elevated concentrations of magnesium, nickel, lead, and phenol and chloroform occurrence reduced response rate in schoolchildren of all ages (RT–test) (R^2 = 0.11–0.88; p < 0.001). We estimated influence exerted by nutrition on the results produced by psychological testing and established the following. Cognitive flexibility in primary schoolchildren primarily deteriorated due to chronic deficiency of protein, calcium and vitamin C in school meals (R^2 = 0.30–0.74; p < 0.0001) and to by 2.5–2.7 times lesser extent due to excessive carbohydrate contents and caloric contents (R^2 = 0.12–0.27; p < 0.0001). Cognitive rigidity in middle schoolchildren went down due to protein, calcium, vitamins C, B1 deficiency, and excessive carbohydrates contents (R^2 = 0.34–0.78; p < 0.0001) and to by 2.6–5.2 times lesser extent due to iron deficiency and excessive caloric contents of meals (R^2 = 0.13–0.15; p < 0.0001). Visual–spatial short–term operating memory in primary school children deteriorated due to calcium and vitamin C deficiency and excessive fat contents (R^2 = 0.51–0.95; p < 0.0001) and to a lesser extent due to protein, vitamins A, B2 deficiency (R^2 = 0.07–0.37; p < 0.0001) This indicator in middle schoolchildren depended on a greater number of nutrition components, in particular, on iron, phosphor, calcium, vitamins A, B1, B2, proteins, and fats (R^2 = 0.25–0.58; p < 0.0001). A response time detected by testing in primary and senior schoolchildren impaired authentically due to calcium and protein deficiency (R^2 = 0.58–0.84; p < 0.0001) and to a lesser extent due to magnesium and vitamin

C deficiency as well as excessive carbohydrate contents (R^2 = 0.13–0.27; p < 0.0001). In middle school, the same effect occurred due to deficiency of magnesium, vitamin C, protein, iron, and calcium (R^2 = 0.15–0.66; p < 0.0001). Next, we estimated effects produced by socioeconomic factors and established that cognitive functions deteriorated in children of all ages due to growing intensity of optional education (R^2 = 0.30–0.71; p < 0.001) whereas growing physical activity increased cognitive flexibility (R^2 = 0.28–0.32; p < 0.001) and the effect was much more apparent in middle and senior schoolchildren, by 1.8–2.5 times (R^2 = 0.27–0.81; p < 0.001). Effectiveness of operating memory directly depends on a socioeconomic status of a family and exposure to tobacco smoke. However, a share contribution made by these two factors does not exceed 6.0–10.0 % and 17.0–27.0 % accordingly for children of all ages (R^2 = 0.03–0.12; p < 0.001–0.02).

Therefore, high intensity of learning, children's blood being contaminated with technogenic chemicals, improper macro- and micronutrient balance in meals as well as some socioeconomic factors raise likelihood of disorders in children's physical development, induce risks of a wide range of somatic pathologies, functional disorders and impaired mental health.

At the same time, the aforementioned factors do not produce any negative effects on physical and mental characteristics as well as on somatic health in case their values conform to optimal levels determined by the accomplished mathematical modeling (Table 2).

Therefore, the existing sanitary-hygienic standards were violated to this or that extent in all the analyzed secondary schools and the analyzed factors deviated from the optimal values determined in our research. Thus, duration of the total educational loads was 900–3150 minutes per week for primary schoolchildren in the first- and third-type schools (the optimal value is 984.3 minutes). Duration of breaks was only 222 minutes per week in the fourth- and fifth-type schools (the optimal value is 345.6 minutes). The smallest educational loads were detected in the third-type school, 22.0 scores a day / 131 scores a week; the greatest ones were detected in the first-type school, 34.0 / 203.0 scores accordingly (the optimal value is 22.0 / 130.0).

Meals were provided with violations in all the analyzed schools. The maximum deficiency of macronutrients was established in the first-type school (45 %); the minimum deficiency, in the fourth- and fifth-type school (5.0 %). Macronutrients levels exceeded their standardized values by 1.2–1.6 times in the second- and third-type school. The minimum deficiency of micronutrients was established in the first-type school (calcium and vitamin A) and the maximum deficiency was detected in third-type school (vitamins B1, B2, C, A, iron, calcium, magnesium and phosphor).We should note that calcium was in deficiency in meals provided by all the analyzed secondary schools.

Having analyzed chemical contamination of children's blood, we established that phenol and lead concentrations exceeded regional background and reference values in children of all ages from all the analyzed secondary schools.

Conclusions. Schoolchildren are simultaneously exposed to risk factors related to the educational process; to harmful environmental parameters, both inside school and beyond; to unfavorable socioeconomic living conditions (the educational process being organized improperly, macro- and micronutrients imbalance in meals provided at schools, children's biological media being contaminated with adverse technogenic chemicals). All this induces disorders in body composition, results in higher morbidity and deteriorates children's mental health.

We took four different types of secondary schools as an example and analyzed them profoundly. This enabled us to develop methodical approaches to substantiating optimal values (or their ranges) for factors related to the education environment as well as the environment beyond the educational process. Conformity with these values results in absence of any impermissible health risks for children. These developed approaches make it possible to determine concrete safe levels of various loads under combined exposure to multiple variable risk factors.

The parameters we determined for the analyzed risk factors in our study do not produce any negative effects on schoolchildren's body even under combined exposure to them. This calls for the necessity to conform to the existing hygienic standards when organizing the educational process and providing meals at school. It is also vital to improve the ecological situation,

Table 2

Optimal values of risk factors that do not produce any negative effects on schoolchildren of all ages even under combined exposure to them

Risk factors	Components of risk factors	Age		
		Primary school	Middle school	Senior school
		Optimal (standard) values		
The educational process	Total educational loads, min/week	984.3 (840.0–1170.0)	1326.4 (1305.0–1620.0)	**1494.0** (1530.0–1665.0)
	Duration of breaks, min/week	345.6 (250.0–360.0)	**454.7** (250.0–420.0)	468.8 (300.0–480.0)
	Recovery index, arbitrary units	0.3	–	–
	An average number of lessons a day	4.6 (4.0–5.0)	–	–
	Educational loads as per subjects, day/week, scores	22.0/130.6 (–/–)	40.4/214.0 (–/–)	44.0/257.0 (–/–)
	Intellectual loads, scores	2.1 (2.3–3.3)	–	–
	Emotional loads, scores	1.1 (1.3–2.3)	–	–
	Monotony of learning, scores	1.8 (2.3–2.8)	–	–
	Intensity of learning, scores	1.7 (1.8–2.7)	–	–
Meals provided at school (breakfast / lunch)	Iron, mg	**3.7** (2.4–3.0)	5.8–6.4 (5.4–6.3)	6.0–6.8 (5.4–6.3)
	Magnesium, mg	**64.5–75.7** (50.0–62.5)	108.8 (90.0–105.0)	100.2–108.1 (90.0–105.0)
	Phosphor, mg	260.7 (220.0–275.0)	426.8 (360.0–420.0)	428.4 (360.0–420.0)
	Calcium, mg	260.6–286.2 (220.0–275.0)	360.3 (360.0–420.0)	383.9–414.6 (360.0–420.0)
	Vitamin A, mg	0.1–0.2 (0.2)	0.2 (0.3)	0.3 (0.3)
	Vitamin B1, mg	0.3 (1.2–0.3)	0.4–0.5 (0.4–0.5)	0.5 (0.4–0.5)
	Vitamin B2, mg	0.3–0.5 (0.3–0.4)	0.5 (0.5–0.6)	0.5 (0.5–0.6)
	Vitamin C, mg	11.8–18.4 (12.0–15.0)	20.0–22.1 (21.0–24.5)	23.3–24.4 (21.0–24.5)
	Proteins, g	19.3 (15.4–19.3)	32.6 (27.0–31.5)	32.3(27.0–31.5)
	Fats, g	**20.0–21.8** (15.8–19.8)	31.6–32.5 (27.6–32.2)	32.8–34.9 (27.6–32.2)
	Crabohydrates, g	81.4 (67.0–83.8)	115.3 (114.9–134.2)	124.9 (114.9–134.2)
	Caloric contents, kcal	585.0–590.0 (470.0–587.5)	846.0 (816.0–952.0)	875.7 (816.0–952.0)
Contaminants in blood	Phenol	0.007 (0.005 ± 0.001)	0.001 (0.005 ± 0.001)	0.009 (0.005 ± 0.001)
	Formaldehyde	**0.004** (0.01 ± 0.001)	**0.005** (0.01 ± 0.001)	**0.005** (0.01 ± 0.001)
	Manganese	**0.003** (0.013 ± 0.004)	**0.003** (0.013 ± 0.004)	**0.003** (0.013 ± 0.004)
	Lead	**0.005** (0.01 ± 0.0067)	**0.007** (0.01 ± 0.0067)	0.010 (0.01 ± 0.0067)
	Nickel	**0.006** (0.015 ± 0.007)	0.010 (0.015 ± 0.007)	0.011 (0.015 ± 0.007)
	Chromium	0.007 (0.003 ± 0.002)	0.010 (0.003 ± 0.002)	0.013 (0.003 ± 0.002)
Socioeconomic factors	Socioeconomic status, scores	0.3	1.4	1.6
	Spare time activities, scores	1.2	2.1	2.1
	Intensity of learning, scores	1.0	1.3	1.3
	Physical activity, scores	0.5	1.7	1.7

to make water treatment procedures more effective and to improve drinking water quality. Interaction between teachers and parents is another significant factor since it helps eliminate gaps in parents' knowledge on how to provide a truly health-preserving environment for their children beyond school.

It is advisable to include biological impedance analysis into periodical medical examinations at school, to maintain close oversight of morbidity among schoolchildren during a school year and to provide relevant psychological testing. There is an acute necessity to develop a standardized procedure for assessing indicators describing intensity of learning in middle and senior school.

Still, we should remember that this study is rather limited since it covers only five secondary schools in Perm region. It is advisable to expand it and analyze secondary schools in other RF regions aiming to perform more profound testing whether the existing standards conform to schoolchildren's physiological needs and whether schoolchildren's life activities are truly safe in the contemporary situation.

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Research article

MYCOTOXINS IN COFFEE AND CHICORY: FROM REGULATED TO EMERGENT

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Coffee is a daily basic food product for many people all over the world. In Russia and some European countries, people who try to pursue healthy lifestyle often prefer chicory as a substitute to coffee. Our research goal was to evaluate occurrence of Aspergillus, Penicillium, Fusarium and Alternaria secondary metabolites in coffee and chicory distributed on the RF market.

29 mycotoxins were determined in 48 samples of coffee and chicory using ultra high-performance liquid chromatography coupled with tandem mass-spectrometric detection (UHPLC-MS/MS).

The range of analyzed contaminants included regulated mycotoxins (aflatoxins, ochratoxin A, deoxynivalenol, fumonisins, T-2 toxin, and zearalenone), their derivatives and structural analogs (A and B trichothecenes), Alternaria metabolites (alternariol, its methyl ether, altenuene, tentoxin), citrinin and several emergent mycotoxins (citreoviridin, cyclopiazonic and mycophenolic acids, enniatins, beauvericin).

To the best of our knowledge, the present study is the first to report results indicating that unregulated emergent mycotoxins occur in the examined products. Chicory samples contained beauvericin (9 of 16 samples, the contents varied from 2.4 to 1173 µg/kg) and enniatin B (6 of 16 samples, 2.8–1109 µg/kg). Green and roasted coffee samples contained mycophenolic acid (11 of 20 samples, 23.5–58.3 µg/kg; 3 of 12 samples, 155.7–712.2 µg/kg accordingly). Several samples were contaminated with aflatoxins, ochratoxin A and fumonisin B2. Their contents in the examined samples did not exceed maximum levels; however, their occurrence indicates a potential health risk for consumers. This requires hygienic assessment and monitoring of these products with the focus on their contamination not only with regulated aflatoxin B1 and ochratoxin A but also with other potentially hazardous mycotoxins.

Keywords: *mycotoxins, emergent mycotoxins, coffee, chicory, ochratoxin A, aflatoxins, contamination, UHPLC-MS/MS.*

Coffee is globally one of the most widely consumed natural beverages. It accounts for 75 % of non-alcoholic drinks' consumption [1]. In the Russian Federation in 2019, coffee consumption exceeded tea consumption by 12 %. Arabica *(Coffea arabica)* and Robusta *(Coffea canephora* var. *Robusta)* are the most widely spread coffee varieties [2]. Besides, there are 125 other varieties including Liberica *(Coffea liberica, Coffea excelsa),* which is grown in South-East Asia and is well-known for its bitter taste; Eugenioides *(Coffea eugenioides)*, grown in Ethiopia; and Cameroon coffee *(Coffea charrieriana)* grown in Cameroon [3]. Health benefits of green coffee are well known at present and it results in growing consumption of beverages based on it [4]. Chicory (*Dorema aucheri*) belongs to *Asteraceae* family and is used as an alternative to coffee. Its taste reminds coffee, but it doesn't contain caffeine.

As any other agricultural products, coffee and chicory can be contaminated with substantial amounts of mold fungi (microfungi) including their toxigenic species. Coffee may be contaminated at any stage in its production, prior to and after harvesting. Coffee tree, being a warm-climate plant, grows only in tropical and subtropical climate. Plants in countries with hot and humid climate are most often

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contaminated with microfungi from *Aspergillus* and *Penicillium* genus that produce the most hazardous mycotoxins (MTs) such as aflatoxins (AFL) and ochratoxin A (OTA) [5, 6]. It is known that fungi from *Aspergillus* species such as *A. carbonarius, A. niger, A. ochraceus* and *A. westerdijkiae* are the main OTA producers in tropical and subtropical coffee plantations and *Penicillium verruculosum, P. brevicompactum, P. crustosum, P. olsonii* и *P.oxalicum* in temperate regions [7, 8]. The capacity of an OTA-producing strains to contaminate the coffee beans depends on several factors such as climatic conditions, storage and transportation, and also processing (wet and dry processing) conditions [9]. Fungi from *Fusarium* genus are also considered natural contaminants in coffee [5].

Most published reports related to coffee bean MT contamination are devoted to its contamination with OTA. There is information about contamination of coffee from Brazil, Vietnam, Guatemala, Indonesia, China, Cote-d'Ivoire [10], the South Korea, Malaysia, Taiwan, the Philippines and Ethiopia with the toxin [11–15]. Meta-analysis carried out by Khanakhan with colleagues [13], gives an opportunity to confirm information about global occurrence of OTA in coffee and coffee beverages in different countries. The lowest occurrence of this toxin was in coffee from the South Korea (3 %), Vietnam (10 %) and Panama (19 %); on the contrary, all samples from Kuwait and Chile were contaminated [13]. OTA was detected not only in green coffee [10, 14, 16] but also in their processing products [8, 11, 12, 17–19]. Coffee contamination with AFL and sterigmatocystin (STC) is reported less frequently [5, 10, 20, 21]. Garcia-Moralez and others found out that all natural coffee samples were contaminated with AFL B1 at the range from 0.25 to 2.33 μg/kg [22]; according to Bessiare with colleagues, 18 % of green coffee samples contained from 0.1 to 1.2 μg/kg AFL B1 [10].

The development and implementation of precise analytical multi-detection methods has allowed carrying out a comprehensive assessment of the contamination of coffee and coffee beverages with a large number of MTs, as well as emergent MTs (EMTs). Fumonisins B2 and B4 have been detected in coffee beans [23]. Other types of coffee and beverages were contaminated with enniatins (ENNs) B, B1, A1, alternariotoxin (alternariol monomethyl ether, AME), beauvericin (BEA), citrinin (CIT) and patulin, fumonisin B1 (FB1), trichothecene MTs and mycophenolic acid (MPA) [8, 10, 17–19, 24]. It has been established that coffee roasting may reduce OTA contents by 97 % depending on the temperature and the particle size [25].

Several countries have established hygienic regulations for MTs contents in coffee. Thus, in the RF the maximum level (ML) of AFL B1 should not exceed 0.005 mg/kg[1]; in the European Union ML OTA is 5 μg/kg in roasted coffee beans and ground roasted coffee and 10 μg/kg in soluble coffee (instant coffee) [26]. OTA contents in green coffee are also regulated in Italy, Finland and Greece at the MLs equal to 8, 10 and 20 μg/kg accordingly [5].

Up to now, an issue related to chicory contamination with MTs in the world has scarcely been given any attention. In the RF, any data on MT contamination of coffee and chicory consumed in the country are practically unavailable.

Our research goal was to evaluate frequency and levels of a wide range of toxicological metabolites: MTs regulated in plant food products (AFL B1, B2, G1, G2; OTA, DON, FB1, FB2, T-2, ZEN); their derivatives

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[1] TR TS 021/2011. O bezopasnosti pishchevoi produktsii: tekhnicheskii reglament Tamozhennogo soyuza (s izmeneniyami na 14 iyulya 2021 goda) / utv. resheniem Komissii Tamozhennogo soyuza ot 09.12.2011 № 880 [CU TR 021/2011. On food products safety: the technical regulations of the Customs Union (last amended on the July 14, 2021), approved by the Decision of the Customs Union Commission on December 09, 2011 No. 880]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/902320560 (November 11, 2021) (in Russian).

and structural analogues (DAS, HT-2, T-2 triol, NEOS - derivative of T-2 toxin; 3- and 15-acDON, FUS X – DON derivatives); cyclopiazonic acid (CPA); citreoviredin (CTV); CIT; as well as EMTs (STC, MPA, ENN A and ENN B, beauvericin (BEA), tentoxin (TEN); toxins produced by *Alternaria* sp. such as alternariol (AON), AME and altenuene (ALT)) in the different coffee varieties including green and black coffee (ground coffee and coffee beans) and chicory.

Materials and methods. Coffee and chicory samples were purchased in retail outlets of Moscow and the Moscow region. Overall, we analyzed twenty samples of green coffee beans (Arabica and Robusta varieties from Central and South America, Africa, India and Indochina) and twelve roasted coffee samples, both beans (7 Arabica samples) and ground coffee (5 samples). Chicory samples included 15 instant ones (13 powder-like and 2 liquid) and one sample of roasted chicory radix cut into small pieces.

Prior to extraction, all samples were mixed thoroughly. 50 g portions of coffee beans and roasted chicory radix samples were milled to a homogenous powder. The samples were prepared according to a modified procedure for determining MTs in green coffee suggested by Bessaire et al. [10]. 1.0 g of powder was weighted into 50 ml centrifuge tube, 10 ml of distilled water were added, mixed and allowed to stay for 10 min for swelling. Next, 10 ml of acetonitrile acidified with acetic acid (1 % of volume) were poured into the sample, mixed, ultrasonicated for 10 minutes and shaken for 10 minutes. After addition of 1 g of sodium chloride and 4 g of anhydrous magnesium sulfate the mixture was centrifuged at 4500 rpm for 15 minutes. An extract aliquot (5 ml) was transferred into the 15 ml centrifuge tube and defatted with 3 ml of hexane by shaking for 10 minutes. Then, 0.7 g of anhydrous $MgSO_4$ was added into the tube and stirred. 3 ml portion of acetonitrile fraction was evaporated to dryness under nitrogen and reconstituted with 100 µl of methanol, followed by 400 µl of milliQ water. After centrifugation, the supernatant was transferred into the chromatography vial for analysis.

Soluble chicory samples were prepared as follows: 1.0 g of thoroughly mixed sample was weighted into 50 ml centrifuge tube, 10 ml of distilled water and 10 ml of acidified acetonitrile (acetic acid, 1 vol. %) were consecutively added and the mixture was thoroughly stirred each time, then it was placed into an ultrasonic bath for 10 minutes and a shaker for 10 minutes. After that, 2 g of sodium chloride were added into the tube and the mixture was centrifuged at 4500 rpm for 15 minutes. 800 µl of the extract were transferred into a microcentrifuge Eppendorf tube and 800 µl of milliQ water were added. After centrifugation, the supernatant was transferred into the chromatography vial for analysis. Each sample was analyzed in two replicates.

Analysis was performed using Vanquish UHPLC system connected with triple quadrupole mass-spectrometric detector with a heated electrospray source TSQ Endura controlled by Xcalibur 4.0 QF2 Software (Thermo Scientific, USA). Analytes were separated on a column filled with octadecyl silica (Titan C18, 2.1 × 100 mm, 1.9 µm, Supelco). The column compartment temperature was 25 °C, the mobile phase flow was 0.4 ml/min, the injection volume was 10 µl.

To perform analysis in positive polarity, the following mobile phases were used: (A) water / methanol (90 / 10 % vol.); (B) methanol / water / acetonitrile (10 / 10 / 80 % vol.), both phases were modified with formic acid (0.1 % vol.) and 1 mM of ammonium formate.

To perform analysis in negative polarity, pH of the phase A was adjusted to 9.0 with aqueous ammonia and equal amount of ammonia was added to the phase B. The gradient scheme was as follows: the start at 0 % B; increase to 100 % B within 20 min; 20–23.5th min, 100 % B; 23.5–24th min, 0 % B; column equilibration at 0 % B from 24th to 26th min.

MS / MS detection was performed in positive or negative electrospray ionization polarities (Tables 1 and 2).

Table 1

MRMs for MTs detected in positive polarity

MT	t_R, min	Parent ion	Parent ion (m/z)	Product ions* (m/z)	Collision energy, V	Fragmentor, V
DON	11.2	$[M+H]^+$	297.1	249.1; 267.1	10.6; 17.9	100
T-2 triol	11.3	$[M+NH_4]^+$	400.2	365.2; 145.2	10; 25	76
FUS X	11.4	$[M+H]^+$	355.4	247.0; 229.1	12.3; 16.0	103
NEOS	11.4	$[M+NH_4]^+$	400.2	215.1; 197.2	16.6; 16.7	79
HT-2	12.3	$[M+NH_4]^+$	442.3	215.1; 263.1	10; 10	91
3- and 15- acDON	13.5	$[M+H]^+$	339.1	137.1; 231.1	10; 12.9	97
AFL G2	14.1	$[M+H]^+$	331.1	245.1; 189.1; 285.1	30; 41; 27	170
AFL G1	14.3	$[M+H]^+$	329.1	243; 200	26; 41	150
FB1	14.4	$[M+H]^+$	722.5	704.5; 352.4	28; 36	217
AFL B2	14.8	$[M+H]^+$	315.1	287.1; 259.0	32; 29	170
DAS	14.9	$[M+NH_4]^+$	384.2	307.2; 247.1	10.3; 14	89
AFL B1	16.1	$[M+H]^+$	313.1	241.0; 213.0	37; 45	166
TEN	16.2	$[M+H]^+$	415.3	312.2; 256.2	19; 29	129
FB2	16.9	$[M+H]^+$	706.5	336.4; 354.4	36; 34	150
MPA	17.5	$[M+H]^+$	321.0	207.0; 303.1	22; 10	113
T-2	18.9	$[M+NH_4]^+$	484.3	215.1; 185.1; 305.2	17; 21; 13	138
CTV	19.1	$[M+H]^+$	403.2	297; 315	10; 10	45
OTA	19.3	$[M+H]^+$	404.1	239; 221	24; 35	123
STC	21.1	$[M+H]^+$	325.1	281.0; 253.0	36; 44	152
CPA	21.8	$[M+H]^+$	337.1	182.0; 196.1	19; 23	165
ENN B	24.6	$[M+NH_4]^+$	657.6	214.2; 527.4	31; 27	142
BEA	25.2	$[M+NH_4]^+$	801.4	244.2; 134.2	32; 54	215
ENN A	25.5	$[M+H]^+$	682.7	210.2; 228.2	24; 24	255

Note: * the first indicated ion is the one used for quantification.

Table 2

MRMs of MTs detected in negative polarity

MT	t_R., min	Parent ion	Parent ion (m/z)	Product ions* (m/z)	Collision energy, V	Fragmentor, V
CIT_1	12.0	$[M+CH_3OH-H]^-$	281	249	10	50
CIT_2	12.0	$[M-H]^-$	249.2	115.2; 205.1	52; 18	200
ALT	14.2	$[M-H]^-$	291.2	189.2; 203	32; 32	188
AON	16.2	$[M-H]^-$	256.9	213; 215; 212.1	22; 25; 32	195
ZEN	20.0	$[M-H]^-$	317.2	175; 73.1; 131.1	23; 18; 28	228
AME	20.1	$[M-H]^-$	271.1	256; 228; 227.1	21; 29; 37	194

Note: * the first indicated ion is the one used for quantification.

The source had the following parameters: the vaporizer temperature was set at 225 °C; spray voltage, 4500 V; the ion transfer tube temperature, 200 °C; sheath gas, 35, aux gas, 10, sweep gas, 2 arb. units (nitrogen in all cases); CID gas (argon), 2 mTorr; dwell time, 100 ms; Q1 and Q3 resolution, 0.7 and 1.4 FWHM accordingly.

Standard solutions of 29 MTs were prepared from dry standards (Sigma Aldrich; Fermentek, Jerusalem, Israel). Stock standards were prepared in acetonitrile (AFL, STC, CIT, trichothecenes of groups A and B, ZEN and its analogues, OTA), methanol (*Alternaria* toxins, ENN A, ENN B, BEA, MPA) or in an "acetonitrile / water" mixture (50 / 50 % vol.)

(FB1, FB2 with a concentration equal to 100 or 500 µg/ml). Standard solutions were used to make a multi-standard and calibration solutions. All the solutions were stored at -18 °C.

To quantify MTs, external calibrations on a "clean" matrix were applied. LOD and LOQ were estimated according to 3-σ and 10-σ criteria: 17 and 52 µg/kg for DON and 3- and 15-acDON toxins; 8.7 and 26 µg/kg for FUS X; 5 and 17 µg/kg for MPA; 4 and 12 µg/kg for T-2 triol; 2.8 and 8.5 µg/kg for CTV and CPA; 2.3 and 6.8 µg/kg for ALT, AON, AME and HT-2 toxin; 1.1 and 3.4 µg/kg for FB1, AFL G2, ZEN and DAS; 0.7 and 2.0 µg/kg for ENN A; 0.5 and 1.7 µg/kg for NEOS, CIT, TEN, ENN B, BEA and T-2; 0.2 and 0.7 µg/kg for OTA and FB2; 0.09 and 0.3 µg/kg for AFL G1 and B2; 0.05 and 0.15 µg/kg for STC and AFL B1. Recovery varied from 60 to 108 %. "Positive" samples were divided into two sub-groups. The first one included samples, containing MTs at concentrations exceeding limit of detection (LOD). The second sub-group included samples contaminated with MT over limit of quantification (LOQ).

Results and discussion. ***Coffee contamination with mycotoxins.*** Occurrence of MTs in 32 samples of green and roasted **coffee** was examined. Six out of twenty-nine analyzed MTs were detected in the samples including MPA, OTA, BEA, AFL B1, AFL B2 and STC. Six percent of green coffee samples were contaminated with regulated AFLs at the levels below 5 µg/kg (0.37 and 1.07 µg/kg). MPA was detected, in 44 % of samples; other toxins were detected less frequently: BEA, in 3 % of the cases; MTs produced by "storage fungi" such as OTA (6 %), AFL B2 (6 %), AFL B1 (3 %). STC was detected in trace quantities (Table 3).

MPA concentrations varied within a wide range from 23.5 to 712.2 µg/kg. All the analyzed samples met the requirements for AFL B1 contents in coffee established in the CU TR 021/2011[1].

A more detailed study of MT contamination of coffee depending on the method of its treatment is presented in Table 4.

The analysis conducted in this study for the first time confirmed the presence of significant amounts of EMTs (MPA and BEA) in the analyzed coffee samples. MPA was detected in 55 % of the green coffee samples (contamination range from 23.5 to 58.3 µg/kg). The occurrence of MPA in roasted coffee was 2 times lower than in ground black and green coffee, while contamination levels amounted to 151.7 and 712.2 µg/kg. BEA was also detected in black ground coffee samples at 0.5 µg/kg.

OTA was detected in isolated samples of roasted coffee beans and green coffee in quantities that were by several times lower than the hygienic standards fixed in the European Union countries. OTA contents in green coffee were by almost 3 times higher than in roasted coffee and amounted to 1.07 µg/kg, which agreed with the published data [5, 10].

Table 3

Occurrence of MTs in coffee and chicory samples

MTs	Samples contaminated with MTs over LOD, %		Contamination, µg/kg	Samples contaminated with MTs over LOQ, %	Contamination levels, µg/kg
	< LOQ	> LOQ			
	Coffee (n = 32)			***Chicory (n = 16)***	
AFL B1	3	–	0.05	6	5.76
AFL B2	6	–	0.09; 0.11	–	–
OTA	3	3	0.37; 1.07	6	1.6
STC	3	–		–	–
MPA	–	44	23.5–712.2	–	–
FB2	6	3	0.2–2.6	–	–
ENN B	–	–	–	38	2.8–1109.0
BEA	3	–	0.50	56	2.4–1173.0

Note: *LOD is limit of detection; LOQ is limit of quantification.

Table 4

Occurrence of MTs in green and black coffee

Toxin	A number of samples		MT contents in contaminated samples, µg/kg		MT contents in samples of the whole series, µg/kg		
	analyzed	contaminated	range	average	M	Me	90 %
Green coffee							
MPA	20	11 (55 %)	23.5–58.3	36.6	20.1	24.1	51.3
AFL B2		2 (10 %)	0.09; 0.11	0.10	0.010	0	0.05
OTA		1 (5 %)	1.07	1.07	0.05	0	0
AFL B1		1 (5 %)	0.05	0.05	0.003	0	0
FB2		1 (5 %)	2.60	2.60	0.13	0	0
Roasted coffee beans							
MPA	7	2 (25.6 %)	155.7; 712.2	434.0	124.0	0	155.7
OTA		1 (14.3 %)	0.37	0.1	0.01	0	0.05
Black ground coffee							
MPA	5	1 (20.0 %)	72.8	72.8	14.6	0	36.4
BEA		1 (20.0 %)	0.46	0.46	0.09	0	0.23

Table 5

Chicory contamination with mycotoxins

Toxin	A number of samples		Contamination range, µg/kg	Average contents in contaminated samples, µg/kg	MT contents in samples of the whole series, µg/kg		
	analyzed	contaminated			M	Me	90 %
BEA	16	9 (56 %)	2.4–1176.2	152.8	85.9	2.5	84.5
ENN B		6 (38 %)	2.8–1109.0	390.5	156.2	0	604.8
AFL B1		1 (6 %)	5.76	5.76	0.64	0	0
OTA		1 (6 %)	1.6	1.6	0.1	0	0

We should note that only green coffee samples were contaminated with AFL: in one samples AFL B1 content was 0.05 µg/kg, in two other samples AFL B2 was found in amounts of 0.09 and 0.11 µg/kg. AFL B1, FB2 and trace quantities of STC were detected only in a Robusta coffee sample. Similar results were obtained on the ground coffee samples; trace quantities of OTA were detected only in a mixture of coffee varieties. The higher MT contamination of Robusta coffee compared to Arabica coffee was also reported by Bessaire and others [5].

Several MTs were rarely identified in the same sample. Two samples were simultaneously contaminated with two toxins, MPA+OTA and MPA+AFL B2. Similar results for green coffee were obtained by other researches [10]. The risk assessment of MT contamination of coffee, based on analyzing the results on this sample of coffee of different varieties and methods of preparation, shows that coffee, in comparison with other products of plant origin, is not a significant source of MT. This assessment indicates that coffee cannot be considered a substantial source of MTs in comparison with other vegetative food products.

In this research, MT contamination of **instant chicory** was studied for the first time. Four toxins were detected as contaminants of this product, the emergent fusariotoxins BEA and ENN B being detected most frequently (Table 5).

More than a half of the samples contained BEA in concentrations from 2.4 to 1176.2 µg/kg. Average contents amounted to 152.8 µg/kg in contaminated samples and 85.9 µg/kg in all the analyzed samples. ENN B was detected in six chicory samples in concentrations ranging from 2.8 to 1109.0 µg/kg. Its average contents reached 390.5 µg/kg in contaminated samples; 156.2 µg/kg, in all the series of samples; 604.8 µg/kg, in 90 %.

Attention should be drawn to the detection in single cases of OTA (1.6 µg/kg) and AFL B1 (5.76 µg/kg) which exceeds hygienic regulation of AFL B1 content, established for some types of plant products in the RF (tea, coffee, cacao and cacao-based products, grains and products made of processed grains).

Liquid chicory samples were also contaminated with EMTs. One sample contained 2.8 µg/kg of ENN B and 3.6 µg/kg of BEA; the other, 1060.2 µg/kg of ENN B and 1172.6 µg/kg of BEA. We should note that AFL B1 that is regulated in food products of plant origin was detected in roasted chicory in the amount of 5.76 µg/kg, together with BEA (3.0 µg/kg).

Conclusions:

1. The procedure for quantification of mycotoxins by ultra-high performance liquid chromatography coupled to tandem mass-spectrometric detection in coffee and chicory has been developed. We have optimized conditions for chromatographic separation and mass-spectrometric detection of 29 MTs. The procedure has been characterized in terms of recovery, limits of detection and quantification.

2. To the best of our knowledge, it has been the first survey of multi-mycotoxin (29 mycotoxins (MTs)) contamination of coffee and chicory present in the RF market. The results indicated wide occurrence of emergent mycotoxins in these products. Occurrence of EMTs, such as MPA and BEA in green and roasted coffee amounted to 47 %; BEA and ENN B were detected in 94 % of chicory samples. MPA concentrations in coffee reached 712.2 µg/kg; maximum ENN B and BEA contents in chicory equaled 1109 and 1173 µg/kg accordingly.

3. Several MTs regulated in food were detected in coffee and chicory samples: OTA, AFL and FB2 – in coffee samples, and AFL B1 and OTA – in chicory. When such carcinogenic toxins as AFL, OTA and fumonisins occur in plant products, this creates a potential health risk when they are consumed with food.

4. The results of our experimental survey on coffee and chicory being contaminated with MTs and EMTs indicate the necessity to perform profound hygienic assessment of plant products that are imported into the RF, especially from regions with tropical and subtropical climate where the environmental conditions are favorable for vegetation of toxicogenic mold fungi from *Aspergillus, Penicillium, Fusarium,* as well as other poorly studied producers of mycotoxins and emergent mycotoxins.

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Competing interests. The authors declare no competing interests.

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Research article

DEVELOPMENT OF A NEW CONCEPT FOR ASSESSING WORK INTENSITY OF CIVIL AVIATION PILOTS

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The article describes a concept for assessing work intensity (WI) developed by the authors. This concept is based on the results produced by comprehensive assessment of the current working conditions, by analyzing the psychophysiological state of civil aviation (CI) pilots in flight, as well as by assessing a contribution made by flight loads and signs of fatigue to an increase in a risk of aviation accidents (AA).

It has been established that, according to sanitary and hygienic profiles, WI levels at all workplaces of civil aviation pilots correspond to harmful working conditions, which are aggravated by exposure to four other harmful factors (noise, microclimate, vibration, and working posture) in 48 % of cases.

The research results have shown that the risks of fatigue increase significantly after 5 hours of flight. This fatigue manifests itself in the growing number of gaze fixations by 11 %; an increase in an average latency period of a complex visual-motor reaction, by 12 %; the growing number of significant errors for flight safety, by 50 %. All these processes occur in the absence of physiological recovery of the cardiovascular system, $p < 0.05$. Pilots who are in a state of fatigue and stress due to violated work and rest regimes tend to have more AA. This accounts for at least 8.4 % of cases from all others causes.

It is proposed to introduce the 3rd degree of harmfulness for strenuous work, as well as new WI indicators for sensory, informational and intellectual loads, such as an increase in a time required to fix the gaze on a device (in %), the frequency of image / value change on a screen (times/min), the volume of information flows per unit of time (bps), and the number of multifunctional devices (more than 10 bits per second). It has been established that the assessment of WI should be supplemented with specific indicators of the flight load and work regimes. These indicators include the number of takeoffs and landings, the number of crossed time zones, the number of stress factors during a flight, and the number of night flight shifts per week. They are directly related to developing fatigue among pilots and an increased risk of AA occurrence.

Keywords: *work intensity, information loads, flight simulators, eye-tracking, fatigue, flight safety, risks of aviation accidents, psychophysiological studies, questioning.*

Work intensity (hereinafter WI) is among the most complicated indicators that describe working conditions. It is very difficult to formalize and regulate quantitatively. The first criteria to assess WI were mentioned about 30 years ago in the Guide R 2.2.013-94 “Hygienic criteria for assessing working conditions as per adverse and hazardous occupational factors, work hardness and intensity”[1] and this was a theoretical breakthrough in occupational medicine. However, these criteria have never been revised since then whereas work process has undergone substantial changes. It has become more productive, intellectual and intensive due to information technologies being implemented into it. These processes make control over WI even harder, especially when it comes down to performing highly intellectual work tasks. It con-

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[1] R 2.2.013-94. Hygienic Criteria for Evaluation of Labour Conditions by Indexes of Harmfulness and Danger of Industrial Environment and Working Process Difficulty and Intensity (approved by the first deputy to the Head of the RF State Sanitary Epidemiologic Surveillance Service and deputy to the RF Chief Sanitary Inspector on July 12, 1994). *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200003682 (March 11, 2022) (in Russian).

cerns not only methodical support but also available assessment criteria being insufficient and limited by too narrow boundaries.

Work performed by pilots who fly modern aircrafts (AC) belongs to the most intensive ones. On one hand, the most sophisticated achievements in avionics are now implemented in civil aviation and it makes AC piloting simpler and easier. On the other hand, this means that pilots are required to mobilize all the functions of their analyzers in order to provide maximum possible concentration, attention focus, prompt decision-making and fast reactions when dealing with constantly changing information.

Assessment of WI for pilots is complicated further due to specific occupational factors at their workplaces. These factors create a whole lot of peculiarities typical for flying including high responsibility; a great number of incoming signals; frequent necessity to make decisions given critical time deficiency; working in shifts with different durations of a shift combined with substantial physiological costs; alternation between day and night shifts; necessity to cross several time zones; developing desynchronosis; possible spatial disorientation and delusions during a flight[2].

The analysis of regulatory and legal documents has revealed the existing gaps in the system for regulation of working conditions for aircraft crewmembers employed in civil aviation. This system is limited to assessing only three occupational factors (noise, microclimate, and lighting). Still, according to some hygienic standards[3], four classical WI indicators are listed among psychophysiological factors (three of them concern sensory loads and the remaining one is about work monotony). However, even this limited list of WI indicators is not sufficient to assess flight burdens on a pilot objectively. We should state that at present noise levels tend to be lower in cabins of up-to-date AC and WI is becoming a leading factor that determines working conditions [1, 2]. It is important to control WI since there is a substantial probability of developing fatigue among pilots, a growing number of errors in their work and, as a result, an elevated risk of aviation accidents.

However, approaches to measuring and assessing WI that are stipulated in basic regulatory documents[4] have certain limitations in their use for this occupational group. To be exact, they do not give an opportunity to assess WI at pilots' workplaces considering multiple action algorithms at different stages in a flight; they have inherent subjectivity of assessment as per specific indicators; they do not involve using up-to-date measuring equipment; they do not regulate conditions for accomplishing relevant measurements (a real flight or a simulator).

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[2] Sanitarno-gigienicheskaya kharakteristika vrednosti, opasnosti, napryazhennosti, tyazhesti truda chlenov ekipazhei vozdushnykh sudov grazhdanskoi aviatsii Rossii: rukovodyashchii dokument (utv. Glavnym gosudarstvennym sanitarnym vrachom RF i Federal'noi aviatsionnyi sluzhboi RF 13, 14 oktyabrya 1997 g.) [The sanitary-hygienic profile of harmfulness, hazard, intensity and hardness of work performed by aircraft crewmembers in Russian civil aviation: the guide (approved by the RF Chief Sanitary Inspector and the RF Federal Aviation Service on October 13, 14, 1997)]. *GARANT: information and legal support*. Available at: https://base.garant.ru/71554050/ (March 12, 2022) (in Russian).

[3] SanPiN 1.2.3685-21. Gigienicheskie normativy i trebovaniya k obespecheniyu bezopasnosti i (ili) bezvrednosti dlya cheloveka faktorov sredy obitaniya (utv. postanovleniem Glavnogo gosudarstvennogo sanitarnogo vracha RF ot 28 yanvarya 2021 goda № 2) [Hygienic standards and requirements to providing safety and (or) harmlessness of environmental factors for people (approved by the Order of the RF Chief Sanitary Inspector on January 28, 2021 No. 2)]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/573500115 (March 12, 2022) (in Russian).

[4] R 2.2.2006-05. Guide on Hygienic Assessment of Factors of Working Environment and Work Load. Criteria and Classification of Working Conditions (approved by G.G. Onishchenko, the RF Chief Sanitary Inspector on July 29, 2005). *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200040973 (March 12, 2022) (in Russian); Ob utverzhdenii Metodiki provedeniya spetsial'noi otsenki uslovii truda, Klassifikatora vrednykh i (ili) opasnykh proizvodstvennykh faktorov, formy otcheta o provedenii spetsial'noi otsenki uslovii truda i instruktsii po ee zapolneniyu: Prikaz Mintruda Rossii ot 24.01.2014 g. № 33n (red. ot 27.04.2020) [On Approval of Procedure for conducting a special assessment of working conditions, Classifier of adverse and (or) hazardous production factors, reporting form on a specific assessment of working conditions and instructions how to fill it in: The Order issued by the RF Ministry for labor and Social Protection on January 24, 2014 No. 33n (last edited on April 27, 2020)]. *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_158398/ (March 12, 2022) (in Russian); MI NTP.INT-17.01-2018. Metodika izmerenii pokazatelei napryazhennosti trudovogo protsessa dlya tselei spetsial'noi otsenki uslovii truda (utv. prikazom General'nogo direktora AO «Klinskii institut okhrany i uslovii truda» A.V. Moskvichevym ot 06.12.2018 № 010-OD) [The methodology for measuring indicators of labor intensity within special assessment of working conditions (approved by A.V. Moskvichev, Managing Director of "Klinskiy Institute for labor protection and working conditions" JSC on December 06, 2018, the Order No. 010-OD)]. Moscow, 2018, 42 p. (in Russian).

All this calls for developing a new concept for assessing WI. This concept for assessing WI at workplaces of civil aviation pilots should rely on control of both functional changes in the body and indicators that provide evidence there is a relationship between occupational factors at pilots' workplaces and an elevated risk of aviation accidents as the most unfavorable outcome at these workplaces.

The concept for WI assessment will make it possible to cover all the specific features typical for flying. These features are associated with sensory, information, intellectual and emotional loads, work monotony and intensive working regimes, in other words, all this combined under the notion "work intensity". This will also help develop relevant activities aimed at improving the system for managing risks associated with fatigue.

Our research goals were to provide scientific substantiation for the WI assessment concept based on results produced by experimental studies of influence exerted by flying and associated loads on functional changes in the nervous system, cardiovascular system, and sensory organs of pilots; on a growing number of errors in work operations during a flight; on establishing a contribution made by fatigue to an increase in a risk of aviation accidents. Another goal was to develop recommendations on making relevant addenda into legal and regulatory documents.

Research materials and methods. The research involved applying analytical examinations, questioning, hygienic studies, time studies, psychophysiological studies, statistical and expert methods. We considered provisions stipulated by the State Standard GOST R ISO 10075-3-2009[5] when selecting the research techniques.

We accomplished experimental studies to assess the psychophysiological state of 120 pilots (aged 41 ± 8 years). The experiment involved simulating a flight using full-flight simulators for Boeing 737-800, Airbus A-320, and Sukhoi Superjet 100 aircrafts that account for 52 % of all the aircraft fleet in the RF civil aviation. Flights with their duration being 340 minutes were simulated based on real situations available in a simulator database (coordinates, height, speed, meteorological conditions, emergencies, etc.). The flights were standardized as per their duration and complexity. Overall, eight different stages in a flight were simulated, each lasting 15 minutes. Three stages did not involve any failures in flight and navigation systems in regular conditions (No. 1, taking off and climbing; No. 2, horizontal flight; No. 3, descending and landing). The other five stages simulated descending and landing with failures of flight and navigation systems in irregular conditions (No. 4, a strong crosswind and fog; No. 5, a strong crosswind, fog and an engine failure; No. 6, a strong crosswind, fog, an engine failure and going on to the second circle; No. 7, a fire in an engine and going on to the second circle; No. 8, a shift in a wind at 1200 meters, going on to the second circle, visual landing). The experiment gave an opportunity to assess errors made by pilots in their operations; the process relied on expert estimates provided by a flight instructor.

Time studies were accomplished in accordance with the Guide on Aircraft Flight Exploitation (GAFE). All the standard operational procedures included into the GAFE were divided into seven groups depending on involved sensory loads: a duration of concentrated observation; density of signals; a number of production objects that were to be observed simultaneously; observation of monitors; loads on the acoustic analyzer; monotony indicators; loads on the vocal apparatus.

We took simple and complex visual-motor reactions (SVMR and CVMR) to analyze operational working capacity and stability of sensorimotor reactions. To do that, we applied UPFT-1/30 "Psychophysiolog" device for psychophysiological testing ("Medicom MTD" NPKF LLC, Russia). We measured 12 indicators including an average reaction time (msec), a total number of errors, and a level of sensorimotor reactions.

Attention focusing was assessed using "BYIBOR" device ("KONTSEPTSYA" JSC. Moscow). We assessed the following indicators:

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[5] GOST R ISO 10075-3-2009. Ergonomic principles of assuring the adequacy of mental workload. Part 3. Principles and requirements concerning methods for measuring and assessing mental workload (approved and validated by the Order of the Federal Agency on Technical Regulation and Metrology dated December 7, 2009 No. 585-st). *KODEKS: electronic fund for legal and reference documentation.* Available at: https://docs.cntd.ru/document/1200075947 (March 17, 2022) (in Russian).

a sum of correct key strokes (quantity); an average reacting time (ART) to signal signs (msec); SD (standard deviation); a sum of "alerting" errors; a sum of logical errors; a sum of omissions.

SMI ETG glasses-like mobile eye-tracker was applied to register and assess indicators of oculomotor activity. We assessed dynamic characteristics of fixations, saccades, and winks (quantity, duration, speed, and path curvature).

We used the same UPFT-1/30 "Psychophysiolog" device for psychophysiological testing ("Medicom MTD" NPKF LLC, Russia) together with Holter monitoring to examine the functional state of the cardiovascular system. Hear rate variability was estimated as per data on statistical, geometric and spectral characteristics.

We questioned 667 pilots and examined data on prevalence of chronic diseases among them. We also analyzed reports on aviation accidents and a contribution made to them by pilots' fatigue resulting from improper work and rest regimes. The reports were issued after 84 investigations of aviation accidents (AA) performed by the Interstate Aviation Committee (IAC) in 2010–2021 [3].

Nominal (qualitative) data were described with absolute values (how many times an indicator recurred in a sampling) and relative frequencies or percents (a percent of this value in the whole sampling). A hypothesis that values of an indicator conformed to normal distribution was tested using Kolmogorov – Smirnov test and Shapiro – Wilk test. Since this distribution was not normal in all the groups, we described them with median values (*Me*) and lower and upper quartile (Q_1; Q_3) calculated in Statistica 10.0.

Results. ***Time studies*** provided an insight into actual sensory loads pilots had to face during a flight. We calculated a number of signals[6] and messages received by a pilot at different stages in a flight, their density per minute/hour, as well as a period a pilot spent performing concentrated observation of the processes involved in a flight (Table 1).

Obviously, a number of signals received by a pilot, their density and a period of concentrated observation are extremely high. For example, during taking off and landing, both pilots had to perform constant control of speed, height, vertical speed, meteorological conditions shown by the locator, relief shown by GPWS, positions of other aircrafts shown by TCAS etc. Given this, values of the aforementioned indicators are far beyond any limits stipulated by regulatory documents[4] for harmful working conditions from the hazard category 3.2. Thus, a period of concentrated observation amounted to 98 %; density of signals

Table 1

Results produced by time studies of regular operational procedures performed by a pilot at different stages in a flight

Flight stages	Number of signals	Time, min	Density of signals per 1 minute / hour	A period of concentrated observation, %
Pre-flight preparations	493	20	25 / 1500	90
AC cabin preparation	1780	30	59 / 3540	100
Towing and starting the engine	603	18	34 / 2040	100
Taxiing	326	10	33 / 1980	100
Taking off	791	10	79 / 4740	100
Climbing	760	20	38 / 2280	100
Horizontal flight	2180	80	27 / 1620	90
Preparing to descend	377	10	38 / 2280	100
Descending	808	20	40 / 2400	100
Landing	361	5	72 / 4320	100
Taxiing after landing and switching the engine off	156	5	31 / 1860	100
Post-flight works	231	15	15 / 900	100
Total in a flight shift	8866	243	37 / 2220	98

[6] A signal was understood as excitation occurring under a specific state or a change in states of production devices that exerted influence on a pilot's sensory organs – visual signals (produced by optical indicators), acoustic signals (acoustic indicators) or signals perceived by skin (tactile indicators). The definition is taken from the MI NTP.INT-17.01-2018[4], item 3.1.7.

per one hour varied from 900 to 4740 at different stages in a flight (2220 per hour on average during a whole flight shift); a period during which pilots had to observe monitors exceeded six hours. Therefore, given all regular operation procedures according to GAFE, actual values of, for example, density of signals received by pilots turned out to be significantly higher than values stipulated by the existing regulations (“more than 300 signals’). This makes it necessary to assign pilots’ working conditions into a category with higher harmfulness as per work intensity, namely the hazard category 3.3.

A number of signals received by a pilot during taking off, for example, requires reacting to them at a speed about 760 msec per one signal[7]. An experimental study showed that an average latent period necessary to select a proper reaction amounted to approximately 330–540 msec [4]. When actual tasks have been performed for a long period, a value of this indicator can grow by 2–4 times and fatigue is very probable. For example, a reaction time of a car driver from the moment a danger was detected to making a decision how to eliminate it varies from 0.4 to 1.6 sec; on average, 1 sec; in the worst scenario, 1.6–2 sec [5]. This reaction time allowed for civil aviation pilots should not exceed 0.5 sec since the density of signals is much higher. Therefore, a number of signals received by a pilot is at the very limit of psychological capacity of human analyzers. When a pilot experiences fatigue and faces substantial overloads due to working under such conditions, errors are very probable and even close to unavoidable.

More than 1000 incoming signals received by pilots per one hour in a flight shift allow concluding that this quantity is much higher than the same parameter for car drivers who receive approximately 700–800 signals per one hour of a work shift that lasts 7–8 hours [5]. Besides, car drivers do not have to observe monitors, to listen what is on the air or to speak with air traffic controllers. Pilots do it constantly using radio headsets. In addition, pilots cannot stop and get some rest in case they feel tired. Therefore, all the indicators prove that work performed by civil aviation pilots belongs to the most intensive ones and it is extremely vital to estimate a number of signals for providing flight safety. Difficulties in calculating a number of signals processed by a pilot during an actual flight are also related to the fact that accomplished procedures on flying an aircraft usually envisage several possible solutions to one task. It is especially true when an unforeseen situation or an emergency occurs (unfavorable meteorological conditions, technical problems, etc.).

According to some research works, it takes a lot of effort to assess sensory loads as per results produced by calculating incoming signals; in addition, such assessments bring a significant uncertainty into ultimate results. Calculation of information loads can become a way to integrally assess volumes of information a pilot has to process. These loads can be calculated using oculography (eye tracking). The maximum information flow of conscious sensory perception is known to be equal to approximately 40 bps[8]. This indicator has been established to be age-dependent since sensory perception goes down by approximately 40 % when a person reaches 60 years.

Issues related to measuring and hygienic assessment of information as a physical factor have been addressed in research works that concentrate on developing “information hygiene” as a specific trend in occupational medicine [6–8]. However, any tasks on determining information loads were solved in such works by using calculated prior methods and relied mostly on assessing volumes of text information produced by workers employed in different brunches on PC over one year. Later works highlight the necessity to compare information produced by people and perceived by them [9, 10]. However, we did not manage to find such studies in available literature sources.

In the present study, the task related to assessing information loads as well as outcomes of their influence on pilots’ functional state was solved by using a comprehensive approach based on actual data obtained in experimental conditions. The study involved using psychophysiological techniques, health self-assessment, revealing correlations between WI and preva-

[7] Matranova I.N. Metodicheskoe rukovodstvo po psikhofiziologicheskoi i psikhologicheskoi diagnostike [The methodical guidelines on psychophysiological and psychological diagnostics]. Ivanovo, “Neirosoft” LLC, 2007, 216 p. (in Russian).

[8] Fundamentals of Sensory Physiology. In: R.F. Schmidt ed. 2nd cor. edition. Berlin, Springer-Verlag, 1981, 267 p.

lence of chronic diseases among pilots as well as occurrence of aviation accidents.

Experimental psychophysiological studies were accomplished in accordance with the approved protocol that envisaged growing intensity of flight loads from stage to stage.

Within the experiment, we performed eye movement testing, assessment of heart rate variability (HRV), CVMR/SVMR, and testing of attention focusing bound to errors in activities. This enabled us to correlate flight loads with functional changes in pilots' bodies as well as to identify exact quantitative volumes of processed information. This quantification considered how frequently one image replaced another on a monitor, information flows from other sources, and a number of multifunctional devices (Table 2). Emotional loads (stress-factors) were calculated as per a number of scheduled taking-offs / landings in difficult conditions with analyzing a number of errors in flying an aircraft.

Results produced by eye-tracking gave grounds for objective assessment of density of signals, a period of concentrated observation, a number of objects that had to be observed simultaneously and how pilots' attention was distributed to cover all of them. The estimated period of concentrated observation varied from 90 % (horizontal flight) to 100 % (pre-flight preparations, taking off, climbing and landing) at different stages in the experiment. The density of signals and messages on average amounted to 4500 per one hour, which is by 15 times higher than the criteria established for intensive labor belonging to hazard category 3.2 as per this indicator. A quantity of objects that should be observed simultaneously varied

Table 2

Indicators of sensory, information, intellectual and emotional loads for pilots in experimental studies with modeling actual flight conditions on a simulator

No.	LI indicators	As per stages in experiment			WI assessment criteria[4,5] for hazard category 3.2	New WI criteria for hazard category 3.3	Expert assessment of WI category (as per average values)
		min.	max.	average			
1	***Sensory loads*** A period of concentrated observation (% of a flight shift)	90	100	95	More than 75[4]	"More than 85"	3.3
2	Density of signals (light, acoustic, tactile) and messages (per 1 working hour during a flight shift, quantity)	5100	8400	4500	More than 300[4,5]	"More than 600"	3.3
3	A number of objects that have to be observed simultaneously (over a flight shift)	25	41	36	More than 25[4,5]	"More than 35"	3.3
4	Observation of monitors (hours per a flight shift)	4,1	6,2	6,1	More than 4/6[4]	"More than 8"	3.2
5	***Monotony*** A period spent on passive observation of a flight process (% of a flight shift)	0	7	6	More than 90[4]	"More than 95"	2
6	***Information loads*** A growing period of gaze fixation on a device (in %)	5	20	15	-	"More than 35" (n.i.*)	3.2
7	Frequency of images/volumes replacing each other on a screen (times/minute)	5	45	30	-	"More than 30" (n.i.*)	3.2
8	Information flow per a unit of time (bps)	5	40	25	-	"More than 100" (n.i.*)	3.2
9	***Intellectual loads*** A number of multifunctional devices (more than 10 bps)	4	4	4	-	"More than 8" (n.i.*)	3.1
10	***Emotional loads*** Work-related stress factors: errors in flying, action algorithm failure, taking offs / landing in unpredictable conditions (a number per a flight shift)	0	20	17	-	"More than 20" (n.i.*)	3.2

Note: *n.i. means this indicator is new.

from 25 (stage No. 2, horizontal flight) to 41 (landing, Nos. 3–6). According to these criteria, pilots' work can be assigned into the hazard category 3.3 as per its intensity.

Observation of monitors (recalculated as per a full regular flight shift) varied from 70 % (4.1 hours) during a horizontal flight to 100 % (6.2 hours) when an aircraft took off (stage No. 1) or landed (3–6, stages No. 5–8). We should note that criteria stipulated in the existing documents for this indicator[4] seem outdated and do not rely on a solid physiological foundation since the hazard category 3.2 covers such working conditions that involve observing visual displays (monitors) being equal to "more than 4 hours". At present, when almost each second workplace is equipped with PC, and information input or reading information on a monitor accounts for more than 50 % of a work time, these boundaries are to be shifted by two hours towards growing without distinguishing a particular type of displayed information. Observation of monitors for more than 8 hours per a work shift allows assigning working conditions into the hazard category 3.3.

A period spent on passive observation of a flight process varied from 0 % (taking off and landing) to 7 % during a horizontal flight. This means no monotony in this kind of work.

Images / values replaced each other on screens of flight and navigation equipment with frequency that was different at different stages in a flight and varied from 5 to 20 (on average 15) times per minute. Information flows per a unit of time varied from 5 to 40 (on average 25) bps. Four different multifunctional airborne devices (more than 10 bps) were used by pilots when different stages in a flight were simulated. These devices were the main flight display, multifunctional display, engine display and on-board computer; their use allowed us to determine intellectual loads pilots had to face. According to these indicators, pilots' work can be assigned into the hazard categories 3.2 and 3.1.

Therefore, three out of ten controlled WI indicators belonged to the hazard category 3.3; 5 indicators, the hazard category 3.2; one indicator, the hazard category 3.1; and only 1 indicator fell within the permissible category. This allows assigning pilots' work into the hazard category 3.3, which is confirmed by the WI indicators determined by simulating an actual flight conditions on a flight simulator.

We analyzed controllable psychophysiological CVMR indicators, attention focusing and HRV in dynamics. The analysis revealed authentic changes in aircraft captains and second pilots both at different stages and by the end of the experiment (Table 3).

The most distinct dynamics was detected in CVMR testing against the results produced by SVMR tests. CVMR testing revealed a decline in correctness by the end of the experiment

Table 3

Results produced by psychophysiological tests on flight simulators

Indicators		Stages in testing		P_{total} / P_{1-8}
		Taking off (Stage 1)	Landing 6 (Stage 8)	
Indicators taken in dynamics as per eye-tracking results				
A number of signals per minute		25.9 [22.1; 31.4]	27.1 [20.8; 35.1]	0.107 / 0.552
Path curvature		2.13 [1.87; 3.14]	2.18 [2.03; 2.35]	0.002 / 0.477
A number of fixations		1.49 [1.11; 1.62]	1.66 [1.51; 1.85]	0.002 / 0.091
CVMR indicators in dynamics				
Average reaction time (ARcT)		409 [390; 440]	461 [392; 558]	0.036 / 0.031
Level of sensorimotor reactions (LoSR)		4.00 [2.25; 5.00]	2.00 [1.25; 3.00]	0.014 / 0.017
Maximum reaction time (MaxRT)		631 [556; 723]	754 [590; 1132]	0.021 / 0.026
Indicators of attention focusing in dynamics				
Minimal reaction time (MinRT)		869 [816; 922]	892 [600; 1235]	0.041 / 0.859
Share of correct answers (SoCA)		100 [90.0; 100]	90.0 [90.0; 100]	0.369 / 0.026
HRV indicators in dynamics				
RMSSD	Aircraft captains	24.4 [22.1; 26.4]	22.9 [16.5; 31.0]	0.178 / 0.032
	Second pilots	35.2 [26.6; 42.8]	32.8 [25.6; 38.1]	0.300 / 0.678
	Both groups	26.4 [22.6; 39.0]	25.6 [20.9; 37.5]	0.131 / 0.085

Note: P_{total} is the significance level in comparing values of dynamic series as per all stages in testing (from taking off to landing 6); P_{1-8} is the significance level in comparing indicators at the marginal stages in testing (only taking off and landing 6).

(by 16.5 %), a growing total number of errors (by 48 %), a growing number of incorrect reactions (by 58 %), a longer average reaction time (by 12.7 %), and a decrease in the integral reliability index (by 17 %).

The data provided by Table 3 and Figure 1 indicate that there was a statistically significant dynamics during all the stages in the experiment as per such CVMR indicators as ARcT (an average reaction time) and LoSR (the level of sensorimotor reactions). It is interesting that ARcT median values were growing steadily from the beginning of testing up to its end. The median had a strong direct statistically significant correlation (r = 0.911, p < 0.001) and its growth rates amounted to 19.5 %. LoSR median values declined steadily from the beginning of testing up to its end and were characterized with a strong direct statistically significant correlation (r = 0.846, p = 0.002), the decrease rate amounted to 50.0 %.

The results produced by analyzing various CVMR indicators in dynamics over the experiment had unidirectional trends. This indicates that changes were developing in the state of pilots' CNS including weaker perception and processing of afferent information as well as developing inhibitory processes. They determined lower effectiveness of the nervous system functioning, including cognitive one, lower working capacities, reliability and safety.

Tests on attention focusing revealed an apparent dynamics as per the minimal reaction time (p = 0.041) during all the stages in the experiment. However, we did not detect any significant differences in this indicator at the beginning and the end of testing (p = 0.859). A different dynamics was detected for a share of correct answers registered at each stage in the experiment. Inter-stage differences in the indicator were not statistically significant (p = 0.369) in most cases apart from differences between the marginal stages where they were statistically significant (p = 0.026). This means the indicators deteriorated and fatigue was developing: the median value of a share of correct answers went down by 10 % from the beginning to the end of testing.

HRV analysis established RMSSD to be the only indicator that correlated with the most significant SVMR indicators and attention focusing indicators. In particular, we revealed statistically significant correlations between RMSSD and a share of correct answers in attention focusing assessment (r = 0.756, p = 0.030) as well as between RMSSD and the average CVMR speed (r = -0.786, p = 0.021). These correlations indicate that in future these indicators (attention focusing, CVMR or HRV) might be introduced as new metrics in fatigue assessment (Figure 2).

The data provided in Table 3 clearly show that such indicators as path curvature and the number of fixations had statistically significant dynamics during all stages in testing. Their growth rates amounted to 2.21 % and 11.8 % for path curvature and the number of fixations accordingly (Figure 3).

The analysis also revealed a strong statistically significant inverse correlation (Figure 3) between RMSSD and such an eye-tracking indicator as the number of fixations (r = -0.747, p = 0.033).

The results produced by analyzing dynamics of psychophysiological indicators showed that fatigue was already present and

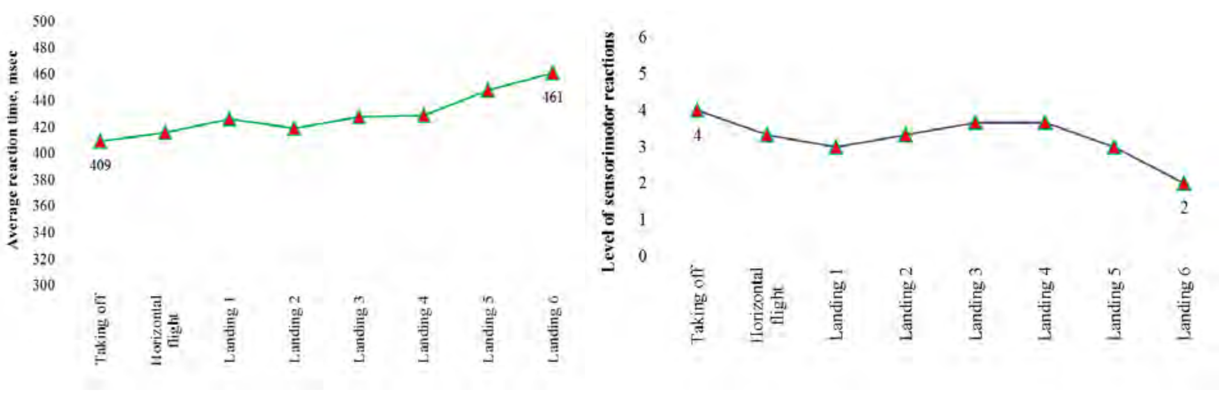

Figure 1. CVMR indicators in dynamics

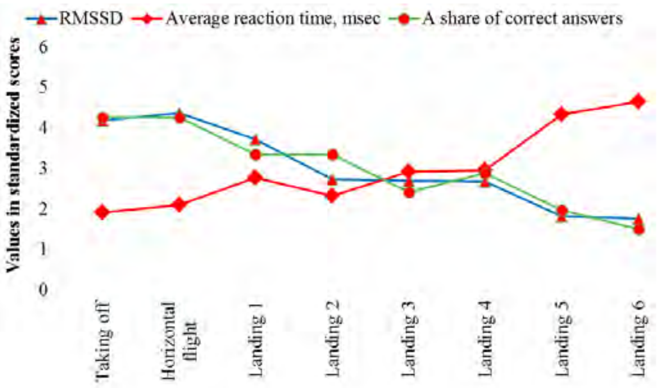

Figure 2. Assessment of correlations between HRV, CVMR and attention focusing

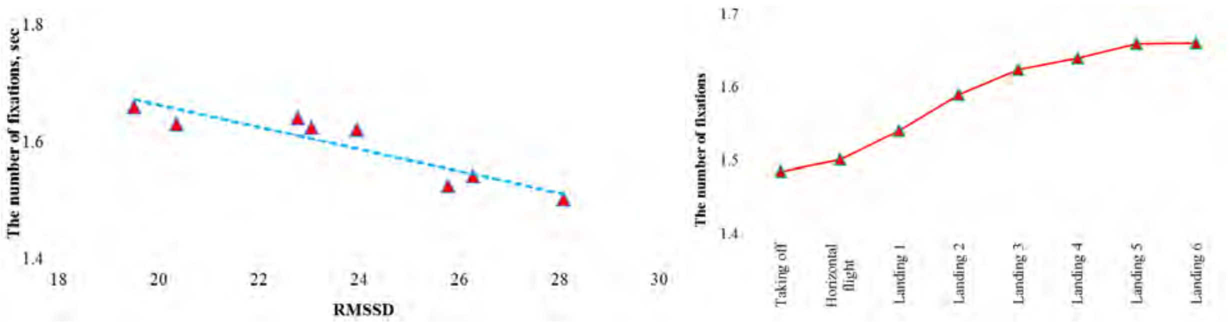

Figure 3. Eye tracking indicators in pilots in dynamics during the experiment

this involved a growing number of errors made by pilots in their operations. Each error was registered by flight instructors who were observing a simulated flight. Errors were detected in flying techniques, navigation, interactions and distribution of attention as well as in maintaining proper radio communication. The significance of these errors was conditionally estimated with scores from one to four (insignificant, correctable, gross or critical). The number and significance of the errors made by pilots turned out to be growing over the experiment and as loads intensified. By the end of the experiment, the differences between the initial and final stages in it were authentic, $p < 0.05$.

RMSSD had a strong and statistically significant correlation with the scores given to the errors ($r = -0.731$, $p = 0.040$). A similar trend was observed regarding correlations between the score given to the errors made by pilots and the share of correct answers in attention focusing assessment ($r = -0.722$, $p = 0.043$). We also detected statistically significant direct correlations between the score given to the errors and path curvature ($r = 0.922$, $p = 0.001$) as well as between the score given to the errors and the number of fixations ($r = 0.905$, $p = 0.002$).

Some aircrews made rather gross errors when flying (for example, they missed a height for going on to the second circle; they did not complete all proper preparations for landing using just one engine; they estimated a situation with engine failure incorrectly; they lost a proper height when landing etc.). The overall number of errors grew by the end of the experiment.

Therefore, the experiment performed on flight simulators involved modeling conditions that were closed to intensive sensory, information, intellectual and emotional loads pilots had to face when flying an up-to-date aircraft during a real flight. According to the level of these loads, pilots' work can be assigned into the hazard category 3.3 as per its intensity. Psychophysiological functions of a pilot can be at the level that imposes a threat to flight safety; the fact is confirmed by the data on errors made by pilots in flying techniques. Impairing psychophysiological indicators in the experiment dynamics were closely related to growing loads and this confirms that WI for pilots actually falls within the hazard category 3.3.

Development of a concept for WI assessment for pilots involved analyzing flight loads and detecting signs of fatigue; this was done based on pilots' self-assessment according to the recommendations by the International Civil Aviation Organization (ICAO) and in line with other research works [11]. According to these recommendations, ***we questioned 667 pilots.*** The results indicate that their work is accompanied with apparent intellectual, sensory and emotional loads and intensive working regimes. We established that more than 70 % of the pilots spent more than 75 % of the total flight time on concentrated observation of the devices; about 30 % of them received more than 300 signals (light or acoustic) per one hour on average during a flight; 60.5 % of the pilots crossed from 2 to 4 different time zones during one flight shift and 18 % of them crossed even more than 4. The pilots often highlighted lack of rest and sleep among factors influencing their fatigue: 1.7 % of them "never" had enough time to rest, 44 % "rarely" had it, and 60 % had only interrupted sleep between flight shifts and they had difficulty falling asleep. A share of pilots who could have episodes of "microsleep" during a flight amounted to 74.3–82.9 %.

The report issued by E.I. Surina, the leading expert on flight safety and human factor and a member of the IATA working panel on FRMS, stresses that it is significant to obtain relevant data on pilots' fatigue by using self-assessment [12]. Thus, according to data provided by voluntary reports (CAA, FAA, NASA), 90 % of pilots consider fatigue the key challenge in their work; they make 30 % of their errors due to fatigue; 7 % of them believe fatigue to be a factor that is hardly manageable with volition. According to some other data, aircraft captains were prone to having aviation accidents during flights that lasted longer than 12 hours (the US National Safety Transportation Board) and 20 % of such accidents are directly or indirectly associated with fatigue (FAA). Forty-three percent of pilots fell asleep at least once during a flight; 31 % stated that they found their second pilot asleep when they woke up (the British Airline Pilots' Association)[9]. According to Russian sources, aviation accidents caused by human factor accounted for approximately 80 % in 2020 as per all types of works [13].

According to questioning performed in Austria (85 %), Sweden (89 %), Germany (92 %) and Denmark (93 %), four out of five pilots feel tired at their workplace. Nevertheless, 70–80 % of pilots who had fatigue did not report fatigability or being incapable to fly [14].

Some factors that cause fatigue produce more apparent tiring effects. They are, for example, multiple taking offs and landings that tire a pilot more than just one flight with the same duration [15]; night flights or flights involving time zones crossing etc. [2, 16]; overtime works that are associated not only with fatigue but also with higher work-related injuries (by 61 %).

We analyzed ***health of civil aviation pilots using data on prevalence of chronic diseases among them.*** The analysis revealed that some diseases were caused by high WI. We detected high prevalence of chronic circulatory diseases (80.6 %), digestive diseases (38.4 %) and diseases of the nervous system (17.4 %) among pilots. They also had authentically higher risks that these diseases would develop (by 8.5, 4 and more than 17 times accordingly) against car drivers whose work is also rather intensive. These diseases were established to be associated with neuro-emotional and sensory loads and they could cause pilots' occupational incapacity, which was also confirmed by other studies.

Examining causes and circumstances of aviation accidents (AA) that occurred in civil aviation in Russia from 2010 to 2021 determined what contribution was made to them by fatigue and stress: 49.7 % of all AA were associated with human factor. Out of them, 8.4 % were caused by pilots' errors resulting from their fatigue due to improper work and rest regimes. In addition, some other factors increased risks of these accidents by 3–5 times: occupational noise, flights in dark, a night shift, total flying hours over a flight shift, month/year and even distribution of flight loads, duration of rest prior to a flight and an annual vacation.

We analyzed data on pilots keeping proper rest and work regimes as per data taken from reports on aviation accidents investigations. The analysis revealed that in some cases daily, monthly or annual standards of

[9] Sostoyanie bezopasnosti poletov v grazhdanskoi aviatsii gosudarstv-uchastnikov soglasheniya o grazhdanskoi aviatsii i ob ispol'zovanii vozdushnogo prostranstva v 2020 g. [Pilots' safety in civil aviation in the member-states of the agreement on civil aviation and air space use in 2020]. *The Interstate Aviation Committee*, 2021, 76 p. (in Russian).

flying hours were violated (from 2.4 to 12 % of cases as per different indicators). Duration of an annual vacation was also improper: almost one third of pilots did not have a vacation for over a year prior to an aviation accident; 18.5 % of aircraft captains had a vacation that lasted 10–29 days, 8 % of second pilots had a vacation of 1–9 days and another 16 %, 10–29 days. Flying hours over the last three days exceeded 13–16 hours in 6–10 % of cases (for both aircraft captains and second pilots), a number of landings varied from five to eight over the same period in 26.8 % of cases (and less than five in the remaining cases). Although we did not establish any violated standards for flying hours (permissible overwork considered), most of the aforementioned cases ended in air disasters. Obviously, improper work and rest regimes and excessive flight loads involve elevated risks of fatigue among pilots and lower flight safety.

Preventive activities aimed at health preservation, labor protection and prevention of accidents primarily rely on ***the legislative base***. A ground document for aircraft crewmembers is the Sanitary Rules SP 2.5.3650-20[10] that stipulates their working conditions as per only three factors. However, the profile of working conditions for airplane and helicopter crewmembers includes practically all known occupational factors and their levels can exceed permissible ones by multiple times. The existing situation is that most work-related factors at pilots' workplaces are not regulated and controlled, though hygienic standards are widely used by those who design and operates aircrafts and by heads of organizations responsible for providing regulated working conditions for pilots and control over their state at workplaces.

Meanwhile, it is well known that exposure to all occupational factors (especially noise, vibration, infrasound, unfavorable ergonomics of a workplace, or an uncomfortable working posture) make for fatigue development among workers[11] [17–19]. When they are not controlled, it does not make pilots' working conditions better or improve flight safety; we should also remember such a risk factor as "overworking", which aggravates their fatigue and neurotic trends [20].

The aforementioned sanitary rules have certain standards for providing safety at workplaces of workers employed by railways, sea and river ships and for air traffic controllers. This can be used as an additional argument for including relevant standards in the SR 2.5.3650-20[10] in the chapter that covers safety provision for air transport. As for vibration, we should note that its standard values for various aircrafts are stipulated in the valid State Standard GOST 23718-2014[12] and occupational diseases associated with exposure to vibration are detected in helicopter pilots. This makes control over this factor mandatory. Regulation of ionizing radiation that exerts its influence on jet plane pilots is included into ICRP, 60, part 1, item136v[13] and Sanitary Rules and Norms SanPiN 2.6.1.2800-10[14] .

Absence of requirements to work-related factors and factors of working conditions makes control over them impossible at workplaces. Due to this, the Order by the RF Ministry of Labor "On approval of peculiarities in accomplishing special assessment of working conditions at workplaces of crewmembers employed in civil aviation" has not been issued yet. A basic complexity in developing "SAWC peculiarities" for crewmembers working in civil aviation was absence of WI assessment criteria. As a

[10] SR 2.5.3650-20. Sanitarno-epidemiologicheskie trebovaniya k otdel'nym vidam transporta i ob"ektam transportnoi infrastruktury (utv. postanovleniem Glavnogo vracha RF ot 16 oktyabrya 2020 goda № 30) [The sanitary-epidemiological requirements for specific means of transport and transport infrastructure objects (approved by the Order of the RF Chief Sanitary Inspector on October 16, 2020 No. 30)]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/566406892 (April 05, 2022) (in Russian).

[11] Suvorov G.A., Shkarinov L.N., Denisov E.I. Gigienicheskoe normirovanie proizvodstvennykh shumov i vibratsii [Hygienic standardization of occupational noise and vibration]. Moscow, Meditsina, 1984, 240 p. (in Russian).

[12] GOST 23718-2014. Passenger and transport airplanes and helicopters. Admissible levels of vibration in saloons and crew cabins and methods of vibration measuring (approved by the EEC and CIS Interstate Council for Standardization, Metrology and Certification (the meeting report issued on May 30, 2014 No. 67-P)). *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200112158 (April 05, 2022) (in Russian).

[13] ICRP Publication 60. 1990 Recommendations of the International Commission on Radiological Protection. *Ann. ICRP*, 1991, vol. 21, no. 1–3.

[14] SanPiN 2.6.1.2800-10. Gigienicheskie trebovaniya po ogranicheniyu oblucheniya naseleniya za schet prirodnykh istochnikov ioniziruyushchego izlucheniya [Hygienic requirements regarding limitation of population exposure due to natural sources of ionizing radiation]. Moscow, Rospotrebnadzor's Federal Center for Hygiene and Epidemiology, 2011, 40 p. (in Russian).

result, necessary requirements are not included into aircraft operating manuals; prevention activities are not developed; problems occur when sanitary-hygienic profiles of working conditions are created; there are no objective grounds for developing a set of activities aimed at preventing fatigue in crewmembers.

Rest and work regime is another significant instrument for providing flight safety. This instrument is not effective enough at present. The Order by the RF Ministry of Transport[15] and the Regulation were issued 17 years ago and need revising. This is further confirmed by results produced by investigating reasons for AA, which showed that work and rest regime was violated in some cases. This led to fatigue among pilots and emergencies (approximately 9 % of AA cases). It is necessary to update the system for regulating work and rest regime and to implement up-to-date mechanisms for control of pilots adhering to it, international experience taken into account.

Discussion. Our analysis of the available regulatory documents indicates that the existing legal and surveillance base for standardization of working conditions at crewmembers' workplaces does not provide necessary control and mitigation of occupational risks. Neither makes it for improving pilots' health and preventing fatigue among them, high work intensity being the basic reason for it.

The comprehensive studies accomplished within this research work allowed us to develop this new concept for WI assessment when dealing with up-to-date intensive work tasks with typically high volumes of perceived and processed information as well as high speed of attention switch and decision-making. These work tasks set high demands for a worker's ability to perform sensorimotor activity under time deficiency. The concept includes a new approach to classifying labor intensity as per its hazard; introduction of the hazard category 3.3 for an indicator that describes sensory loads and for other indicators suggested for control of information, intellectual, and emotional loads (with quantitative criteria); alterations in the conceptual apparatus together with making relevant changes in the regulatory and legal documents. The suggestions have been developed on the example of assessing work intensity at workplaces of civil aviation pilots but they can be used for other occupations as well provided necessary adaptation to their specificity.

The concept is supported with the results produced by the comprehensive assessment of the existing working conditions for civil aviation pilots; analysis of pilots' functional state during a flight, which, among other things, included oculography, a method used for these purposes for the first time; data on prevalence of stress-factors among pilots; results of the questioning performed among crewmembers; as well as the results of assessing what contribution flying loads and fatigue made to occurrence of aviation accidents.

At present occupational morbidity has declined drastically and a probability that a grave occupational pathology would develop has become extremely low. At the same time, exposure levels that underlie assigning working conditions into a category with high hazard have not changed for many occupations; they have become even higher for WI. Work intensity does not have a direct correlation with developing occupational diseases; however, it can cause occupational incapacity and emergencies due to human factor. Such factors include not only WI but also microclimate, infrasound, electromagnetic fields, and lighting environment. Assessment of harmful working conditions as per all existing hazard categories, including 3.1–3.4 and 4, is stipulated for all the aforementioned factors, except WI.

According to ICD-10[16], issues related to work, in particular, "stressful work schedule"

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[15] Ob utverzhdenii Polozheniya ob osobennostyakh rezhima rabochego vremeni i vremeni otdykha chlenov ekipazhei vozdushnykh sudov grazhdanskoi aviatsii Rossiiskoi Federatsii: Prikaz Mintransa Rossii ot 21 noyabrya 2005 g. № 139 (red. 17.09.2010 g.) [On Approval of the Regulation on peculiarities of work and rest regime for crewmember employed in civil aviation in the Russian Federation: The Order by the RF Ministry of Transport dated November 21, 2005 No. 139 (last edited on September 17, 2010)]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/901964448 (April 07, 2022) (in Russian).

[16] Mezhdunarodnaya klassifikatsiya boleznei 10-go peresmotra (MKB-10) (utv. prikazom Minzdrava Rossii ot 27.05.97 g. № 170 (red. ot 12.01.1998)) [International classification of diseases, 10th revision (ICD-10) (approved by the Order of the RF Public Healthcare Ministry on May 27, 97 No. 170 (last edited on January 12, 1998))]. *The international statistical classification of diseases and health issues, the 10th revision, online version*. Available at: https://mkb-10.com/ (March 18, 2022) (in Russian).

(ICD code Z 56.3) are among factors that are potentially hazardous for health and are related to psychosocial circumstances. This allows assigning the WI factor at workplaces (including those of civil aviation pilots) to work-related factors that can cause health hazards and this is fixed in the legislation.

WI induces unfavorable changes in workers' functional state thereby increasing occupational risks associated with injuries and emergencies. Given that, we suggest making the following alterations to determining the hazard category 3.3 of working conditions as per labor intensity.

The hazard category 3.3 (harmful working conditions, the 3rd degree) is applied to working conditions when a worker is exposed to harmful and (or) hazardous occupational factors exposure to which can induce such functional changes in a worker's body that can lead to developing occupational diseases with average or grave severity (including those with loss of working ability) and/or occurrence of chronic diseases caused by working conditions and/or high probability of an injury and an elevated risk of emergencies.

Intellectual load is a load when work is estimated considering intellectual activities performed by a worker. Intellectual load at workplaces of civil aviation pilots is assessed as per the number of multi-functional devices (more than 10 bps) in an aircraft cabin.

Information load is a quantitative measure of an information flow received by a worker per a unit of time, bps.

A multifunctional device is a device with an information flow going through it exceeding 10 bps.

This research has shown a possibility to perform objective assessment of visual signals using oculography (eye-tracking). However, so far there have been no available physiological criteria for assessing work performed by a pilot when this device is used. Our data gave an opportunity to suggest such criteria based on comparing oculography results and current sensory loads with results produced by simultaneous physiological studies that involved assessing SVMR, CVMR and HRV as well as with a number of errors made by a pilot when flying an aircraft as flight loads became more intensive. Oculography results were scaled as per intensity depending on signs of growing fatigue. This intensity was determined by an increase in a time of fixation on a device (in %), frequency of images/values replacing each other on a screen (times/minute), information flow volume per a unit of time (bps), and a number of multifunctional devices (more than 10 bps).

Specific indicators describing flight loads are especially significant in WI for civil aviation pilots. They include duration of a flight shift (which can exceed 10 hours when it comes down to long-distance flights); a number of taking offs and landings and a number of time zones crossed during one flight shift; a number of night flight shifts per week. These indicators are considered "work regimes". The criteria to assess them were developed based on work and rest regime regulations, results produced by investigating aviation accidents in civil aviation and pilots' health self-assessment.

Our research results indicate it is necessary to make ranges for the WI indicators wider and include the hazard category 3.3 for them.

Table 4 provides the criteria developed for assessing work intensity at workplaces of crewmembers.

Conclusions. The research results indicate that boundaries for hazard categories of working conditions as per indicators fixed in regulatory documents[4] are not sufficient for assessing WI at pilots' workplaces. This necessitated developing more precise criteria and introducing an additional hazard category of working conditions as per work intensity, 3.3, as well as developing new indicators for assessing information, intellectual and emotional loads.

We have developed new criteria for assessing WI for pilots who had to face highly intensive flight loads. These criteria are substantiated with the results produced by psychophysiological studies on flight simulators and confirmed by the questioning among aircraft crewmembers, detected regularities in prevalence of chronic diseases among them, and established cause-effect relationships with an increase in a risk of aviation accidents in civil aviation.

Given intensive flight loads pilots are exposed to, their psychophysiological functions can impair down to a level that imposes a threat to flight safety. This is confirmed by the data of physiological studies; errors made by pilots in flying techniques, navigation, distribution of attention, and radio communication

Table 4

Hazard categories of working conditions as per WI for civil aviation pilots

Indicator	Hazard category of working conditions			
	permissible		harmful	
	2	3.1	3.2	3.3
Sensory loads				
Duration of concentrated observation (% of a flight shift)	Less than 50	51–75	76–85	More than 85
Density of signals (visual and acoustic) and messages on average per 1 hour of a flight shift, units	Less than 175	176–300	301–600	More than 600
The number of objects that have to be observed simultaneously per 1 working hour	Less than 10	11–25	26–35	More than 35
Observation of monitors and devices (hours per a flight shift)	Less than 6	from 6 to 8	from 8 to 10	10 and higher
Duration of loads on the acoustic analyzer (hours per a flight shift)	Less than 6	from 6 to 8	from 8 to 10	10 and higher
Loads on the vocal apparatus (hours per week)	Less than 20	from 20 to 25	from 25 to 30	More than 30
Information loads				
Longer duration of fixation on a device (% of a total flight)	Less than 10	from 11 to 20	from 21 to 35	More than 35
Frequency of image/values changing on a screen (times/hour)	Less than 5	from 6 to 15	from 16 to 30	More than 30
Information flow volume per minute (bps)	Less than 5	from 6 to 10	from 11 to 100	More than 100
Intellectual loads				
The number of multifunctional devices (more than 10 bps)	1–3	4–5	6–7	More than 7
Emotional loads				
Work-related stress factors: errors in operation, action algorithm failure, taking offs and landings under unpredictable conditions (a number per a flight shift)	Less than 10	from 11 to 15	from 16 to 20	More than 20
The number of conflicts (per a shift)	Less than 3	from 4 to 6	from 7 to 9	More than 9
Monotony of loads				
Time spent on passive observation of a flight process (% of a total shift)	Less than 80	from 81 to 90	from 91 to 95	More than 95
Work regime				
Duration of a flight shift (hours)	Less than 8	9	10	More than 10
The number of taking offs/landings (per a flight shift)	1–2	3–5	6–8	More than 8
The number of taking offs/landings (per week)	1–6	7–10	11–14	More than 14
The number of night flight shifts (per week)	1–2	3	4	More than 4
The number of crossed time zones (per a flight shift)	1–3	4–5	6–7	More than 7
The number of crossed time zones (per week)	1–6	7–12	13–18	More than 18

maintenance during the experiment that involved modeling a flight on a flight simulator; and by the results of the accomplished questioning and data taken from reports issued after investigations of actual aviation accidents.

An efficient legislative base for regulation and control of pilots' working conditions, WI standardization that is adequate to actual flight loads, and established differentiated work and rest regimes are mandatory for mitigating occupational health risks for civil aviation pilots and preventing fatigue among them. The latter is a leading factor that can reduce risks of aviation accidents and provide flight safety.

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Research article

INTEGRATED MODEL OF HEALTH RISK ASSESSMENT FOR WORKERS HAVING TO WORK OUTDOORS UNDER EXPOSURE TO COOLING METEOROLOGICAL FACTORS

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Natural resources extraction involves continuous exposure to cooling meteorological factors typical for open production grounds. This necessitates relevant health risk assessment and management of health risks caused by exposure to these harmful occupational factors. However, the available risk assessment models do not provide a possibility to perform complete assessment of the existing risks created by exposure to meteorological hazards.

The study design included the following. We performed hygienic assessment of working conditions and health of workers employed by "Samotlorneftegaz" Joint Stock Company (JSC) who had to perform their work tasks under exposure to cooling meteorological factors on open production grounds; the assessment involved calculating the group health risk. Individual peculiarities were assessed using subjective (547 people took part in questioning) and objective assessment methods (76 people took part in estimating thermal state of their bodies and 54 people participated in thermometry with cold stress). Finally, we assessed prior and posterior risks.

The prior group risk assessment made it possible to identify risk groups who had a significant risk of developing occupational and non-occupational diseases and to rank working places as per health hazards. The posterior risk assessment confirmed the results produced by the prior risk assessment regarding potentiating negative effects produced by cooling meteorological factors. The assessment of developing general and local thermoregulation disorders revealed that certain individual peculiarities made a substantial contribution to their development. Among them, we can mention long-term outdoor work (60 % of work time or more) under exposure to cooling meteorological factors; a chronic pathology; tobacco smoking. The results produced by this study allowed us to suggest an integrated model for risk assessment, management and communication about health risks caused by working under exposure to cooling meteorological factors.

Keywords: *outdoor work, oil production, cooling meteorological factors, health risk assessment, prior risk, posterior risk, individual peculiarities in outdoor work.*

In the Russian Federation, 69.7 % of all the regions are completely or partially located in areas with arctic climate and climate that is considered just as harsh [1].

Almost 80 % of all natural resources in the country (more than 90 % of natural gas and 75 % of oil) are concentrated in the northern regions [2, 3]; naturally, such global companies as PJSC Rosneft Oil Company and PJSC Gazprom have large production complexes there.

Although technological processes applied in oil production have never ceased to develop,

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health risks for workers employed in the industry remain rather high [4, 5, 6–9].

Technological processes at oil production enterprises involve spending a lot of time outdoors since workers have to cover long distances during a work shift moving from one place to another. Several authors mention a possibility that working conditions might deteriorate due to indirect effects produced by cooling microclimate and resulting changes in intensity of impacts exerted by some other harmful occupational factors on workers' bodies [10–15]. Complex exposure to adverse and (or) hazardous occupational factors as well as to adverse climatic conditions creates high occupational risks[1]. Therefore, it is vital to assess and manage health risks for workers who are exposed to cold at their workplaces [16].

There is no available procedure for assigning working conditions into a specific hazard category as per exposure to cooling microclimate on open grounds [17]. This creates certain difficulties for performing hygienic assessment of working conditions and health risk assessment as well as for accomplishing preventive activities aimed at mitigating this risk factor.

The existing risk assessment models mostly concentrate on meteorological parameters when it comes down to exposure to cooling meteorological factors [18–20]. However, they do not provide a possibility to assess the existing risk integrally, including its aspects related to work record, working process peculiarities, and individual reactions to cold.

Our research goal was to develop an integrated model of health risk assessment for workers who have to work outdoors under exposure to cooling meteorological factors.

Materials and methods. Our study concentrated on health and working conditions of workers employed at an oil production facility. It was conducted at the following production grounds belonging to Samotlorneftegaz Joints Stock Company (JSC): the oil treatment and pumping workshops No. 1 and 2 (OTPW No. 1 and 2); the oil treatment and deposit workshops No. 1 and 2 (OTDW No. 1 and 2); and the environmental recovery workshop (ERW). Several occupational groups participated in the study including operators of the dehydrating and desalting unit (DDU operators); compressor unit operators (CU operators); operators dealing with units for pumping working substance into a bed (PWSB operators); repairmen [21].

Climate on the analyzed territory is harsh with the overall cold season lasting up to 270 days. The region is located in the climatic zone II (III) with average winter temperature being -18 $^{\circ}$C.

Hygienic assessment of working conditions was based on the results produced by production control (PC) and special assessment of working conditions (SAWC) for the period from 2014 to 2018.

Microclimate at workplaces was assessed in accordance with the Guidilines R 2.2.2006-05[2]. The equivalent temperature was determined as per data obtained by daily monitoring of air temperature and velocity that was performed by the information and analytical system (IAS) of the enterprise.

Prior health risk caused by exposure to occupational noise, whole-body vibration, chemicals in workplace air, work heaviness and cooling microclimate on open grounds in the cold season [21] was assessed as per the previously developed models[3].

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[1] O Strategii razvitiya Arkticheskoi zony Rossiiskoi Federatsii i obespecheniya natsional'noi bezopasnosti na period do 2035 goda: Ukaz Prezidenta RF ot 26.10.2020 № 645 [On the strategy for the Arctic zone development in the Russian Federation and national security provision for the period up to 2035: The RF President Order issued on October 26, 2020 No. 645]. *Prezident Rossii [web-site]*. Available at: http://www.kremlin.ru/acts/bank/45972 (March 02, 2022) (in Russian).

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The prevalence of various pathologies among workers was analyzed as per results produced by periodical medical examinations (PME). Overall, 1063 workers participated in them [5]. To detect any statistical differences in workers' health, we created two study groups made of workers who spent the shortest period per week outdoors and the longest one [5]. Overall, group I included 616 workers with the following occupations: DDU operators (192 people), repairmen (80 people) and process unit operators (344 people). They had to perform their work tasks on open grounds for a period from 10.5 to 14.0 hours a week, that is, up to 35 % of the total working time. Group II was made up of 447 workers including DDU operators (128 people) and repairmen (319 people) who spent from 24 to 31 hours a week working on open grounds, that is, 60 % of their total working time or even more.

Posterior risk was assessed in accordance with the guide[4]. We chose 95 % confidence interval as a statistical reliability measure ($p < 0.05$).

Individual peculiarities related to working on open grounds were assessed using subjective (547 people took part in questioning) and objective assessment methods (76 people took part in estimating thermal state of their bodies[5] and 54 people participated in thermometry with cold stress[6]).

We questioned the workers using our own original questionnaire. It contained 35 questions about working conditions, occupation, work record, health, lifestyle, and some other factors.

Thermal state of workers' bodies was estimated in normal conditions, 2 hours prior to working under exposure to cold and 2 hours after it. We used the following direct indicators to describe thermal state: body and skin temperature, self-feeling of being warm or cold, and heat content. Body temperature was taken in the axillary crease; skin temperature, on five different spots on a worker's body surface. Overall, we took more than 1000 measurements [21].

Local thermoregulation disorders with cold stress were estimated in a specially allotted warm room at the studied enterprise prior to starting work in cold outdoor conditions. An examined participant spent 10 minutes in sedentary posture to provide thermal adaptation; then, according to the procedure, a worker had to submerge his hands into cold water and keep them there until local discomfort occurred. Then, the temperature was measured in dynamics during 25 minutes until it reached its initial level.

All the results were statistically analyzed with MS Excel 2010 and Statistica 10 applied software packages.

Results and discussion. We calculated prior health risks caused by exposure to major harmful occupational factors, work record at selected workplaces being taken into account [5, 21, 22]. The results are provided in Table 1.

Occupational noise was the leading health risk factor at most workplaces. Cooling microclimate on open grounds was also identified as a leading health risk factor at certain workplaces, including PWSB operators of KNS-6 (group pumping station) at the OTPW No. 1 and repairmen dealing with DNS-4 (booster pump station) and KNS-6 at the ERW [21].

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[6] Voprosy rannei diagnostiki i profilaktiki pri sosudistykh narusheniyakh u gornorabochikh Zapolyar'ya: metodicheskie rekomendatsii [Issues related to early diagnostics and prevention of cardiovascular diseases in miners working beyond the Polar Circle: methodical guidelines]. In: A.V. Ivanov, A.S. Kononov, S.K. Kashulin eds. Kirovsk, Scientific research laboratory for complex issues of occupational hygiene with clinical picture of occupational diseases of the RSFSR Public Healthcare Ministry, 1981, 17 p. (in Russian).

Table 1

Prior health risks for workers with different work record of work under exposure to harmful occupational factors

Work record, years	Prior risk					
	Noise	Microclimate in cold season	Whole-body vibration	Work heaviness	Chemical factor, non-carcinogenic risk	Total risk
DDU and DNS-1 operators at the OTPW No. 1						
10	*0.133*	0.02	≤0.02	≤0.02	0.000453	*0.151*
15	**0.162**	0.02	≤0.02	≤0.02	0.00053	**0.179**
20	**0.184**	*0.05*	≤0.02	≤0.02	0.00059	**0.225**
25	**0.203**	*0.10*	≤0.02	0.02	0.00063	**0.297**
30	**0.218**	**0.16**	≤0.02	*0.05*	0.00067	**0.376**
DDU operators of CRP at the OTDW No. 1						
10	**0.184**	0.02	≤0.02	≤0.02	0.00023	**0.201**
15	**0.219**	0.02	≤0.02	≤0.02	0.00027	**0.235**
20	**0.245**	*0.05*	≤0.02	≤0.02	0.00030	**0.283**
25	**0.267**	*0.10*	≤0.02	0.02	0.00032	**0.354**
30	**0.286**	**0.16**	≤0.02	*0.05*	0.00034	**0.430**
PWSB operators of KNS-1E at the OTPW No. 1						
10	*0.093*	0.02	≤0.02	≤0.02	0.000347	*0.111*
15	*0.116*	0.02	≤0.02	≤0.02	0.000409	*0.134*
20	*0.134*	*0.05*	≤0.02	≤0.02	0.00045	**0.178**
25	*0.149*	*0.10*	0.02	≤0.02	0.00049	**0.250**
30	**0.162**	**0.16**	*0.05*	≤0.02	0.00051	**0.332**
PWSB operators of KNS-6 at the OTPW No. 1						
10	*0.055*	0.02	≤0.02	≤0.02	0.000043	*0.074*
15	*0.069*	0.02	≤0.02	≤0.02	0.000051	*0.088*
20	*0.082*	*0.05*	≤0.02	≤0.02	0.000056	*0.128*
25	*0.093*	*0.10*	≤0.02	≤0.02	0.00006	**0.184**
30	*0.102*	**0.16**	≤0.02	≤0.02	0.00006	**0.246**
TAKAT-1,2,3 vacuum compressor operators at the OTDW No. 1						
10	*0.119*	0.02	≤0.02	≤0.02	0.000233	*0.137*
15	*0.145*	0.02	≤0.02	≤0.02	0.00027	**0.162**
20	**0.166**	*0.05*	≤0.02	≤0.02	0.00030	**0.208**
25	**0.184**	*0.10*	0.02	≤0.02	0.00032	**0.281**
30	**0.199**	**0.16**	*0.05*	≤0.02	0.00034	**0.361**
VKS-28 vacuum compressor operators at the OTPW No. 2						
10	**0.166**	0.02	≤0.02	≤0.02	0.00035	**0.183**
15	**0.199**	0.02	≤0.02	≤0.02	0.00041	**0.215**
20	**0.223**	*0.05*	≤0.02	≤0.02	0.00045	**0.262**
25	**0.245**	*0.10*	≤0.02	≤0.02	0.00049	**0.321**
30	**0.262**	**0.16**	≤0.02	≤0.02	0.00051	**0.380**
Repairmen of DNS-4 and KSP-6 at the ERW						
10	*0.055*	0.02	≤0.02	≤0.02	0.01473	*0.088*
15	*0.069*	0.02	≤0.02	≤0.02	0.01488	*0.101*
20	*0.082*	*0.05*	≤0.02	≤0.02	0.01499	*0.141*
25	*0.093*	*0.10*	≤0.02	0.02	0.01507	**0.212**
30	*0.103*	**0.16**	≤0.02	*0.05*	0.01514	**0.295**

Note: health risk rates that correspond to significant risk of occupational diseases ($Risk_{OD} \geq 0.16$) are given in bold; moderate risk rates that correspond to significant risk of non-occupational diseases ($Risk_{OD} \geq 0.05$ and < 0.16) are given in italics.

It is obvious that different occupational factors make different contributions to the total risk; these contributions can be either significant or insignificant for occupational diseases occurrence depending on a workplace. Significant total risk rates for occupational diseases occurrence (more than 16 %) were detected for workers with work record being 10 years who worked as DDU operators at the central reservoir park (CRP) grounds in the oil treatment and deposit workshop No. 1 and vacuum compressor unit (VKS-28) operators in the OTPW No. 2. Significant total risk was established for those workers with work record being 15 years who worked as DDU operators of the booster pump station (DNS-1) in the OTPW No. 2 and TAKAT-1,2,3 vacuum compressor operators in the OTDW No. 1. Workers with their work record being 20 years had significant total risk at workplaces of PWSB operators at the group pumping station (KNS-1E) in the OTPW No. 2. Those with work record being 25 years had this level of risk at workplaces of PWSB operators at the group pumping station KNS-6 in the OTPW No. 1 and repairmen at the booster pumping station DNS-4 and group pumping station KSP-6 in the environmental recovery workshop (ERV) [21].

Exposure to cooling microclimate makes a substantial contribution to occupational and non-occupational incidence among workers [5]. This contribution made by cooling meteorological factors to the total health risk varied depending on work record and a workplace. It was insignificant during the 1st year of working and rose to 65.1 % when work record reached 30 years. When work record was equal to 5 years, the contribution made by cooling meteorological factors varied from 13.3 % for DDU operators at the central reservoir park (CRP) grounds in the oil treatment and deposit workshop No. 1 to 37 % for PWSB operators at the group pumping station KNS-6 in the OTPW No.1. When work record reached 30 years, the contribution made by cooling meteorological factors to the total risk rose to its maximum and varied from 37.2 % for DDU operators at the CRP grounds in the OTDW No. 1 to 65.1 % for PWSB operators at the KNS-6 in the OTPW No. 1 (Table 2).

Table 2

Contributions made by cooling meteorological factors to the total health risks at the examined workplaces depending on work record

Occupational group	Workplace	Work record significant for OD occurrence* (years)	Contribution made by cooling meteorological factors to risks of somatic and occupational diseases (%)					
			Work record (years)					
			5	10	15	20	25	30
DDU operators	DNS-1 OTPW No. 2 (*n* = 10)	15	18.0	13.3	11.2	22.2	33.6	42.5
	CRP OTDW No. 1 (*n* = 24)	10	13.3	10.0	8.5	17.7	28.3	37.2
PWSB operators	KNS-6 OTPW No. 1 (*n* = 7)	25	37.0	27.0	22.7	39.1	54.4	65.1
	KNS-1E OTPW No. 2 (*n* = 3)	20	24.7	18.0	14.9	28.1	40.0	48.2
CU operators	TAKAT-1,2,3 VCU OTPW No. 1 (*n* = 4)	15	19.8	14.6	12.3	24.0	35.6	44.3
	VKS-28 OTPW No. 2 (*n* = 4)	10	14.7	10.9	9.3	19.1	31.2	42.1
Repairmen	DNS-4 ERW (*n* = 52)	25	29.4	22.7	19.8	35.5	47.2	54.2
	KSP-6 ERW (*n* = 51)	25	29.4	22.7	19.8	35.5	47.2	54.2

Note: * OD means occupational diseases.

The research involved using the health risk assessment procedure. According to it, we applied models for assessing prior group health risk that helped us determine contributions made by specific factors into the total risk. A time study performed at workplaces was a vital stage in hazard identification. This study was performed at workplaces where workers had to deal with various work tasks during their work shift and an amount of time spent working on open grounds was of fundamental importance for health outcomes in a whole number of cases. Thus, it was reported that workers who performed their work tasks on open grounds for 60 % of their working time or even longer had a high risk of a developing chronic pathology [21].

Posterior risk assessment revealed that exposure to harmful occupational factors combined with cooling meteorological factors had a direct correlation with morbidity since RR was higher than 1 for priority categories of diseases, both on average and as per its upper and bottom limits [22].

Since etiological fractions were higher than 50 % as per these categories of diseases, we can conclude there is a strong correlation here. Therefore, diseases of the circulatory system (RR = 2.87, CI: 2.36–3.48, $p < 0.001$), diseases of the ear and mastoid process (RR = 2.49, CI: 1.85–3.36, $p < 0.001$), diseases of the nervous system (RR = 5.12, CI: 3.21–8.16, $p < 0.001$), diseases of the musculoskeletal system (RR = 3.18, CI: 2.46–4.09, $p < 0.001$), diseases of the digestive system (RR = 3.35, CI: 2.04–5.48, $p < 0.001$) and diseases of the respiratory system (RR = 4.9, CI: 2.64–9.25, $p < 0.001$) can be considered occupational and associated with long periods spent by workers on open grounds under exposure to cold (Table 3) [21].

The next stage in our research involved assessing individual peculiarities based on the questioning results as well as the results produced by field and model tests.

Thermal regulation disorders were assessed subjectively and objectively in workers who were exposed to cooling meteorological factors at their workplaces. As a result, we determined what individual peculiarities made for developing local and overall thermal regulation disorders. They were a long period spent working outdoors, for 60 % of the total working time or even longer (RR = 3.0; CI: 1.20–7.45; $p = 0.017$); chronic pathology including diseases of the circulatory system (RR = 1.46; CI: 1.30–1.63; $p < 0.0001$), diseases of the ear and mastoid process (RR = 1.33; CI: 1.20–1.47; $p < 0.0001$), endocrine, nutritional and metabolic

Table 3

Posterior health risks for workers who spend the longest time on open grounds

№	Category of diseases as per ICD-10	Relative risk (RR) (95 % confidence interval (CI))	Sensitivity, %	Specificity, %	Etiological fraction EF, %	Statistic indicators
1	Diseases of the circulatory system	2.87 (2.36–3.48)	67.6	69.6	65.2	χ^2 = 129.56; **$p < 0.001$**
2	Diseases of the ear and mastoid process	2.49 (1.85–3.36)	64.4	62.0	59.8	χ^2 = 39.52; **$p < 0.001$**
3	Diseases of the digestive system	3.35 (2.04–5.48)	70.8	60.0	70.1	χ^2 = 26.26; **$p < 0.001$**
4	Diseases of the nervous system	5.12 (3.21–8.16)	78.8	61.7	80.5	χ^2 = 60.46; **$p < 0.001$**
5	Diseases of the musculoskeletal system	3.18 (2.46–4.09)	69.7	65.5	68.5	χ^2 = 91.30; **$p < 0.001$**
6	Diseases of the respiratory system	4.90 (2.64–9.25)	78.2	59.9	79.6	χ^2 = 31.07; **$p < 0.001$**

Table 4

Risks of developing local and overall thermal regulation disorders for workers with individual peculiarities who have to work on open grounds during the cold season

№	Individual peculiarities	Relative risk (RR), 95 % confidence interval (CI), significance level (p)	
		Local thermal regulation disorders	Overall thermal regulation disorders
1	Tobacco smoking	2.69 (1.23–5.88) $p = 0.007$	1.13 (1.02–1.27) $p = 0.0378$
A	Smoking intensity from 11 to 20 cigarettes a day	4.17 (1.33–13.04) $p = 0.005$	$p > 0.05$
B	Smoking for more than 20 years	$p > 0.05$	1.23 (1.05–1.43) $p = 0.043$
2	Health disorders		
A	Diseases of the circulatory system	1.88 (1.43–2.46) $p < 0.0001$	1.46 (1.30–1.63) $p < 0.0001$
B	Diseases of the ear and mastoid process	$p > 0.05$	1.33 (1.20–1.47) $p < 0.0001$
C	Diseases of the musculoskeletal system and connective tissue	1.61 (1.25–2.13) $p = 0.0008$	1.35 (1.22–1.48) $p < 0.0001$
D	Endocrine, nutritional and metabolic diseases	2.19 (1.62–2.96) $p = 0.0001$	1.31 (1.16–1.48) $p = 0.015$
E	Diseases of the nervous system	1.57 (1.19–2.07) $p = 0.003$	$p > 0.05$
3	24.0–31.0 hours per 40-hour working week spent working outdoors (60 % of the total working time or even longer)	1.92 (1.18–3.14) $p = 0.005$	3.0 (1.20–7.45) $p = 0.017$

diseases (RR = 1.31; CI: 1.16–1.48; $p = 0.015$), diseases of the musculoskeletal system (RR = 1.35; CI: 1.22–1.48; $p < 0.0001$), diseases of the nervous system (RR = 1.57; CI: 1.19–2.07; $p = 0.003$); and tobacco smoking (RR = 1.13; CI: 1.02–1.27; $p = 0.0378$) (Table 4).

All these individual peculiarities were determined for workers employed at the studied enterprise who have to work on open grounds in the cold season.

The results produced by this personified assessment of thermal regulation disorders in workers necessitate considering individual peculiarities within health risk assessment and give an opportunity to develop targeted medical and preventive activities for this category of workers.

The research accomplished successfully, we were able to suggest an integrated model for risk assessment, risk management and information about health risks associated with working on open grounds in the cold season. The model considers the results produced by assessing group occupational risks and individual peculiarities of a worker (Figure).

Conclusions:

1. Quantitative prior risk assessment gave an opportunity to identify workers' groups with a significant risk of developing occupational and non-occupational diseases. It also allowed ranking workplaces as per "health hazards" and developing preventive activities aimed at reducing negative effects produced on workers' health by cooling microclimate on open production grounds, harmful occupational factors as well as factors related to work process.

2. Posterior risk assessment confirmed the results produced by prior risk assessment regarding potentiating negative effects produced by cooling meteorological factors combined

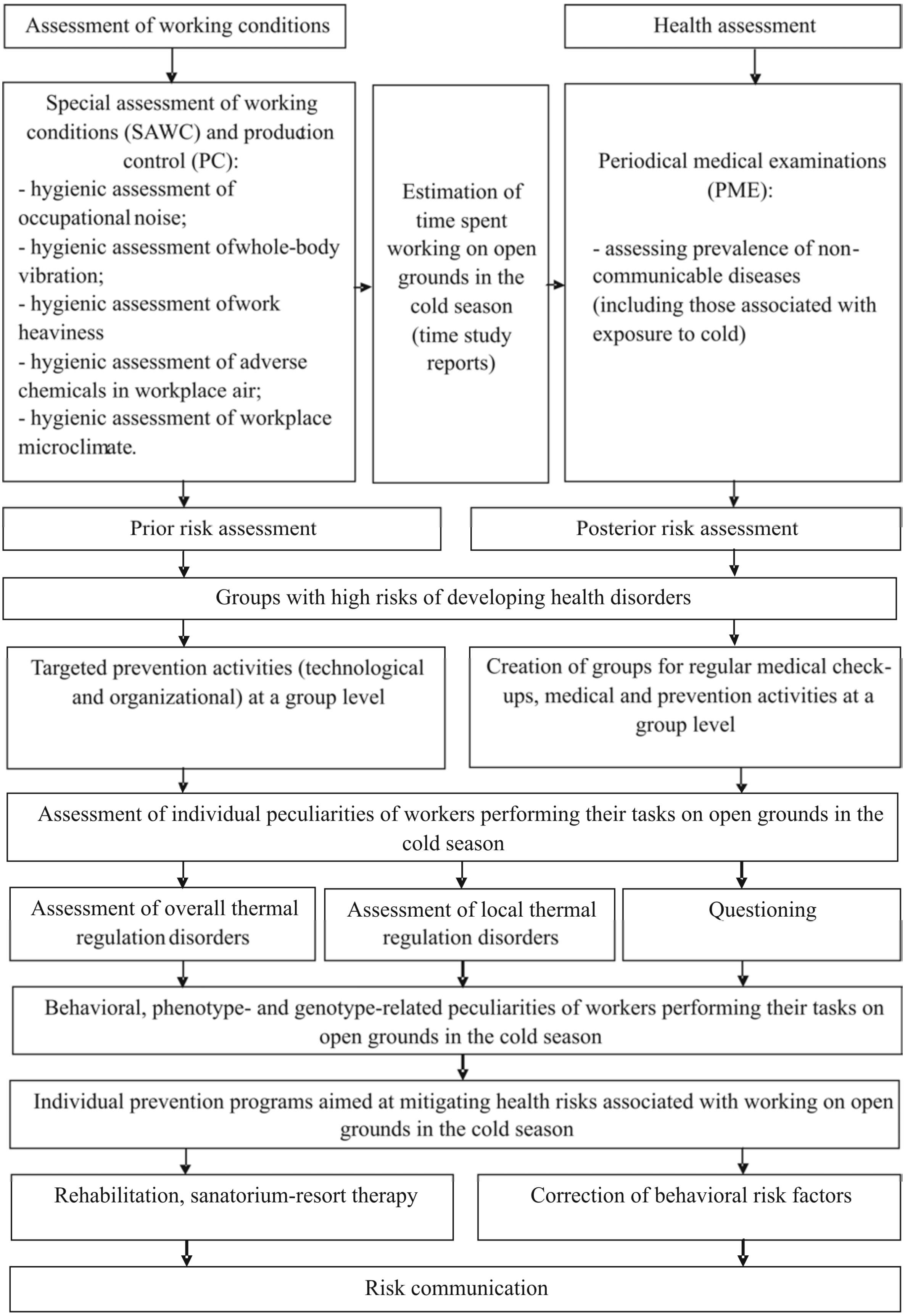

Figure. The model for risk assessment, management and communication regarding health risks associated with working on open grounds during the cold season with harmful occupational factors on health of workers from specific occupational groups who have to spend more than 60 % of their total working time on open grounds.

3. Identified individual peculiarities necessitate considering them within health risk assessment and make it possible to develop targeted personified medical and preventive activities for these occupational groups.

4. We have developed and suggested an integral model for risk assessment, risk management and communication about health risks for workers who have to work on open grounds under exposure to cooling meteorological factors. This model gave grounds for developing targeted (primary and secondary) prevention activities aimed at mitigating risks and communication about them. These activities included technological and administrative measures to reduce risks and to shorten exposure duration; use of personal protective equipment; correction of behavioral risk factors; organization of preliminary and periodical medical examinations, regular medical check-ups and health-improving rehabilitation programs.

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Research article

ASSESMENT OF SCIENTISTS' LIFESTYLE AND RISK FACTORS AFFECTING THEIR PROFESSIONAL EFFICIENCY

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People involved in scientific research should keep their cognitive status high since this is necessary for preserving their intellectual potential and maintaining their work efficiency. Given that, it seems important to determine what impacts scientific work might have on mental health, to estimate potential disorders and to develop a strategy aimed at preventing cognitive impairments. Our research goals were to perform screening assessment of executive functions, to examine signs of premature ageing and to explore behavioral and social risk factors among Russian researchers.

We accomplished a cross-sectional study with 213 researchers employed by state scientific institutions in Moscow participating in it; they were 116 women and 97 men aged from 23 to 78 years (their average age was 45.48 ± 15.33 years).

As a result, we established that risk factors causing a decline in professional efficiency were rather frequent among the participants. Probable cognitive disorders were detected in 9.85 % of them and we should note that these disorders were not age-related. We detected signs of senile asthenia in 3.28 % of the participants and senile depression in 2.34 %. Two thirds of the participants had subclinical depression (74.6 %). Only one fifth of the respondents (19.71 %, n = 42) did not have any cognitive impairments, asthenic syndrome, or depression. A quarter of the researchers (25.34 %) were not sufficiently committed to healthy lifestyle. Low physical activity established for 79.3 % of the respondents was the major risk factor; among others, we can mention irrational nutrition, primarily among those researchers who worked with students; poor stress management skills among physicians who combined clinical practice with science; difficulties in interpersonal relationships among people who dealt solely with research.

It is necessary to implement corporate programs aimed at prevention and rehabilitations for researchers in order to preserve their scientific activity and professional efficiency as well as to extend their professional longevity

***Keywords:** professional longevity, researchers, doctors, teachers, intellectual work, quality of life, cognitive functions, lifestyle.*

Scientists play a significant role in the development of the contemporary world as they create new concepts, form opinions, analyze great volumes of variable data, research and suggest new scientific methods [1]. Research work, just as any other intellectual one, differs from physical labor since it exerts greater loads on the nervous system. These loads can result in negative health outcomes [2, 3]. Research work also involves the necessity to perform multiple functions, to process great volumes of information and to face substantial psychoemotional stress [3]. It is especially true when it comes down to researchers who combine either science and clinical practice or science and teaching. Nowadays, this combina-

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tion of two different professional roles is quite typical [4]. Such overloads can lead to burnout and various health disorders [5, 6]. On the other hand, many authors believe intellectual work to be a factor that protects from cognitive ageing [7–9].

Researchers should keep their cognitive status high since this is necessary for preserving their intellectual potential and maintaining their work efficiency. Given that, it seems important to determine what influence research work has on mental health; to estimate potential disorders; and to develop a strategy aimed at preventing cognitive impairments [7].

Cognitive functions decline with age; the process is known as cognitive ageing. It is becoming a most outstanding challenge for public healthcare in the 21st century [10–12]. Previous studies describe a significant age-related decrease in such cognitive functions as executive functions, short-term memory, sequence thinking, information processing speed and naming speed, visual and verbal memory [13].

Literature analysis has revealed two major trends in relevant studies [14–16]. They either concentrate on estimating negative factors that cause cognitive ageing and poor executive functions (hypertension, apolipoprotein E, type 2 diabetes mellitus, cardiovascular and cerebrovascular diseases), on one hand [17–18]; or they aim to detect protective factors (education, intellectual activity, physical activity, giving up smoking, a proper diet), on the other hand [19–20].

There are no data available in literature that can describe researchers in Russia as a specific population group or provide some insight into risk factors that can reduce their professional efficiency. However, such studies are necessary for developing prevention and rehabilitation programs aimed at preserving intellectual potential and extending professional longevity.

Our research goals were to perform screening assessment of executive functions; to examine signs of premature ageing; and to explore behavioral and social risk factors among Russian researchers.

Materials and methods. We accomplished a cross-sectional study with 213 researchers employed by state scientific institutions in Moscow participating in it; they were 116 women and 97 men aged from 23 to 78 years (their average age was 45.48 ± 15.33 years).

Having assessed general health of the participants, we established that 28.31 % of them had chronic diseases; 43.3 % were practically healthy; and only 28.3 % had perfect health. Hypertension prevailed among chronic diseases accounting for 50.0 % (the 1st place). It was followed by diabetes mellitus and metabolic disorders (15.0 %, the 2nd place) and oncological diseases (10.0 %, the 3rd place).

The researchers who participated in the screening were distributed in different age groups as follows:

- 8.9 % were aged 20–30 years (n = 19);
- 20.57 %, 30–40 years (n = 44);
- 17.9 %, 40–50 years (n = 38);
- 16.9 %, 50–59 years (n = 36);
- 16.4 %, 60–69 years (n = 35);
- 19.33 % were older than 70 years (n = 41).

A period dedicated to scientific and research work varied from 1 year to 50 years (the median was 24.8 years). The greatest shares of the participants had working experience of 20–30 years (28.86 %) and 5–10 years (21.03 %). They were followed by the researchers with their working experience being equal to 30–40 years (19.09 %) and 40–50 years (18.5 %). A share of the researcher with short working experience (from 1 to 5 years) was rather small (12.52 %).

We created a screening test-card to obtain data on the quality of life and cognitive status of the participants. The test-card included several validated questionnaires in Russian that were printed on paper and handed out to the participants.

The participants were offered to fill in the following questionnaires:

1) Cognitive Difficulties Scale by McNair and Kahn (to assess cognitive loads and cognitive activity);

2) "Age is not an obstacle" (an intellectual anamnesis in young and middle age, intellectual activity);

3) Geriatric Depression Scale (GDS);

4) Health Promoting Lifestyle Profile (HPLP), an international questionnaire validated for use in Russia;

5) SF-36, a non-specific survey that measures quality of life, a version validated for use in Russia. Standard indicators for different age groups and the population in general were taken from "SF-36 Health Survey: Manual and Interpretation Guide" by J.E. Ware (1993)[1]. The Guide contains average indicators describing quality of life for people from different age groups who do not have any chronic diseases but have certain risk factors in their life (the 1st and 2nd health groups as per the WHO classification).

Results. The participants left school at the age from 15 to 18 years (the average age was 17.13 ± 1.04 years). The share of the participants who completed post-graduate studies or were taking them at that moment amounted to 76.05 % (*n* = 162). Seventy-three point seven percent (*n* = 157) defended their thesis for Candidate of Sciences degree at the average age being 35.53 ± 3.44 years (from 29 to 46 years).

Theses for Doctor of Sciences degree were defended by 44.6 % of the participants (*n* = 95) at the average age of 48.5 ± 6.85 years (from 38 to 57 years).

Almost 70 % of the participants (69.95 %, *n* = 149) were given a title "Associate Professor" at the average age of 38.38 ± 4.11 years (from 33 to 49 years); 41.78 % of the researchers (*n* = 89) were granted a Professor title at the average age 58.31 ± 10.42 years (from 45 to 66 years). Our sampling did not include any Academicians or Corresponding members of the Russian Academy of Sciences.

Forty-seven point four percent of the participants (*n* = 101) combined research work with teaching. On average, teaching experience amounted to 17.15 ± 7.20 years (from 1 year to 25 years).

The share of the participants who combined their researcher work with clinical practice, either in the past or when the study was conducted, amounted to 35.21 % (*n* = 75). On average, medical experience amounted to 16.06 ± 5.93 years (from 4 years to 31 years). Thirty-seven people among the participants were involved only in research activities (17.3 %).

Social aspects regarding living conditions were as follows. Most researchers (79.81 %, *n* = 170) owned their housing and the remaining 20.18 % rented it (*n* = 43). People who got married accounted for 79.34 % (*n* = 169) of the participants and the average age of getting married amounted to 26.77 ± 4.79 years (from 20 to 38 years). Only 53.84 % of all those people who got married (*n* = 91) were not divorced when this study was conducted. Seventy-nine point eight one percent of the researchers (*n* = 170) had children, from one to three (1.8 ± 0.7 on average).

Cognitive functions and signs of premature ageing. According to the results of "**Cognitive Disorders Scale"** as per McNair and Kahn, 89.67 % (*n* = 191) of the participants did not have any functional cognitive disorders. Probable cognitive disorders were detected in 10.3 % of the researchers (*n* = 22) (the total score exceeded 42). Average test results amounted to 27.23 ± 11.26 scores (from 9 to 49 scores) (Table 1).

We applied the **"Age is not an obstacle"** test to detect any signs of premature ageing. As a result, we did not establish any signs of senile asthenia in 74.17 % of the respondents (*n* = 158). Still, certain deviations were revealed in 25.8 % of the participants. Pre-asthenia was established in 22.5 % (*n* = 48); the results obtained for 3.28 % (*n* = 7) of the respondents indicated they had certain signs of senile asthenia. The average score estimate in the **"Age is not an obstacle"** test amounted to 2.06 ± 0.71 scores (from 0 to 5 scores) (Table 1).

According to the results of **"Geriatric Depression Scale"**, only 22.5 % of the researchers did not have any signs of depression (*n* = 48). We detected subclinical depression in 74.6 % of the participants (*n* = 159) and the results obtained for 2.34 % (*n* = 5) of them

[1] Ware J.E. SF-36 Health Survey: Manual and Interpretation Guide. USA, Health Institute, New England Medical Center Publ., 1993.

Table 1

The results produced by the screening tests in the overall group and subgroups determined as per activity types

Scales	Total ($n = 213$)	Researchers ($n = 37$)	Researchers-physicians ($n = 75$)	Lecturers ($n = 101$)
Cognitive screening (score)	27.23 ± 11.26	29.14 ± 12.77	33.62 ± 15.31*	22.21 ± 10.05
"Age is not an obstacle" (score)	2.06 ± 0.71	1.90 ± 0.55	2.86 ± 1.23*	1.65 ± 0.72
Geriatric depression scale (score)	7.38 ± 3.19	6.73 ± 3.12	7.95 ± 2.97	7.41 ± 3.33

Note: * means an authentic difference ($p < 0.05$) between physicians and lecturers.

Table 2

Life quality indicators as per SF-36 scores in the overall group and subgroups determined as per activity types

Domain	Total ($n = 213$)	Researchers ($n = 37$)	Researchers-physicians ($n = 75$)	Lecturers ($n = 101$)
PF	65.03 ± 15.50	91.07 ± 39.2	**44.66 ± 17.06***	62.60 ± 20.21
RP	52.65 ± 21.0	54.16 ± 26.71	50.55 ± 20.52	53.08 ± 20.0
BP	86.55 ± 17.40	96.04 ± 32.15	83.01 ± 33.78	83.23 ± 38.96
GH	51.76 ± 22.4	49.4 ± 19.39	45.13 ± 17.45	57.09 ± 23.11
VT	59.77 ± 19.1	56.34 ± 21.44	63.72 ± 20.6	59.38 ± 28.4
SF	84.06 ± 22.2	82.44 ± 37.03	86.38 ± 31.70	83.56 ± 39 ± 67
RE	61.21 ± 19.9	65.08 ± 28.42	**52.27 ± 19.34***	64.38 ± 27.06
MH	63.62 ± 22.0	64.97 ± 25.81	68.09 ± 26.3	60.16 ± 23.32
Physical wellbeing	44.39 ± 18.55	48.39 ± 20.75	**39.75 ± 12.04***	44.95 ± 10.44
Mental wellbeing	46.59 ± 20.09	43.60 ± 19.43	49.27 ± 18.66	46.65 ± 12.99

Note: * means an authentic difference ($p < 0.05$) between physicians and lecturers.

indicated actual depression. An average score as per GDS amounted to 7.38 ± 3.19 (from 4 to 11 scores) (Table 1). We also compared indicators between the subgroups with different activity types within the total sampling. Researchers who combined scientific work with clinical practice turned out to have more apparent cognitive disorders and asthenia signs in comparison with researchers who also worked with students ($p = 0.01$ and $p = 0.02$ accordingly). This might be due to greater stress and workloads.

Researchers' quality of life. We analyzed **quality of life** with the SF-36 survey version that was validated for use in Russia. According to the results, average indicators were established as per most scales among Russian researchers (Table 2). The following average scores were obtained for the analyzed sampling: PF = 65.03 ± 15.50 %, RP = 52.65 ± 21.0 %, BP = 86.55 ± 17.40 %, GH = 51.76 ± 22.4 %, VT = 59.77 ± 19.1 %, SF = 84.06 ± 22.2 %, RE = 61.21 ± 19.9 %, MH = 63.62 ± 22.0 %. General physical wellbeing amounted to 44.39 ± 21.27 %; general mental wellbeing, 46.59 ± 22.90 %.

We detected authentic differences in physical wellbeing between the subgroups with different activity types. It was significantly poorer among researchers-physicians than among people who were involved only in research ($p < 0.0001$), in particular, as per the "physical functioning" scale ($p < 0.0001$) and the "emotional role functioning scale" ($p = 0.03$) (Table 2).

Quality of life tended to decline with age among the analyzed researchers, just as it is the case with population in general. People aged 50–59 years had lower score estimates as per several scales against those aged 20–29 years. In particular, the indicators were lower as per the physical functioning (81.8 ± 22.8 % against 95.2 ± 10.2 %, $p = 0.04$), bodily pains (79.3 ± 30.9 % against 94.8 ± 9.9 %, $p = 0.03$)

and physical role functioning (75.0 ± 43.3 % against 93.4 ± 14.0 %, $p = 0.006$). Still, vitality and social functioning tended to improve with age since the lowest scores were detected among people aged 20–29 years (65.5 ± 22.8 % and 78.2 ± 22.3 % accordingly), then they grew among the participants aged 30–39 years (75.5 ± 11.0 % and 91.6 ± 10.8 % accordingly) and then, in general, remained stable without significant falls with age.

The best mental health was detected among people aged 30–39 years and older than 50–59 years. People who were older than 60 years tended to have lower scores as per the physical functioning scale than those aged 20–29 years (82.2 ± 17.5 %, $p = 0.02$) but higher scores as per emotional role functioning (81.4 ± 37.6 % against 63.1 ± 44.3 %). Overall, life quality of the researchers who were older than 60 years turned out to be higher than life quality of those aged from 50 to 59 years.

We analyzed sex-related peculiarities of life quality and revealed a difference in physical functioning. Men had higher scores as per this scale (94.8 ± 10.3 %) against women (85.0 ± 18.3 %, $p = 0.006$). On average, according to J.E. Ware[1], men tended to enjoy higher quality of life than women did, in particular, as per such indicators as vitality and physical role functioning.

Still, this trend was rather ambiguous among the researchers. For example, according to our data, women had higher scores as per the social functioning and the emotional role functioning scales ($p > 0.05$). Having compared life quality indicators obtained for the analyzed researchers with those obtained for population in general, we established that the researchers had authentically higher scores as per “bodily pains” (89.9 ± 17.4 % against 75.1 ± 23.69 %, $p = 0.008$) and “vitality (68.8 ± 19.1 % against 60.8 ± 20.9 %, $p = 0.04$). However, they had lower scores as per “emotional role functioning” (60.2 ± 1.9 % against 81.26 ± 33.04 %, $p = 0.001$) (Table 2).

More profound analysis of domains that described quality of life involved considering age-related differences between different age groups. As a result, certain peculiarities were detected in comparison with population in general. Thus, the researchers aged 30–39 had better scores as per “bodily pains”; the researchers aged 50–59 years had lower scores as per physical role functioning. We detected authentically lower scores as per emotional role functioning in age groups from 20 to 59 years. It is interesting to note, that this indicator grew among the researchers older than 60 years and reached the level typical for population in general.

As a whole, the participants who were older than 60 years had better quality of life than population in general; in particular, their indicators were higher as per the following scales: physical functioning, physical role functioning, bodily pains and vitality.

Correlations between cognitive functions and quality of life. The total score as per Cognitive Disorders Scale had positive correlations with the following SF-36 scales: “General health” ($r = 0.48$, $p = 0.0032$), “Vitality” ($r = 0.43$, $p = 0.002$), “Social functioning” ($r = 0.61$, $p = 0.0001$), “Mental health” ($r = 0.59$, $p = 0.0003$). We did not detect any correlations with age ($p > 0.05$).

The total score of the “Age is not an obstacle” test had positive correlations with such SF-36 scales as “Physical functioning” ($r = 0.45$, $p = 0.004$) and “Vitality” ($r = 0.38$, $p = 0.013$).

The total score as per GDS had positive correlations with “Mental health” ($r = 0.66$, $p = 0.0002$) and “Vitality” ($r = 0.57$, $p = 0.0037$) domains in the SF-36 survey.

Only one fifth of the respondents (19.71 %, $n = 42$) did not have cognitive disorders, asthenic syndrome or depression. This group also tended to have better quality of life than other participants who had certain deviations in the screening tests ($p = 0.003$ for physical health and $p = 0.001$ for mental health).

We detected impaired cognitive functions in one quarter of the participants and five of them were younger than 35 years. This phenomenon occurs due to subclinical depression and depression.

Subclinical depression as a deviation that prevailed in the tests (74.6 % of the respondents) and its frequency was the same in all age groups. Pre-asthenia and asthenia were established in one quarter of the participants (25.8 %); this means the disorder is rather frequent among researchers due to high psychoemotional loads.

All the researchers who had senile asthenia also suffered from depression or subclinical depression. Impaired cognitive functions did not have any correlations with pre-asthenia ($p > 0.05$).

Researchers' lifestyle. We examined what lifestyle was typical for the analyzed researchers using a version of Health Promoting Lifestyle Profile (HPLP) that was validated for Russia. As a result, we can state that in general the respondents' commitment to healthy lifestyle was quite satisfactory. The average score estimate amounted to 132.75 ± 56.31 for the whole group. Most analyzed researchers (73.7 %, $n = 157$) had a score estimate that fell within "good commitment to healthy lifestyle". The "excellent" score (more than 169) was detected only for 0.93 % ($n = 2$); 2.34 % ($n = 5$) of the respondents had a score lower than 90, which meant poor commitment to healthy lifestyle; 23.00 % ($n = 49$) had a "moderate" score (Table 3).

Having analyzed specific SF-36 scales, we detected the lowest scores for physical activity (on average, the score amounted to 12.28 ± 5.70, which meant "poor") and stress management (the average score was 19.26 ± 7.54, which meant "moderate"). The highest scores were detected as per "Interpersonal relationships" and "Nutrition" (the average scores were 28.47 ± 13.07 and 25.70 ± 11.8 accordingly, which meant "good"). Data might be inaccurate since the respondents filled in the questionnaire themselves.

We did not detect any statistically significant differences between the subgroups with various activity types ($p > 0.05$).

If we study the answers given to the HPLP questionnaire for the total group more profoundly, we cannot fail to notice low scores for the answers regarding physical activity. Seventy-three point seven percent of the respondents did not do any exercises regularly; 71.8 % did not have substantial physical loads three times a week; 80.6 % did not have any physical activity in their free time; 63.7 % did not do any power exercises; 63.12 % of the respondents stated they did not do sports with proper intensity; and 61.2 % did not have any physical loads in their everyday life. The overwhelming majority of the respondents noted that even if they did any sports, they did not usually take their pulse (66.8 %) or train until target pulse rates were reached (86.25 %).

As for nutrition, 72.3 % of the analyzed researchers preferred a diet with low cholesterol contents; 81.2 % tended to eat 2 to 4 portions of fruit every day. All the respondents (100 %) had from 3 to 5 portions of vegetables every day; 93.1 % had from 6 to 10 portions of complex carbohydrates every day; 58.0 % had 2 or 3 portions of milk products every day; 100 % tried not to have more than 2 or 3 portion of protein food; 88.7 % usually had breakfast. Nevertheless, 88.9 % usually failed to read labels on food products to examine their structure and 39.3 % did not limit sugar and sugar-containing food products in their rations.

Table 3

HPLP results in the total group and subgroups as per activity types

Scales	Total ($n = 213$)	Researchers ($n = 37$)	Researchers-physicians ($n = 75$)	Lecturers ($n = 101$)
Health self-responsibility	21.6 ± 9.44	22.97 ± 8.3	22.33 ± 10.21	20.35 ± 9.37
Physical activity	12.28 ± 5.70	12.11 ± 3.55	10.84 ± 3.81	13.27 ± 3.95
Nutrition	25.70 ± 11.8	25.52 ± 11.6	26.64 ± 11.52	25.21 ± 10.55
Spiritual growth	22.31 ± 10.7	23.73 ± 11.19	22.66 ± 8.59	21.28 ± 8.42
Interpersonal relationships	28.47 ± 13.07	29.30 ± 13.27	27.24 ± 10.76	28.75 ± 12.1
Stress management	19.26 ± 7.54	19.54 ± 9.23	19.02 ± 7.22	19.26 ± 6.28
Total score	132.75 ± 56.31	136.26 ± 58.81	131.73 ± 50.44	131.36 ± 52 ± 71

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Aggregated data on the analyzed subgroups

Risk factor	Total ($n = 213$)	Researchers ($n = 37$)	Researchers-physicians ($n = 75$)	Lecturers ($n = 101$)
Cognitive disorders	9.85 %	10.8 %	10.6 %	8.9 %
Pre-asthenia	22.5 %	21.62 %	**26.6 %***	19.8 %
Asthenia	3.28 %	2.7 %	**4.0 %****	2.9 %
Subclinical depression	74.6 %	62.16 %	**81.3 %****	74.25 %
Senile depression	2.34 %	2.7 %	2.6 %	1.9 %
Low commitment to healthy lifestyle	2.34 %	2.7 %	**4.0 %***	0.9 %
Moderate commitment to healthy lifestyle	**23.0 %**	**24.3 %**	**24 %**	**21.7 %**
Low health self-responsibility	4.6 %	0 %*	0 %*	**9.9 %**
Low physical activity	**79.37 %**	**85.0 %**	**95.6 %* ****	**67.56 % ***
Improper nutrition	2.8 %	2.7 %	1.3 %*	**3.9 %**
Low spiritual growth	1.4 %	**2.7 %**	1.3 %	0.9 %**
Poor interpersonal skills	0.93 %	**5.4 %**	0 %**	0 %**
Poor stress management	2.34 %	0 %	**5.3 %* ****	0 %

Note: * means the difference from lecturers is authentic; ** means the difference form researchers is authentic, $p < 0.05$.

Apparently, the analyzed researchers tended to have rather poor stress management skills. Fifty-seven point five percent of them did not find enough time to relax every day; 82.5 % of the respondents did not use any special techniques to control stress; 93.6 % noted they could not find even 20 minutes a day to meditate or relax; 83.6 % of the respondents were not ready to slow down in their work to avoid excessive fatigue. Still, 86.8 % had enough sleep and 75.5 % of the respondents tried to find some balance between work and rest.

The analyzed researchers were quite responsible for their health since they were ready to contact a doctor in case of any unusual signs or unpleasant symptoms (71.8 %); they were interested in prevention (79.2 %) and alternative opinions regarding their diagnosis (84.4 %). However, 81.25 % of the respondents gave a negative answer to the question “Do you examine your body at least once a month?” Rather few respondents were interested in various health programs (11.25 %) and even fewer participated in them (3.75 %).

When it comes down to interpersonal relationships, the analyzed researchers were ready to discuss their problems with their family or friends (84.0 %), had a possibility to enter intimate relations (84.9 %) and tried to keep earnest relationships with those around them (95.4 %). Seventy-six point two percent of the respondents tried to resolve conflicts by discussion.

Although the score given to spiritual growth was average, most researchers were sure that they were developing positively (53.1 %); 96.1 % were focused on their future; 70.6 % pursued long-term goals; 69.3 % felt themselves at peace; 96.8 % were open for new challenges.

Risk factors that may cause a decline in researchers’ professional efficiency. Given all the obtained data, we can state that there was rather high prevalence of risk factors that may cause a decline in professional efficiency among the analyzed researchers. We detected probable cognitive disorders in 9.85 % and those disorders were not age-related; 3.28 % had signs of senile asthenia; 2.34 %, signs of senile depression. Two thirds of the respondents suffered from subclinical depression (74.6 %). One quarter of the researchers were not sufficiently committed to health lifestyle (25.34 %). Low physical activity detected in 79.3 % of the respondents was the major issue (Table 4).

When we divided the overall group into several subgroups with different activity types, we detected certain peculiarities related to distribution of risk factors that might cause a decline in professional efficiency. Thus, pre-asthenia and asthenia were significantly more frequent among those researchers who combined scientific work with clinical practice ($p < 0.01$).

Subclinical depression was the least frequent among people who were involved only in research work; it was the most frequent among those combining research work with clinical practice (the difference between the subgroups was authentic at $p < 0.05$).

Researchers-physicians were committed to health lifestyle much poorer than others, especially in comparison with lecturers ($p < 0.01$); they were also rather bad at managing stress, worse than either researchers or lecturers ($p < 0.001$). As for physical activity, lecturers had the highest score; physicians, the lowest ($p < 0.01$) (Table 4).

Conclusions:

1) The prevalence of risk factors that might cause a decline in professional efficiency was rather high among the analyzed researchers. We detected cognitive disorders, which were not age-related, in 9.85 % of them; 3.28 % had signs of senile asthenia; 2.34 %, signs of senile depression. Two thirds suffered from subclinical depression (74.6 %). Only one fifth of the respondents (19.71 %, $n = 42$) did not have cognitive disorders, asthenic syndrome, or depression.

2) One quarter of the researchers were rather poorly committed to healthy lifestyle (25.34 %). Low physical activity detected in 79.3 % of the respondents was the major risk factor; others included improper nutrition, especially among those researchers who combined scientific work with teaching; poor stress management skills in physicians who combined research work and clinical practice; difficulties with interpersonal relationships among respondents who were involved only in research.

3) It is necessary to implement corporate programs aimed at prevention and rehabilitations for researchers in order to preserve their scientific activity and professional efficiency as well as to extend their professional longevity.

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Research article

OCCUPATIONAL HEALTH RISK FOR WORKERS FROM BASIC OCCUPATIONAL GROUPS EMPLOYED AT COPPER AND ZINC ORE MINING ENTERPRISES: ASSESSMENT AND MANAGEMENT

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A great share of workers employed at polymetallic ores mining have to face harmful working conditions at their workplaces. To provide safe working conditions for them and to preserve their health is a vital task occupational medicine has to tackle.

Polymetallic ore mining enterprises employ certain common technological processes; nevertheless, there are specific features depending on ore mining techniques and the mineralogical composition of different ores. These features determine differences both in working conditions and in occupational risks of developing occupational morbidity (OM) and work-related morbidity (WRM).

By now, there have been enough studies on peculiarities of occupational health risks for workers employed at sulfide ore mines, copper-nickel ore mines and ferruginous quartzite mines. Considerably less attention has been given to assessing occupational risks for workers dealing with mining and processing copper-zinc ores.

We performed complex clinical and hygienic examinations at a major copper-zinc ore mining enterprise located in the Southern Urals. The research results gave grounds for determining a category of working conditions, establishing formation peculiarities and the structure of occupational and work-related diseases among workers from various occupational groups.

Occupational risks were assessed considering hygienic and medical-biological indicators.

We established the highest occupational health risks for shaft sinkers, followed by drilling unit operators, timberers, excavator drivers, load haul dumper (LHD) operators and underground self-propelled machine (USPM) operators.

The research results gave grounds for developing a conceptual model of assessing and managing occupational risks in the branch. The urgency of developing and implementing activities aimed at risk mitigation should be determined depending on how validated a risk is and on its rates established for specific occupational groups.

Keywords: *occupational risk, workers, copper-zinc ores, ore mining, workers' health, hygienic and biomedical aspects.*

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At present, providing safe working conditions and preserving workers' health are among the most challenging tasks for the state to solve. Solutions to them should be based on managing occupational risks (OR) including hazard identification, OR assessment and measures aimed at their mitigation[1].

According to the Order issued by the RF Ministry of Labor on December 28, 2021 No. 926[2], an employer can select a procedure for occupational risk assessment depending on specific production, hazards and/or harmful occupational factors existing at workplaces. As stipulated by the aforementioned Order, health risks for workers may be assessed using the procedure described in the Guide R 2.2.1766-03[3] when it comes down to personified assessment.

This procedure involves identifying harmful occupational factors, assessing OR as per hygienic and biomedical health indicators, and determining urgency of activities aimed at OR mitigation.

This procedure is especially suitable for workers who are exposed to harmful working conditions at their workplaces and who have high health risks associated with occupational diseases and work-related ones.

By now, principles and criteria of OR assessment have been tested on occupational groups of workers employed in various branches including those with high health risks at workplaces [1, 2].

Enterprises that deal with polymetallic ore mining belong to productions with high health risks for workers. A share of workplaces with working conditions that do not conform to hygienic standards varies from 30 to 65 % in this branch and workers employed at such enterprises have high risks of developing occupational or work-related diseases (OD or WRD) [3, 4].

Enterprises dealing with polymetallic ore mining employ certain common technological processes; nevertheless, there are peculiarities depending on ways to mine ores, physical and chemical properties of ores, climate and geographical conditions in places where ore deposits are located. All these peculiarities lead to differences in both working conditions and OR occurrence [5–9].

Polymetallic ore mining is associated with risks of occupational diseases of the nervous system (NS), musculoskeletal system (MSS), respiratory system and hearing organ [10, 11].

Occupational pathology of respiratory organs (chronic dust bronchitis, pneumoconiosis) depends on the mineralogical structure of ore dust, size and shape of its particles, as well as exposure levels and duration [12–14].

Apart from silicon dioxide, ore dust can contain such toxic elements as platinum, nickel, chromium, vanadium, manganese, mercury, arsenic, and uranium [15–17]. Some of these chemicals can produce genotoxic and carcinogenic effects [18–20]. Given that, several researchers have pointed out the necessity to determine several classical biomarkers such as the comet assay, micronucleus assay and chromosome aberrations [21, 22].

In addition to ore dust, workplace air can contain exhaust gases from internal combustion engines. These gases are a complex mixture of carbon oxide, nitrogen, aldehydes and sulfur dioxide [23].

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[1] Trudovoi kodeks Rossiiskoi Federatsii ot 30.12.2001 № 197-FZ (red. ot 25.02.2022) (s izm. i dop., vstup. v silu s 01.03.2022); prinyat Gos. Dumoi 21.12.2001 [The Labor Code of the Russian Federation issued on December 30, 2001 No. 197-FZ (last edited on February 25, 2022) (with alterations and addenda that came into force on March 01, 2022); passed by the State Duma on December 21, 2001]. *KonsultantPlus*. Clauses 208, 209, 212. Available at: http://www.consultant.ru/document/cons_doc_LAW_34683/ (March 25, 2022) (in Russian).

[2] Ob utverzhdenii Rekomendatsii po vyboru metodov otsenki urovnei professional'nykh riskov i po snizheniyu urovnei takikh riskov: Prikaz Mintruda i sotszashchity RF ot 28.12.2021 № 926 [On Approval of the Recommendations on selecting procedures for assessing occupational risks and their mitigation: The Order by the RF Ministry of Labor and Social Security dated December 28, 2021 No. 926]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/728029758 (March 23, 2022) (in Russian).

[3] R 2.2.1766-03. Occupational hygiene. Guidelines on occupational risk assessment for workers' health. Organizational and methodological aspects, principles and criteria; approved by G.G. Onishchenko, the RF Chief Sanitary Inspector and the First Deputy to the RF Public Healthcare Minister on June 24, 2003. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/901902053 (March 23, 2022) (in Russian).

The most common harmful occupational factors at ore mining enterprises include, among other things, occupational noise and vibration created by technological equipment, perforators and mining machinery [24–26].

Many works by foreign and Russian researchers have concentrated on formation of occupational health risks for workers dealing with mining various polymetallic ores (sulfide, copper-nickel, copper-zinc, ferruginous quartzite, and platinum ores) and provide quite comprehensive data on the subject [27–30].

When assessing occupational risks at enterprises dealing with mining various polymetallic ores, authors most often use such indicators as a hazard category of working conditions, occupational morbidity, work-related morbidity, and mortality [2, 9, 10, 18, 26].

This research is topical since health disorders among workers employed at copper-zinc ore mining enterprises have not been given enough attention. This concerns both workers dealing with mining copper-zinc ore in general and specific occupational groups at such productions (personified risks).

Our research goal was to perform hygienic and biomedical assessment of occupational risks for workers employed at a copper-zinc ore mining enterprise and to develop a system for managing them.

Research object and techniques. Overall, six enterprises located in Bashkortostan mine and process copper and copper-zinc pyrite ores. These enterprises produce 70 % of zinc and 30 % of copper mined in the Russian Federation. We chose the largest mining enterprise in the republic as our model one for clinical and hygienic examinations. This enterprise employs conventional technologies and equipment typical for mining at similar ore deposits.

Occupational risks were assessed for the enterprise as a whole; personified occupational health risks were assessed for basic occupational groups at the enterprise made of workers dealing with open-pit and underground mining. These occupations included drilling unit operators, excavator drivers, shaft sinkers, timberers, LHD operators and USPM operators. To assess cause-effect relations between diseases and work, we created a reference group that was made of engineers and technicians with permissible working conditions at their workplaces. Their age was similar to that of workers from the main test group.

Overall assessment of working conditions was performed based on results produced by our own hygienic examinations as well as data produced by special assessment of working conditions (SAWC) performed at the examined enterprise by a specialized organization and provided by the enterprise administration.

Actual levels of exposure to harmful occupational factors were detected in conformity with the existing regulatory and methodical documents and using verified measuring devices included into the State Registry.

Our own hygienic assessment covered several harmful occupational factors identified at workplaces of workers from the selected occupational groups. They included a chemical factor (adverse chemicals); occupational noise and vibration (whole-body and local); lighting (natural or artificial); ionizing and non-ionizing radiation; exposure to predominantly fibrogenic aerosols (PFA) (silicon dioxide in copper-sulfide ore dust, silica dust (cement)); microclimate; work heaviness and intensity.

The results produced by these hygienic examinations made it possible to determine respective hazard categories of working conditions according to the provisions fixed in the Guide R 2.2.2006-05[4].

Occupational risks were assessed as per hygienic criteria and biomedical indicators in conformity with the Guide R 2.2.1766-03[3] as well as the Guide edited by N.F. Izmerov[5]. We

[4] R 2.2.2006-05. Occupational hygiene. Guide on Hygienic Assessment of Factors of Working Environment and Work Load. Criteria and Classification of Working Conditions; approved by G.G. Onishchenko, the RF Chief Sanitary Inspector on July 29, 2005; came into force on November 01, 2005. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/1200040973 (March 23, 2022) (in Russian).

[5] Professional'nyi risk dlya zdorov'ya rabotnikov: rukovodstvo [Occupational health risks for workers: the guide]. In: N.F. Izmerov, E.I. Denisov eds. Moscow, Trovant, 2003, 448 p. (in Russian).

considered such indicators as annual detected occupational morbidity, average annual occupational morbidity per 10,000 workers and occupational diseases index (I_{OD}) over 2011–2020, as well as work-related morbidity (relative risk (*RR*) with 95 % confidence interval (CI) and etiological fraction (EF)).

Occupational morbidity at the enterprise as a whole was compared with the data on occupational morbidity in Bashkortostan[6] and the Russian Federation[7] (RF) taken from official sources.

We determined a category of an occupational risk for each considered indicator using a five-score scale for it (negligible, moderate, average, high and extremely high). The category was estimated both for the enterprise as a whole and for specific occupational groups.

Statistical analysis was performed with IBM SPSS Statistics 21 software package (IBM, USA). Distributions were checked for normalcy using Kolmogorov – Smirnov test.

Results and discussion. Even though up-to-date equipment with great unit power was installed and all major technological processes employed at the examined enterprise were mechanized, a share of workplaces with harmful working conditions according to SAWC remained rather high and exceeded 50 %. It reached even 100 % in production divisions dealing with open-pit and underground ore mining.

We established several occupational risk factors influencing health of workers from all the occupational groups involved in underground ore mining. These factors were determined as per both SAWC results and results produced by our hygienic studies and included the following: noise generated by technological equipment, copper-zinc ore dust emitted into workplace air, adverse chemicals, unfavorable microclimate, total absence of natural light, as well as work heaviness and intensity.

When a category of working conditions was determined for activities that involve occupational contacts with PFA, copper-zinc ore dust being one of them, this required preliminary chemical analysis of mining rocks for determining a mass % of silicon dioxide in them. The analysis made it possible to select an appropriate hygienic standard, the maximum permissible average shift concentration (MPC_{as}), and the further steps in a procedure for assessing fibrogenic effects produced by aerosols on lung tissue depending on their intensity.

Thus, in case silicon dioxide accounts for 10–70 % in a rock, MPC_{as} is equal to 2 mg/m^3 and an aerosol has a more apparent fibrogenic effect. We established that a mass fraction of silicon dioxide amounted to 3.2–8.4 % in the examined ore dust; this corresponded to MPC_{as} being equal to 4 mg/m^3 and weak fibrogenic effects.

Hygienic studies revealed that dust suppression by using water, a method that has become quite popular over the last decades, provides lower ore dust contents in workplace air. Average shift concentrations of silicon dioxide did not exceed permissible levels at basic workplaces.

Timberers have to prepare a cement solution used in shotcrete sprayers that splash it on the walls inside underground tunnels to strengthen them. Due to this process, workplace

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[6] O sostoyanii sanitarno-epidemiologicheskogo blagopoluchiya naseleniya v Rossiiskoi Federatsii: materialy k gosudarstvennomu dokladu po Respublike Bashkortostan (2011–2020 gg.) [On sanitary-epidemiological welfare of the population in the Russian Federation: the data on Bashkortostan (2011–2020)]. *Rospotrebnadzor's Regional Office in Bashkortostan*. Available at: http://02.rospotrebnadzor.ru/documen/state_reports_on_RB/ (March 11, 2022) (in Russian).

[7] O sostoyanii sanitarno-epidemiologicheskogo blagopoluchiya naseleniya v Rossiiskoi Federatsii: Gosudarstvennyi doklad (2011–2020 gg.) [On sanitary-epidemiological welfare of the population in the Russian Federation: The State Report (2011–2020)]. *The Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing*. Available at: https://www.rospotrebnadzor.ru/documents/documents.php?back_url_admin=%2Fbitrix%2Fadmin%2Fiblock_admin.php%3Ftype%3Ddocuments%26lang%3Dru%26admin%3DY&clear_cache=Y&arrFilter_ff%5BNAME%5D=%EE+%F1%EE%F1%F2%EE%FF%ED%E8%E8+%F1%E0%ED%E8%F2%E0%F0%ED%EE-%FD%EF%E8%E4%E5%EC%E8%EE%EB%EE%E3%E8%F7%E5%F1%EA%EE%E3%EE+%E1%EB%E0%E3%EE%EF%EE%EB%F3%F7%E8%FF&arrFilter_pf%5BVID_DOC%5D=97&arrFilter_pf%5BNUM_DOC%5D=&arrFilter_pf%5BDAT_DOC%5D=&arrFilter_pf%5BGOD%5D%5BLEFT%5D=&arrFilter_pf%5BGOD%5D%5BRIGHT%5D=&set_filter=%CD%E0%E9%F2%E8&set_filter=Y (March 11, 2022) (in Russian).

air in such zones contained silica dust (cement) aerosols with weak fibrogenic effects. When dried cement powder was poured into sprayers and then mixed with water, concentrations of silica dust were by up to 2.1 times higher than its permissible level in workplace air.

Powerful up-to-date equipment used in technological processes produced vibration and acoustic effects. Noise generated at workplaces of workers from all the examined occupational groups exceeded permissible hygienic levels for this type of activity and this concerned both open-pit and underground mining. Working conditions were considered hazardous as per exposure to noise and their hazard category varied from 3.1 to 3.3.

Microclimate in mine faces was determined by rather low air temperature (from +12 to +16 °C) and elevated humidity (80–90 %) due to dust suppression by using water.

Working conditions for workers in underground mines were characterized with absence of any natural light and therefore were considered hazardous as per this factor. Devices that compensated for ultraviolet deficiency were installed in mines and this made it possible to achieve a reduction in the hazard category at these workplaces, from 3.2 to 3.1.

Since the mined ores contained chemical admixtures with natural radiation, dosimetric control of radiation at workplaces was implemented at relevant underground locations and in production workshops. Levels of ionizing radiation did not exceed the existing hygienic standards for mining operations.

We compared hazard categories of working conditions determined as per results produced by our hygienic studies and by SAWC and revealed certain differences as per such factors as vibration and work heaviness. They did not exert any significant influence on the overall assessment (Table 1).

A hazard category as per each harmful occupational factor detected at the analyzed workplaces varied from permissible (category 2) to hazardous, from category 3.1 to category 3.4.

The results produced both by SAWC and our hygienic studies indicated that the overall assessment of working conditions at workplaces of workers from the basic occupational groups dealing with underground ore mining allowed assigning them into the hazard category 3.2–3.4, occupational risks varying from average to very high (Table 2).

Workers dealing with open-pit mining were mostly exposed to vibration and noise at their workplaces together with copper-sulfide dust, unfavorable microclimate and work heaviness. Their working conditions were assigned into hazard categories 3.2 and 3.3 with occupational risks being high at their workplaces (Tables 1 and 2).

Table 1

Key occupational factors and categories of working conditions for workers from basic occupational groups at the copper-sulfide ore mining enterprise

Occupations	Vibration	Noise	Micro-climate	PFA	Lighting	Adverse chemicals	Work heaviness	Work intensity	Result
Open-pit mining									
Drilling unit operator	2 / 2*	3.3 / 3.3	3.1 / 2	2 / 2	2 / 2	2 / 2	3.1 / 3.1	3.1 / 3.1	3.3 / 3.3
Excavator driver	2 / 3.1	3.1 / 3.1	2 / 2	2 / 2	2	2 / 2	3.1 / 3.1	3.1 / 3.1	3.2 / 3.2
Underground mining									
Shaft sinker	2 / 3.1	3.4 / 3.4	3.1 / 3.1	2 / 2	3.1 / 3.1	2 / 2	3.1 / 3.1	2 / 2	3.4 / 3.4
Drilling unit operator	2 / 2	3.3 / 3.3	3.1 / 3.1	2 / 2	3.1 / 3.1	2 / 2	2 / 3.1	2 / 2	3.3 / 3.3
Timberer	2 / 2	3.1 / 3.1	3.1 / 3.1	3.1 / 3.1	3.1 / 3.1	2 / 2	3.1 / 3.1	2 / 2	3.2 / 3.2
LHD operator	2 / 2	3.2 / 3.2	2 / 2	2 / 2	3.1 / 3.1	2 / 2	2 / 2	3.1 / 3.1	3.2 / 3.2
USPM operator	2 / 2	3.1 / 3.1	2 / 2	2 / 2	3.1 / 3.1	2 / 2	2 / 2	3.1 / 3.1	3.2 / 3.2

Note: * means working conditions category as per SAWC / working conditions category as per results of our hygienic studies.

Table 2

Personified occupational risks for basic occupations at the copper-sulfide ore mining enterprise

Indicators	Open-pit mining		Underground mining				
	Drilling unit operator	Excavator driver	Shaft sinker	Drilling unit operator	Timberer	LHD operator	USPM operator
Category of working conditions*, **	3.3	3.2	3.4	3.3	3.2	3.2	3.2
Risk category	high	average	extremely high	high	average	average	average
Average annual occupational morbidity over 10 years, ‰	98.1	134.5	333.0	108.1	47.1	22.2	14.9
Risk category	high	high	high	high	above average	above average	average
Occupational diseases index I_{OD}*, **	0.38	0.22	0.50	0.49	0.49	0.32	0.30
Risk category	high	average	extremely high	high	high	high	high
Work-related morbidity* RR	3.1	3.0	4.3	3.1	2.7	1.8	1.9
EF, %	66.1	65.2	77.8	66.1	65.0	45.3	47.5
Causation	high	high	extremely high	high	high	average	average
The resulting number of indicators with a specific risk category	4 – "high"	2 – "high", 2 – "average"	3 – "extremely high", 1 – "high"	4 – "high"	2 – "high", 1 – "above average", 1 – "average"	1 – "high", 1 – "above average", 2 – "average"	1 – "high", 3 – "average"

Note: * means the assessment accomplished as per R 2.2.1766-03[3]; **, as per the Guide edited by N.F. Izmerov[5].

Occupational morbidity is known to be a direct indicator showing how working conditions influence workers' health [10, 11]. Given that, we analyzed occupational morbidity at the enterprise as a whole and in specific occupational groups involved in open-pit and underground ore mining.

Over the period from 2011 to 2021, annual detected occupational morbidity varied from 5.6 to 29.31 cases per 10,000 workers; this meant the morbidity rate corresponded to average–high occupational risks and was by 10.0–19.0 times higher than overall morbidity in Bashkortostan and by 4.5–15.3 times higher than the morbidity in the RF as a whole. Average annual morbidity over 10 years amounted to 1.7 cases per 10,000 workers at the enterprise as a whole and corresponded to low occupational risk.

The data analysis revealed the highest occupational morbidity rates among workers dealing with ore mining. They accounted for 85.7 % of all the occupational diseases registered at the enterprise. Average annual OM among workers dealing with ore mining varied from 14.9 to 333.0 cases per 10,000 over 10 years (Table 2). We should note that these rates were by 8.8–195.9 times higher than at the enterprise as a whole.

We calculated this indicator for specific occupational groups considering actual numbers of workers in them. The results showed the highest OM rates among timberers, 333.0 cases per 10,000 workers; they were followed by excavator drivers, 134.5 cases per 10,000 workers; and drilling unit operators, 108.1 per 10,000 workers. These results confirm that the indicator is much more informative for specific occupations in comparison with the same indicator calculated for the enterprise in general.

Overall, 61 cases of occupational diseases were registered at the examined enterprise over the observation period. Diseases of the musculoskeletal system prevailed in the structure of accumulated occupational morbidity (26.9 %), the next were sensorineural hearing loss (25.0 %) and vibration disease (23.3 %). They were followed by diseases of the peripheral nervous system (17.3 %) and diseases of the respiratory organs (7.5 %).

We analyzed how cases of occupational diseases were distributed in specific occupational groups. Figure 1 provides the results.

The index I_{OD} that considered a probability of an occupational risk and severity of an occupational disease amounted to 0.33 for sensorineural hearing loss; 0.33, polyneuropathy; 0.25, vibration disease; 0.13, chronic bronchitis.

Chronic non-communicable diseases detected in workers during periodical medical examinations (PME) belonged to the following main groups: diseases of the musculoskeletal system (33 %); diseases of the nervous system (17.6 %); diseases of the circulatory organs (13.3 %); diseases of the respiratory organs (12.5 %); diseases of the ENT organs (11.3 %).

The leading role belonging to occupational factors and factors related to labor process was confirmed in workers from various occupational groups only for diseases of the musculoskeletal system (dorsopathy and arthropathy), circulatory diseases (hypertension) and respiratory diseases (chronic bronchitis). Occupational causation of these diseases varied from 1.6 to 4.3 as per a relative risk and from 42.3 to 77.8 as per etiological fraction. This means that occupational causation varied from average to extremely high (Table 3).

Frequency of other chronic non-communicable diseases in ore miners did not have any authentic differences from the same indicators in the reference group.

Shaft sinkers had the highest occupational risk rates as per all the analyzed indicators (three indicators rated "extremely high" and one indicator rated "high"); drilling unit operators followed (four indicators rated as "high"); then, timbereres (two indicators rated as "high", one as "above average" and one as "average"); excavator drivers (two indicators rates as "high and two as "average"); LHD operators (one indicator rated as "high", one as "above average" and two as 'average"); and USPM operators (one indicator rated as 'high" and three as "average").

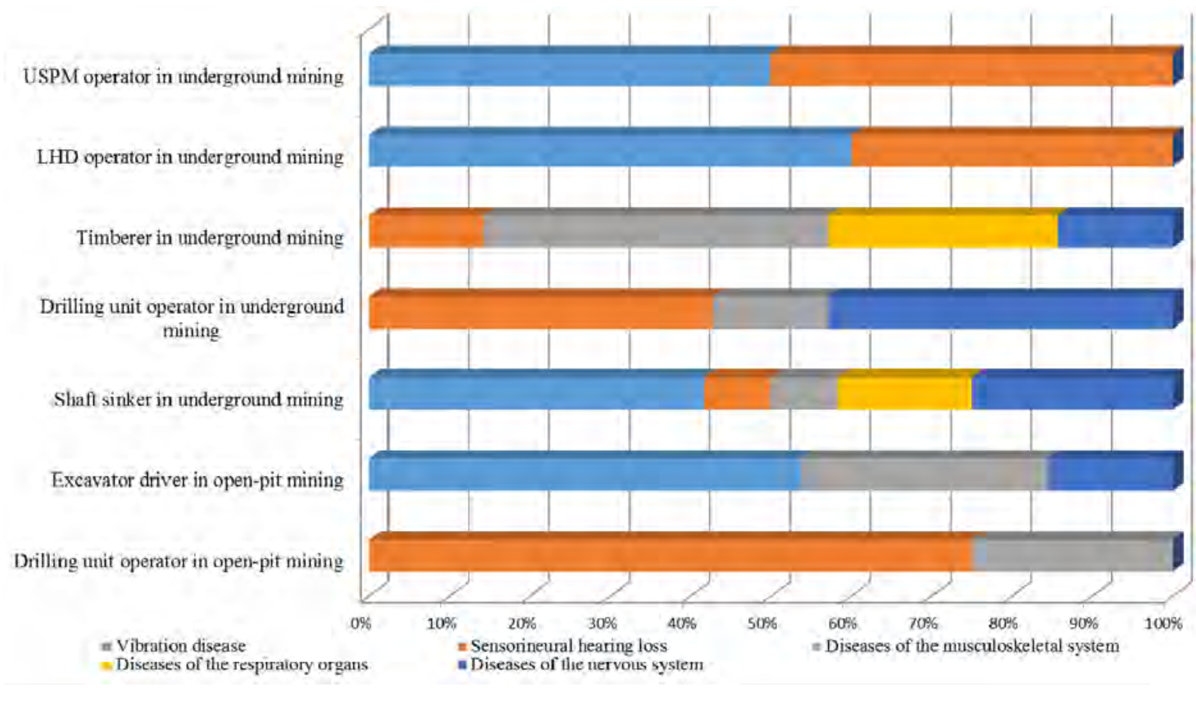

Figure 1. The structure of occupational diseases among workers form basic occupational groups at the copper-sulfide ore mining enterprise

Table 3

Occupational causation of health disorders among workers from the basic occupational groups

Mining type, occupation	Disease	*RR*	Range (95 % CI)	EF, %	Causation
1	2	3	4	5	6
Open-pit mining					
Drilling unit operator	Dorsopathy	3.1	1.6–4.7	66.0	high
	Arthropathy	3.1	1.7–4.6	66.1	high
	Chronic bronchitis	1.9	0.9–3.0	47.3	average
	Hypertension	1.8	0.7–3.0	45.3	average
Excavator driver	Dorsopathy	3.0	1.5–4.6	65.2	high
	Arthropathy	2.5	1.1–4.0	61.0	high
	Chronic bronchitis	1.6	0.5–2.7	43.3	average
	Hypertension	1.6	0.5–2.7	43.3	average
Underground mining					
Shaft sinker	Dorsopathy	4.3	3.1–5.5	77.8	extremely high
	Arthropathy	3.3	1.8–4.8	67.3	extremely high
	Chronic bronchitis	2.7	1.1–4.2	64.2	high
	Hypertension	1.8	0.7–3.0	45.3	average
Drilling unit operator	Dorsopathy	3.1	1.6–4.7	66.0	high
	Arthropathy	3.1	1.7–4.6	66.1	high
	Chronic bronchitis	1.9	0.9–3.0	47.3	average
	Hypertension	1.8	0.7–3.0	45.3	average
Timberer	Dorsopathy	2.7	1.2–4.2	65.0	high
	Arthropathy	2.6	1.1–3.9	61.5	high
	Chronic bronchitis	1.8	0.7–3.0	43.0	average
	Hypertension	1.7	0.8–3.1	42.3	average
LHD operator	Dorsopathy				
	Arthropathy	1.8	0.7–3.0	45.0	average
	Chronic bronchitis				
	Hypertension	1.8	0.7–3.0	45.3	average
USPM operator CM	Dorsopathy				
	Arthropathy	1.8	0.7–3.0	47.2	average
	Chronic bronchitis				
	Hypertension	1.9	0.9–3.0	47.5	average

Therefore, our research results made it possible to assess occupational health risks considering hygienic and biomedical indicators and to determine risk categories both for the enterprise in general and for the basic occupational groups.

We established that working conditions for workers dealing with copper-sulfide ore mining belonged to the hazard category 3.2–3.4 and occupational risks at these workplaces were average and extremely high.

Average annual occupational morbidity varied from 14.9 to 333.0 cases per 10,000 for different occupational groups over the analyzed 10 years. It was by 8.8–195.9 times higher than the same indicator taken for the enterprise as a whole. This means it is quite reasonable to determine this indicator for specific occupations. Consequently, assessment of personified occupational risks for specific occupational groups provides data that are more authentic.

Although occupational risks taken as per average annual occupational morbidity over 10 years were assessed as high (more than 50 cases) for shaft sinkers, drilling unit operators (open-pit and underground mining), and excavator drivers, numeric values of this indicators were by 2.5–22.0 times different in various occupational groups. We believe that the aforementioned criteria could become more significant if their more precise and more profound quantification was performed and their gradation was given according to relevant assessment scales described in the Guide edited by N.F. Izmerov.[5]

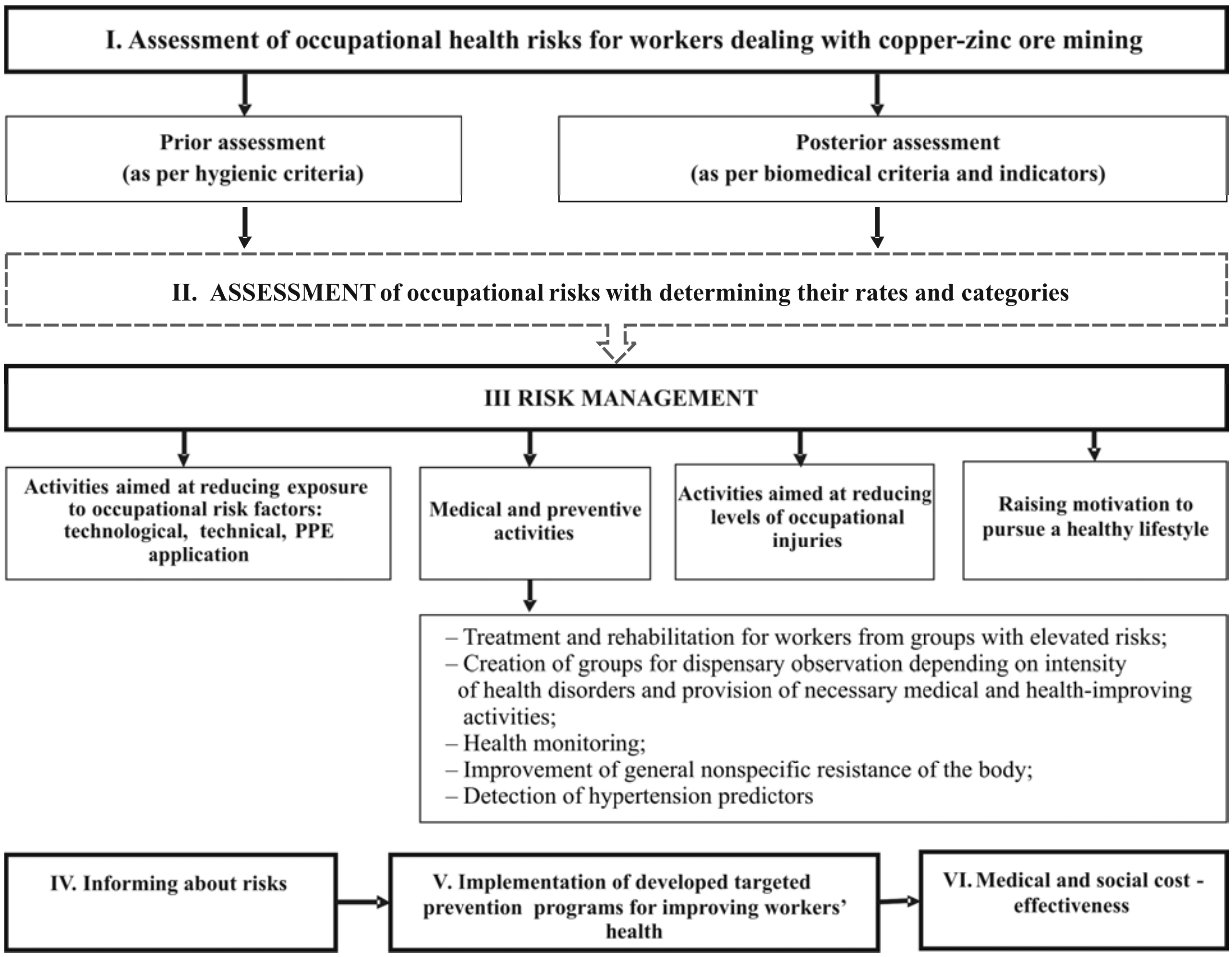

Figure 2. The system for assessing and managing occupational health risks for workers employed at copper-sulfide ore mining enterprises

We also think that occupational risk assessment requires using not only indicators that describe how many occupational diseases have been detected in the current year but also "accumulated" occupational morbidity that makes it possible to establish peculiarities in formation of its structure.

Intensity of exposure to occupational factors as well as work heaviness determines the maximum values of etiological fraction in the development of such diseases of the musculoskeletal system as dorsopathy and arthropathy.

Shaft sinkers had the highest occupational health risk as per all the analyzed indicators; they were followed by drilling unit operators, timberers, excavator drivers, LHD operators and USPM operators.

Conclusion. We have established high occupational health risks for workers from the basic occupational groups dealing with copper-zinc ore mining. These risks need to be mitigated immediately.

Given that and based on the systemic approach to health risk analysis, we have developed a system for assessing and managing occupational health risks for workers employed at copper-sulfide ore mining enterprises (Figure 2).

The system for OR management involves technical, technological, organizational, medical and preventive activities. Their urgency is to be determined as per detected categories of occupational risks.

Periodical medical examinations that include physical fitness testing, creation of groups with elevated "risks" of occupational diseases and dispensary observation are important components in prevention.

Implementation of the system will depend on effective interactions between employers, workers, and medical organizations responsible for providing medical assistance to workers employed at mining enterprises.

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Research article

YOUNG STUDENTS' LIFESTYLE AS A HEALTH RISK FACTOR DURING THE COVID-19 PANDEMIC UNDER VARIOUS ANTI-EPIDEMIC STRATEGIES

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Various strategies have been implemented to prevent the COVID-19 spread both in Russia (self-isolation) and in Belarus (restrictive measures). They can be considered an unordinary stress-inducing situation that involves drastic changes in a lifestyle.

Our research goal was to analyze students' attitudes towards basic lifestyle components in both countries under various anti-epidemic strategies.

We interviewed 876 students from Krasnoyarsk who were self-isolated for 2.5 months and 1140 students from Grodno who did not face strict quarantine restrictions. We performed comparative assessment of changes in basic lifestyle components that occurred during the pandemic.

We established certain changes in subjective health self-assessment (more than a half of the students described it as bad), emotional state (subjective comfort index was between its acceptable level and a trend towards its deterioration). Acute deficiency of usual physical activity was mentioned by 35.4 % of the respondents from Krasnoyarsk and 29.5 % of their counterparts from Grodno ($p < 0.01$). Twenty-three point nine percent of the students from Grodno and 26.6 % from Krasnoyarsk gave up adhering to healthy sleep and nutrition regimes and this resulted in uncontrollable growth in body mass. The complex index of positive changes in a lifestyle, its maximum being seven scores, amounted to 4.15 ± 1.56 scores among the respondents in Krasnoyarsk against 4.46 ± 1.48 scores in the reference group ($p < 0.01$). Some respondents resorted to taking psychoactive substances in their search for subjective stability. Seven point seven percent of the students in Grodno and 4.8 % of their counterparts in Krasnoyarsk started smoking during that period; 28.9 % and 46.2 % of the respondents accordingly increased frequency and volumes of alcohol consumption ($p < 0.01$).

Therefore, the present study concentrated on analyzing specific attitudes towards lifestyles among students in two countries under various anti-epidemic strategies. The results provide significant information for both public healthcare organizations and educational establishments since they can be used as grounds for suggesting activities aimed at maintaining students' wellbeing and providing wider opportunities for young people to pursue a healthy lifestyle.

Keywords: *lifestyle, physical health, mental health, students from universities in Russia, students from universities in Belarus, COVID-19 pandemic, lockdown, anti-epidemic strategies.*

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In an extreme situation, when many restrictive measures have become a part of everyday life, it is especially vital to examine attitudes towards lifestyle and its components [1, 2]. The new COVID-19 coronavirus infection pandemic can be considered a good example here [3] since it has already influenced people's attitudes towards basic components in their lifestyles (physical activity, body tempering, daily routines, nutrition, and refusal to take any psychoactive substances) and is still affecting them [4, 5]. Available research results indicate that anti-epidemic measures vary from country to country; still, basic actions are quite similar and are primarily aimed at producing effects on classical components in any epidemic process. They should influence a source of an infection, block ways of its spread, and raise population resistance to it through creating and enhancing immunity [6–8]. There are ongoing discussions about advisability of different restrictive or permissive measures taken in various countries as a response to the COVID-19 spread. Some people believe that strict measures are not justified [9, 10]; the others argue in favor of extreme restrictive quarantine-like actions [11]. Each country chooses its own way to fight against the pandemic and undergoes an unique "natural experiment" created by the COVID-19 spread [12, 13]. Quarantine measures to fight against the infection were instantly introduced in Russia and in most European countries just as the first pandemic wave started. As opposed to most countries, Belarus refused from introducing strict quarantine measures from the very beginning of the pandemic and the society's lifestyle was preserved in the republic without any grave restrictions or panic. The country did not impose complete or partial limitations on social contacts and people were solely informed about necessary safety precautions and were asked to adhere to them [14–16]. In Russia, self-isolation became a major issue since it led to drastic changes in lifestyle [2]; it is considered an independent stress-factor that impairs people's physical and mental health [17].

Effects produced by pandemic restrictions on lifestyle and its components (self-isolation was introduced several times in 2020 in Russia) can be examined by comparing attitudes of people from two closely related cultures (students in Belarus and Russia) who have quite much in common regarding their lifestyles and culturological components as well as speak the same language. Students are a social group that adapts to new conditions rapidly and easily; therefore, they are an interesting contingent for a comparative study [5].

A freedom to move around and physical activity in general decreased dramatically when strict anti-epidemic restrictions were introduced [18]. The coronavirus pandemic made students and lecturers in Russian higher education institutions switch to distance learning while in Belarus hybrid learning was introduced (conventional learning combined with partial use of information and communication technologies when necessary). Learning became more intense due to arising difficulties in mastering new technologies, requirements not being defined clearly, technical capacities related to distance learning, and impaired activity of the body functional systems. All this created risks of psychosomatic disorders [19]. Since we had necessary data provided by students from both countries regarding various aspects of their lifestyles and their physical and mental health, we were able to perform comparative analysis of two statistical samplings. The analysis completed, we attempted to estimate peculiarities of physical activity, compliance with self-isolation, adherence to healthy wake and sleep regime as well as keeping healthy diets, bad habits, and general health during the COVID-19 pandemic under different anti-epidemic strategies adopted in two countries to prevent the infection spread.

Our research goal was to analyze students' attitudes towards basic lifestyle components in both countries under various anti-epidemic strategies; our respondents were students from Belarus (Grodno) and Russia (Krasnoyarsk).

Research materials and techniques. Our respondents were full-time students of the 2nd–4th year in medical and pedagogical higher education institutions in Grodno and Krasnoyarsk. Overall, 2016 people took part in the study; future teachers accounted for 64.1 %, and future doctors, for 35.9 %. These specialties were selected due to future occupations with their certain peculiarities associated with the necessity to work with people, rendering assistance in various situations and promoting healthy lifestyle by personal example.

Another reason that makes this study vital is associated with estimating anti-epidemic strategies adopted in Belarus and Russian to fight the infection spread since they determine students' lifestyle. The study took place when the pandemic was at its peak and the anti-epidemic strategies adopted at that moment in two countries differed significantly. In Russia, the total lockdown was introduced at the federal level. Anti-COVID-19 measures were introduced by the Order of the RF Chief Sanitary Inspector No. 15, IV, issued on May 22, 2020. The Order stipulated strict self-isolation at a local level, quarantine measures were implemented, and students switched to distance learning. Simultaneously, preventive activities aimed at hygienic education became more intense both during lectures and beyond them (for example, hygienic tests, online exhibitions of posters and healthy lifestyle contests). A lot of attention was paid to improving mental health (online consultations provided by a psychologist); senior students and supervisors volunteered to help junior students to adapt to this unusual situation. In Belarus, life was organized in the same way and the society did not have to face drastic changes; still, certain restrictions were implemented ("The methodical guidelines on organizing educational processes in education institutions during the COVID-19 spread"). Nevertheless, these two different approaches adopted both in Russia and Belarus can be considered an unordinary stress-inducing situation for population [20], young students included.

Our study relied on a specifically designed questionnaire that included questions aimed at detecting changes in students' lifestyle and its components, in particular, their physical activity, diet, wake and sleep regime, as well as use of psychoactive substances. The study was accomplished online at the end of 2020 when all the participating students had already gained certain experience in living under new conditions. An online survey is an optimal way to get information; it gives an opportunity to obtain primary data in a short time under restrictions at the height of the pandemic [7]. Prior to the research, all the respondents were informed about its goals and methodology as well as it being anonymous and confidential. An access to the online questionnaire, which was located on Google Forms, was granted to a respondent only after he or she gave its clear consent to take part in the study.

We questioned two groups of students. The first one was made of students attending higher education institutions in Krasnoyarsk, Russia (n = 876; an average age was 20.7 ± 1.64 years; 16 % males, 84 % females). These students were self-isolated from March to June 2020 during the pandemic and had to switch to distance learning. The second group included students from Grodno in Belarus (n = 1140; an average age was 20.4 ± 1.93 years; 20 % males, 80 % females) who had to face certain restrictions without strict quarantine measures.

Female students prevailed in these two student samplings due to specificity of medical and especially pedagogical higher education institutions. Table 1 provides data on how respondents were distributed depending on their chosen occupation and sex.

All the data were statistically analyzed with Statistica 13 PL software package. Data analysis involved calculating absolute and relative frequencies and using descriptive statistics techniques. Prior to analyzing quantitative indicators, we estimated whether the analyzed values complied with the normal distribution law for a variational series. This was done with Shapiro – Wilk test. Given that the data were not distributed normally, we applied non-parametric statistics techniques. Quantitative indicators were given as $\bar{X} \pm \sigma$ ($\bar{X}$ is a simple mean and σ is standard deviation),

Table 1

Respondents' groups considering their future occupation and sex, abs. (%)

Occupation	Grodno (n = 1140)		Krasnoyarsk (n = 876)		Both cities (n = 2016)	
	Males	Females	Males	Females	Males	Females
Total	225 (19.7)	915 (80.3)	140 (16.0)	736 (84.0)	365 (18.1)	1651 (81.9)
Pedagogical	113 (15.5)	618 (84.5)	34 (8.1)	385 (91.9)	147 (12.9)	1003 (87.2)
	731 (64.1)		419 (47.8)		1150 (57.0)	
Medical	112 (27.4)	297 (72.6)	106 (23.2)	351 (76.8)	218 (25.2)	648 (74.8)
	409 (35.9)		457 (52.2)		866 (43.0)	

Me (median) and Q_{25}–Q_{75} (interquartile range). We applied Mann – Whitney *U*-test to assess validity of differences between them. Qualitative indicators were compared using Pearson's chi-squared test (Pearson's χ^2). The critical significance level (*p*) was taken as 0.05 when statistical hypotheses were tested.

The study was accomplished in conformity with all the ethical standards stipulated by the Declaration of Helsinki and the EU Directives (8/609EU). It did not infringe on human rights, did not impose any threats for participants and fully conformed to ethical requirements fixed for biomedical research [21, 22].

Results and discussion. We chose young students as our research object. We estimated how respondents were distributed as per sex and future occupations with χ^2 criterion and established similarities between the groups, that is, they belonged to the same general totality.

Our social survey revealed that when students from both groups had to face either self-isolation or certain restrictions in their everyday life, this resulted in changes in their subjective health self-assessment and emotional state and also led to deficiency of habitual activity. Lifestyles of most respondents apparently deviated from recommended standards regarding such vital components as sleep duration, diet, physical activity, intensity of educational loads, and use of psychoactive substances. Health self-assessment turned out to be negative in more than a half of the cases. The students from Krasnoyarsk complained their health was bad during self-isolation in 54.3 % of the cases. A share of the students from Grodno with negative health self-assessment was authentically lower (52.8 %). One fifth of the students did not notice any deterioration of their health; 21.8 % of the students from Grodno and 23.5 % of the students from Krasnoyarsk stated their health was either normal or good. Emotional state of most respondents also tended to be unstable due to lack of activity, including physical one. The subjective comfort index that reflects the existing functional state was between its acceptable level and a trend towards its deterioration (50.9 ± 12.4 and 50.8 ± 14.2 scores as per "The scale for subjective comfort assessment by A.B. Leonova" [23] in both examined groups).

While being either self-isolated or living under certain restrictions, 1111 (54.8 %) of the respondents changed their attitudes towards their health drastically and made them more rational, 708 (61.6 %) of the students from Grodno and 403 (46.0 %) of their counterparts from Krasnoyarsk accordingly. Lower values obtained for Krasnoyarsk might be due to students not being ready to face such an extreme situation as a complete lockdown.

Self-isolation induced a decrease in physical activity. Three hundred and ten (35.4 %) of the respondents from Krasnoyarsk lost part of their interest in physical exercises. The students from Grodno (the reference group in this study) also had lower physical activity at that period but a decrease was a bit less apparent (mentioned by 336 people or 29.5 %). One fifth of the respondents, trying to find a way out and realizing how important physical activity was for their health, started doing morning exercises and physical training during a day; they also tried to adhere to rational daily regimes and to plan their activities. A number of the respondents from Krasnoyarsk who had morning exercises and physical training during a day grew by 191 people (21.8 %), which was higher than a number of their counterparts from Grodno who did the same, 188 people (16.5 %). A number of the respondents who tried to plan their daily routines in an optimal way was practically the same in both groups, 493 (56.3 %) students from Krasnoyarsk and 674 (59.1 %) students from Grodno. A half of the respondents had a shorter sleep than recommended and we did not reveal any statistically significant differences between the groups as per sleep duration.

Although many respondents had positive opinions about changes in their diets and eating habits, most still were unsatisfied with outcomes of these changes. One fourth of the respondents, 273 (23.9 %) students from Grodno and 233 (26.6 %) students from Krasnoyarsk did not keep healthy diets. As a result, such students (especially female ones) often noted that their body mass increased. Six hundred and sixty (57.9 %) students from Grodno and 414 (47.3 %) students from Krasnoyarsk related changes in their lifestyle to searching for stability and feeling themselves safe. A small share of the respondents fell back on taking psychoactive substances in their search for subjective stability. Eighty-eight (7.7 %) students from Grodno and 42 (4.8 %) students in Krasnoyarsk started smoking, 38.9 % and 46.2 % of the respondents accordingly mentioned that they started drinking more often and consuming alcohol beverages in greater volumes.

Tables 2 and 3 provide data on frequency of changes in students' lifestyles and deficiency of their habitual activities due to self-isolation or restrictions.

We summed up all the responses as per seven scales that reflected a positive approach and a wish to improve one's lifestyle. As a result, we calculated the complex index of positive changes in lifestyle. It amounted to 4.46 ± 1.48 scores out of maximum seven scores (Me = 5, Q_{25}–Q_{75} = 4–6) among the respondents from Grodno and to 4.15 ± 1.56 scores (Me = 4, Q_{25}–Q_{75} = 3–5) among the respondents from Krasnoyarsk (Mann – Whitney test, $Z = 4.7$, $p < 0.001$). A share of students who did not have any changes in their lifestyle did not exceed 1.0 % in either group.

Table 2

Peculiar attitudes towards lifestyle in the examined groups, abs. (%), (95%-confidence interval)

Answer	Grodno (n = 1140)	Krasnoyarsk (n = 876)	Both cities (n = 2016)
I try to keep a certain daily routine	674 (59.1) (56.3–61.9)	493 (56.3) (53.0–59.6)	1167 (57.9) (55.7–60.1)
	$\chi^2 = 1.64$, $p = 0.2$		
I do morning exercises regularly	188 (16.5) (14.3–18.6)	191 (21.8) (19.1–24.5)	379 (18.9) (17.1–20.5)
	$\chi^2 = 9.2$, $p < 0.01$		
No, I do not drink or smoke	696 (61.1) (58.2–63.9)	471 (53.8) (50.5–57.1)	1167 (57.9) (55.7–60.1)
	$\chi^2 = 10.8$, $p < 0.001$		
I walk outdoors	703 (61.7) (58.9–64.5)	450 (51.4) (48.1–54.7)	1153 (57.2) (55.0–59.4)
	$\chi^2 = 21.4$, $p < 0.0001$		
I spend the whole day working on a PC or using a phone	250 (21.9) (19.5–24.3)	319 (36.4) (33.2–39.6)	569 (28.2) (26.3–30.2)
	$\chi^2 = 51.3$, $p < 0.0001$		
I do not keep a healthy diet	273 (23.9) (21.5–26.4)	233 (26.6) (23.7–29.5)	506 (25.1) (23.2–27.0)
	$\chi^2 = 1.9$, $p = 0.1$		
I have started smoking	88 (7.7) (6.2–9.3)	42 (4.8) (3.4–6.2)	130 (6.5) (5.4–7.5)
	$\chi^2 = 7.0$, $p < 0.01$		

Table 3

Deficiency of habitual activities during the period when anti-epidemic measures were in force, abs. (%), (95%-confidence interval)

Answer "I do not have enough…"	Grodno (n = 1140)	Krasnoyarsk (n = 876)	Both cities (n = 2016)
Walking / doing sports outdoors	336 (29.5) (26.8–32.1)	310 (35.4) (32.2–38.6)	646 (32.0) (30.0–34.1)
	χ^2 = 7.96, p < 0.01		
Entertainment, new excitements	556 (48.8) (45.9–51.7)	432 (49.3) (46.0–52.6)	988 (49.0) (46.8–51.2)
	χ^2 = 0.06, p = 0.8		
Communication with teachers, a possibility to discuss something that is difficult to understand	262 (23.0) (20.5–25.4)	428 (48.9) (45.6–52.2)	690 (34.2) (32.2–36.3)
	χ^2 = 147.3, p < 0.0001		
Cultural events (going to museums, theaters, etc.)	494 (43.3) (40.5–46.2)	412 (47.0) (43.7–50.3)	906 (44.9) (42.8–47.1)
	χ^2 = 2.74, p = 0.09		
Socializing with friends / acquaintances	565 (52.1) (46.7–52.5)	520 (59.4) (56.1–62.6)	1085 (53.8) (51.6–56.0)
	χ^2 = 19.1, p < 0.001		
Freedom to move around the city	478 (41.9) (39.1–44.8)	384 (43.8) (40.6–47.1)	862 (42.8) (40.6–44.9)
	χ^2 = 0.73, p = 0.39		
Stability, feeling safe	660 (57.9) (55.0–60.8)	414 (47.3) (43.9–50.6)	1074 (53.3) (51.1–55.5)
	χ^2 = 22.5, p < 0.0001		

The survey results indicate that changes in major lifestyle components that occurred when various restrictions were in force during the pandemic were associated with several factors. These factors were limited freedom to move around, specificity of distance or hybrid learning, limited direct contacts with friends and teachers [8]. These results reflect common trends associated with changes in lifestyle such as more frequent negative health self-assessments and assessments of emotional state, lack of habitual activity, loss of stability, feeling oneself unsafe.

There are certain differences in frequency of changes regarding lifestyle components under different anti-epidemic strategies aimed at fighting the COVID-19 spread. Many authors note that at the first stages in the pandemic students turned out to be disorganized, they were not able to adhere to basic healthy lifestyle [2]. At the same time, some of them adapted their daily routines quite soon and introduced various productive components into them. They, for example, helped relatives do house chores, helped younger siblings do their school homework, wrote research articles, participated in online conferences, contests and grants for students by making presentations. Some students even had to find a job so that they could help their family to pay expenses.

It became vital to search for ways to motivate students to keep healthy diets, to do sports or exercises and to adhere to other components of healthy lifestyle. When self-isolated people were unable to do sports or exercises at home or, even able, were not interested in doing them, it could lead to their complete refusal from any physical activity. Meanwhile, physical activity was becoming more and more necessary due to growing stress, on the one hand, and significant amounts of accumulated energy that needed to be spent, on the other hand [24].

Self-isolated students from Krasnoyarsk had limited possibilities to have any physical activity within closed spaces, thereby reducing its volumes and making it much less variable. A situation being uncertain and limitations being only prolonged made students ignore planning and abandon rational daily routines, spend more time playing or working on PC, stick to unhealthy diets and adverse eating habits, as well as take psychoactive substances "to calm down" (smoking, alcohol or drugs). On the other hand, self-isolation led to a situation when quite a substantial share of students started doing more physical training including regular morning exercises. The existing stressful situation made students concentrate on ways how to get distracted from unpleasant thoughts, finding something positive in life, looking for a possibility to learn something new (distance and hybrid learning). The study [25] revealed that mental withdrawal and emotion-based strategies aimed at coping with the pandemic were rather ineffective since they could enhance psychological stress in students of higher education institutions. However, it is a bit early to estimate effectiveness of these strategies for coping with an emergency without available longitude data. Still, it does not exclude the necessity to develop preventive recommendations on how to preserve physical and mental health and wellbeing [26, 27].

Our research results indicate that actions aimed at optimizing lifestyle during the pandemic were quite similar but their implementation by the students was rather different due to different estimates of the situation itself as well as available opportunities and resources. Different strategies aimed at fighting the coronavirus infection influenced frequencies of changes in basic components of students' lifestyle. The respondents from Grodno more often mentioned they refused to believe in what was happening and this was combined with denying the reality. This might be due to absence of strict restrictions, specific ways to inform population about the epidemiological situation and, consequently, not so drastic changes in usual lifestyle.

Psychoactive "calming" substances were used rather rarely by the respondents with the aim to change lifestyle and achieve at least imaginary stability and safety. Nevertheless, the students from Krasnoyarsk tended to drink alcohol more often; this might be due to looking for a stronger "anti-stress substance". The students from Grodno started smoking during that period more frequently though. These detected differences can be explained either by stricter control performed by family or absence of it. Some authors note that family exerts substantial influence on personal behavior and adherence to preventive activities [7]. Unfortunately, even support provided by close relatives or friends was not enough for some students to overcome this difficult situation without resorting to alcohol and smoking.

Conclusions. Self-isolation and restrictions during the pandemic highlighted all the issues related to active searching for new opportunities to improve one's lifestyle. Specific quarantine measures adopted in different countries resulted in different decisions on how to optimize basic components of students' lifestyle.

Students who only had to face certain restrictions and switched to hybrid learning tried to pursue more active lifestyle more frequently, they planned their daily routines and chose to spend their time more actively and reduce periods of working on PC as opposed to their self-isolated counterparts. At the same time, young students who had to face the complete lockdown tried to have more physical activity by doing morning exercises or physical training during a day.

Given the still existing unfavorable epidemiological situation, this study can be used to develop recommendations for students to help them survive self-isolation in the most optimal way. Besides lifestyle peculiarities that are typical for students (unbalanced diets, sleep deprivation, and use of psychoactive substances), attention should be paid to specific ones that occur during self-isolation (a substantial decrease in physical activity, changes in educational loads, and limited social contacts).

The results provide data that are important for both public healthcare organizations and education institutions since they can help develop useful recommendations aimed at maintaining students' wellbeing and giving them wider opportunities to pursue healthy lifestyle.

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Research article

INFECTION OF PERSONNEL WORKING IN CLINICAL AND DIAGNOSTIC LABORATORIES: QUALITATIVE ANALYSIS AND RISK ASSESSMENT

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Personnel who work in laboratories and directly deal with detecting and examining pathogenic biological agents (PBA) in human biomaterials have to face high risks of becoming infected. At present, working conditions at workplaces of personnel in such laboratories are to be analyzed and checked thoroughly with subsequent implementation of relevant correction measures.

We performed qualitative analysis of infection risks in clinical and diagnostic laboratories using a reason tree and event tree analysis and determined a risk probability range for an ending event considering combined effects produced by preconditions.

We revealed basic reasons why personnel in medical laboratories became infected when working with PBA. The events were considered at three levels and four directions in their development. We performed mathematical calculation of possible event combinations and determined the whole probability range for occurrence of the events. Quantitative risk analysis showed that a probability of a person becoming infected remained within $0.9 \cdot 10^{-4}$–$0.9 \cdot 10^{-3}$ range even in case of the most unfavorable outcome. The study provides a well-substantiated conclusion about peculiarities of work tasks accomplished in laboratories; we established that laboratory personnel who were involved in determining drug resistance of microbacteria had the highest risks of infection. The most hazardous scenarios of emergencies were identified; they made the highest contribution to the analyzed risk. We established that a probability of personnel becoming infected that starts with the value being $1.3 \cdot 10^{-6}$ occurs when immune prevention is neglected and a disease is revealed too late.

It is advisable to analyze ways how emergencies develop in medical laboratories since this helps to make necessary amendments in the system and influence factors of its functioning. This analysis procedure gives an opportunity to select the most relevant measures for protection and prevention of emergencies involving PBA leakage out of all the available ones. These measures can reduce risks of infection for personnel down to their acceptable levels.

Keywords: *occupational risk, working conditions, laboratory personnel, infection, pathogenic biological agents, hazard analysis, risk assessment.*

Over the whole history of occupational risk assessment, risks caused by exposure to physical and chemical factors have been those studied most frequently. Chemical factor has always been given special attention within hygienic assessment of risks at workplaces [1]. Undoubtedly, this is due to its prevalence in the overall structure of occupational incidence among all occupational groups over the whole period of research in the sphere [2]. In our country, a term "occupational risk" was first introduced by N.F. Izmerov and E.I. Denisov in 1959; however, biological factors first attracted any attention when occupational pathologies were assessed only in the early 1990ties. Still, this factor is largely neglected. It is rather typical to underestimate its effects on working conditions for many occupational groups or specific occupations. Special assessment of working conditions (SAWC) gives preference exactly to physical factors. We cannot consider this situation well grounded since this means that a mechanistic approach prevails in hygienic assessment of factors existing in the working environment.

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Appendix 9 to the Order by the RF Ministry of Labor and Social Security No. 33n dated January 24, 2014 stipulates that, regardless of concentrations of pathogenic microorganisms, working conditions that involve dealing with them should be assigned into the relevant hazard category without any measurements[1]. Biological factor is determined by a contact with infectious agents. According to the rules of strict biological safety, microorganisms are not determined in workplace air [3]. At the same time, the Order No. 29n dated January 28, 2021[2] fixes the following list of biological factors: producing fungi, protein and vitamin concentrates (PVC), nutrient yeast, mixed fodders, enzymatic drugs, biological stimulators, allergens used in diagnostics and treatment, blood components and preparations, immunobiological drugs, infected materials and materials suspected to be infected with microorganisms from 3–4 pathogenicity groups (hazard) or helminthes [4]. The same applies to biological materials that are already infected or suspected to be infected with, among other things, microorganisms from 1–2 pathogenicity groups (hazard), hepatitis viruses and HIV, biological toxins (animal, fish or plant poisons), animal and plant dust including that with bacterial contamination. At present, the list is added with COVID-19 viral cultures and isolates.

All the aforementioned components are predominantly dealt with in laboratories where personnel is directly involved into examining and establishing occurrence of pathogenic biological agents (PBA) in human biomaterials.

Occupational activities in any laboratory include multiple sections with different work tasks on handling infected materials. These activities involve large volumes of manual labor, intensive use of specialized laboratory equipment as well as technical devices for control over ambient air, disinfection equipment etc. Given that, a risk rate of infection in a laboratory depends on both relevance of applied infection control measures and on awareness about the issue among laboratory personnel. Studies with their focus on assessing risks for personnel associated with an environment in closed spaces were accomplished and described by N.V. Eremina [5]. New guidelines on biological safety in laboratory conditions were issued in 2020 due to occurrence of the new coronavirus (2019-nCoV). According to them, each laboratory can perform local (within a specific organization) risk assessment to make sure that its personnel have all competences necessary to perform laboratory tests in safe conditions and to check that relevant risk control measures are available to them [6].

Some authors took efforts to perform retrospective analysis of reasons for emergencies with PBA; methods for analyzing risks of emergencies when working with pathogenic biological agents were examined in the dissertations by the V.N. Khramov and E.A. Stakovskii [7]. However, these methods most fre-

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[1] Ob utverzhdenii Metodiki provedeniya spetsial'noi otsenki uslovii truda, Klassifikatora vrednykh i (ili) opasnykh proizvodstvennykh faktorov, formy otcheta o provedenii spetsial'noi otsenki uslovii truda i instruktsii po ee zapolneniyu (s izmeneniyami na 27 aprelya 2020 goda): prikaz Ministerstva truda i sotsial'noi zashchity RF № 33n ot 24.01.2014 [On Approval of Procedure for conducting a special assessment of working conditions, Classifier of adverse and (or) hazardous production factors, reporting form on a specific assessment of working conditions and instructions how to fill it in: The Order issued by the RF Ministry for labor and Social Protection on January 24, 2014 No. 33n (last amended on April 27, 2020)]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/499072756 (November 12, 2021) (in Russian).

[2] Ob utverzhdenii Poryadka provedeniya obyazatel'nykh predvaritel'nykh i periodicheskikh meditsinskikh osmotrov rabotnikov, predusmotrennykh chast'yu chetvertoi stat'i 213 Trudovogo kodeksa Rossiiskoi Federatsii, perechnya meditsinskikh protivopokazanii k osushchestvleniyu rabot s vrednymi i (ili) opasnymi proizvodstvennymi faktorami, a takzhe rabotam, pri vypolnenii kotorykh provodyatsya obyazatel'nye predvaritel'nye i periodicheskie meditsinskie osmotry: prikaz Minzdrava Rossii ot 28.01.2021 № 29n [On Approval of the Procedure for mandatory preliminary and periodical medical examinations of workers stipulated by the part 4 of the clause 213 in the RF Labor Code, a list of medical contraindications to accomplishing works tasks under exposure to harmful and (or) hazardous occupational factors, as well as work tasks which require mandatory preliminary and periodical medical examinations: the Order by the RF Public Healthcare Ministry dated January 28, 2021 No. 29n]. *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_375353/ (November 12, 2021) (in Russian).

quently rely on using analytics or conventional statistical analysis techniques, which makes their use a bit "subjective".

Our research goal was to assess risks of infection and biological hazards for personnel employed at clinical and diagnostic laboratories of a public healthcare organization.

Research objects and techniques. Our research object was a clinical and diagnostic laboratory of a public medical organization. Working conditions in the selected laboratory conformed to the existing legislation. We selected formal analysis techniques to be used in our study. They provide the highest "objectivity" since they are performed at the qualitative level; at the same time, facts are separated from stereotypical opinions, and only scientifically grounded judgments are considered [8]. Quantification was performed manually with using all possible variants how events would develop and all probabilities that personnel would become infected.

Fault tree and event tree methods give an opportunity to consider functional interrelations between various elements in a system as logical schemes that allow for interdependence between faults of elements or element groups [9]. Generally, both fault trees and event tress are just a visual illustrating the simplest probabilistic models. However, they are of special interests for experts involved in exploiting, maintaining and supervising technical objects. When such a scheme is available to them, these experts can not only find the most critical event among all possible ones but also assess an expected associated risk if a relevant event tree is added with necessary statistical data. These operations do not require any substantial knowledge on probability theory [10].

Research results. We analyzed infection of personnel employed in laboratories of public healthcare organizations and involved in dealing with PBA, established reasons for infection and created a tree-like scheme, which is shown in Figure 1.

When creating this reason tree, we distributed events as per different levels. They are places from left to right in the scheme, from the zero level to the fifth one; this does not

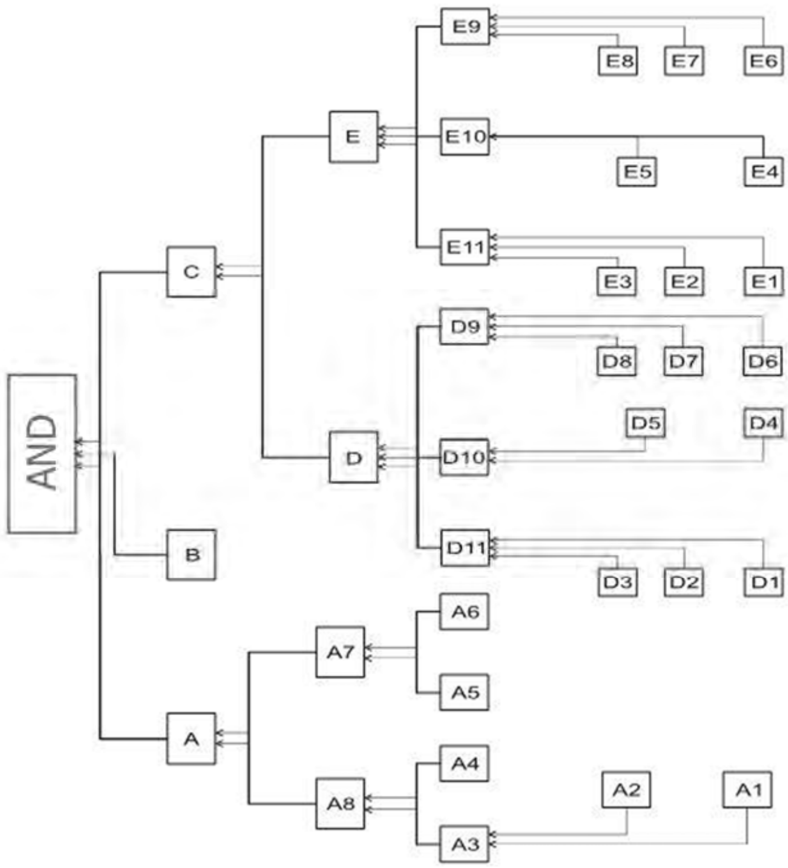

Figure 1. Tree analysis. A reason tree for infection of laboratory personnel

contradict to the logic of creating and reading it. The main (end) event is located at the zero level, followed by events belonging to the first level (some events among them might be initial ones), then the second level and up to the fourth one according to the suggested scheme [11].

Let us enumerate all the initial events necessary to induce the analyzed infection. At the first level, there are events that directly lead to personnel becoming infected:

A is existing biological peculiarities (a biological burden on an object that significantly increases risks of infection);

B is human factor being present in a system;

C is microbacteria occurring in the air or on surfaces inside a laboratory.

The following blocks on the path A are: A8 is a burden crated by microbacteria; A7 is a person's health; A6 is concomitant diseases (diabetes mellitus); A5 is an overall decline in immunity; A4 is the primary resistance and persistence of microbacteria; A3 is multiple drug resistance; A2 is a disrupted treatment scheme; A1 is lack of proper funding.

We can see two categories of preconditions with the same significance on the path C:

E is violation of sanitary rules and standards: E11 means US-radiation has been performed improperly; E10, rules and standards for disinfection have been violated; E9, technical failure of equipment; E8, a decrease in bactericide flow due to voltage changes; E7, equipment has been removed from service too early due to defects; E6, equipment has not been replaced when necessary, its service life has been exceeded (a natural fall in a bactericide flow); E5, improper disinfection; E4, improper concentration of a disinfectant; E3, failure to switch on a lamp; E2, radiation has been performed for a shorter period than required; E1, improper exploitation (just after cleaning);

D is an emergency associated with microbacteria emission: D11 is improper working procedures; D10, an error (lacking experience, nervous overstrain); D9, an expert has lost attentiveness; D8, a decrease in concentration and attention; D7, improper waking and sleeping regime; D6, attention has been moved to another object (a distraction); D5, a new procedure; D4, a young expert; D3, lack of competence needed to apply a new methodology; D2, negligence; D1, lack of knowledge.

The analysis traces an interrelation between preconditions and an end event. Infection can occur already at a moment when a person contacts a bacterium, that is, at the BC combination. The block A elevates this risk and sometimes is the most critical determinant in this event. We cannot possibly single out one certain precondition when trying to determine which exact precondition leads to the main event most rapidly.

This tree has a peculiarity, which is that all the reasons at the level going from left to right can be considered equal. This is because each of the existing reasons can equivalently lead to an event of the higher level. For example, the events D9, D10, D11 can equally be minimal preconditions for the event D to occur. They, in their own turn, result from other equal preconditions. They are mostly represented by the human factor and cannot be neglected by definition. Another peculiarity is that we do not consider any reasons for experts to be within this system. This fact is a priori associated with the reality where most actions aimed at examining a biomaterial in microbiological and bacteriological laboratories have to be performed by people, either manually or by using relevant technical devices and equipment. Therefore, we can totally neglect a probability of their presence in this system.

The probability of the main event P(I) occurs due to a combination of an expert being in a zone with elevated risks and a certain amount of microbacteria (b) that is present on a given surface or environment. This surface can be clothing and the environment is, for example, ambient air inside a room or a box. Another case (a) is organisms having a certain biological peculiarity. Creation of various scenarios as per emergency types logically converts to a technology for hazard quantification [12].

a) $P(I) = P(A) \cdot P(B) \cdot P(C)$

b) $P(I) = P(B) \cdot P(C)$

Each probability of previous events can be given as per the same scheme, for example, regarding a biological burden:

$P1(A) = P(A8) \cdot P(A7)$;

$P2(A) = P(A8) + P(A7) - P(A8) \cdot P(A7)$.

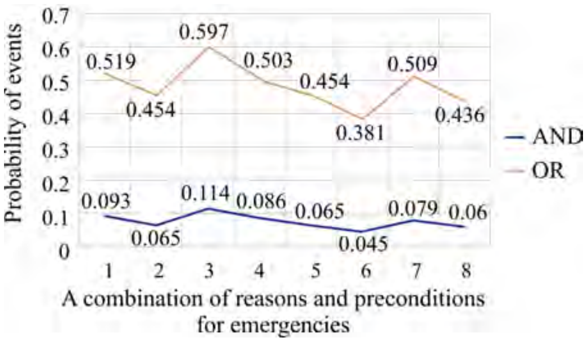

Figure 2. The results produced by calculating probabilities of events as per the paths E and D in the scheme

Since the events A1, A2, A4, A5, A6, D3, D2, D1, D5, D4, D8, D7, D6, E1, E2, E3, E4, E5, E6, E7, E8 are statistically dependent on each other, that is, occurrence of one can result in occurrence of another, then A1 = A2 = A4 = ……….. = E7 = E8. We can calculate their value out of the total probability of these events by dividing 1 by a number of basic events: 1 / 21 = 0.0476.

First, we had to find the probabilities A7 and A8 by considering all possible combinations of the events. The event A7 can occur due to two variants: "AND", "OR", consequently:

$P_1(A7) = P(A5) \cdot P(A6) = 0.0476 \cdot 0.0476 =$
$= 0.0226$;

$P_2(A7) = P(A5) + P(A6) – P(A5) \cdot P(A6) =$
$= 0.0476 + 0.0476 – 0.0476 \cdot 0.0476 = 0.0929$.

Similarly, we found all the probabilities that the event A8 would occur considering all combinations of events in the variants "AND" and "OR". Quantitative analysis revealed that the total probability of the event A varied within 0.0015–0.216 depending on a single precondition or their combinations.

We also determined P(E), or a probability that sanitary rules and standards would be violated; the probability of the event E may vary from 0.213 to 0.375 depending on a combination of factors. Similarly, we calculated probabilities as per the preconditions from the group D and established that the events preceding an error could also overlap, for example, due to improper waking and sleeping regime and any other event that would provoke an expert to abruptly get distracted from manipulations being performed at the moment. It seemed logical to calculate this probability as well [13]: $P_2 (D9) = P (D8) + P (D7) \cdot P (D6) – P (D8) \cdot P (D7) \cdot P (D6) = 0.049$.

To determine the whole range of probabilities that a certain event would occur, we calculated all possible combinations of events. The results are provided in the Figure 2.

Figure 3 shows an "event tree" in a situation when an analyzed biomaterial with PBA has been splashed. The scenario approach with an emergency involving PBA splashing makes it possible to determine [14]:

- four analyzed outcomes: no infection, recovery, disease, fatal outcome;
- five bifurcation stages, that is, stages where separation or qualitative restructuring takes place; in our case, a division into 2–3 paths (outcomes);
- a logical-probabilistic chain that includes [15]:

a) an initiator – an emergency involving splashing and formation of liquid droplet aerosol (the frequency of this initial event is equal to 1);

b) the influencing factor of the 1st order – dispersity of an aerosol;

c) the influencing factor of the 2nd order – a probability to become infected;

d) the influencing factor of the 3rd order – a period before an emergency was detected;

e) the influencing factor of the 4th order – effective measures to eliminate the emergency, taken or not taken;

f) the factor of the 5th order – an outcome (there can be three possible ones: recovery, disease, fatality).

Particles with PBA can occur in air inside a laboratory due to procedures involving aerosol formation. Coarsely dispersed aerosol (liquid droplet diameter is > 5 μm) disperses within one meter away from its source. Typically, such aerosols rapidly deposit from air on skin, clothing and work surfaces in a room. After liquid droplets in an aerosol dry out, finest particles (droplet nuclei) occur and their diameter varies from one to five μm. Each such particle can contain from one to several viable microbacteria. They can remain

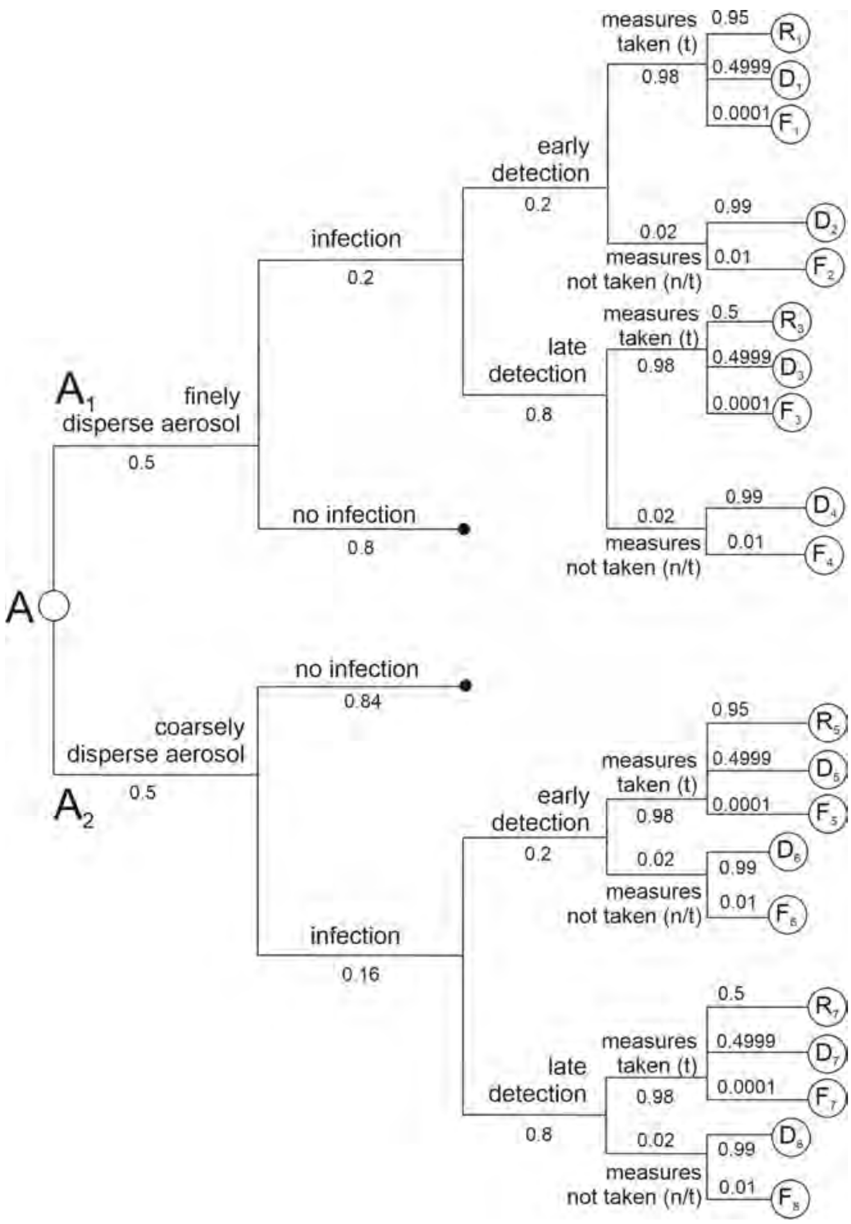

Figure 3. A tree analysis. The event tree when an analyzed biomaterial with PBA has been splashed

viable for a long period, enter the lung alveoli when inhaled, and, consequently, can induce an infection[3].

When a finely dispersed aerosol occurs with its particles being less than 5 μm in diameter, particles deposit slower, they are retained in air for a longer period, and a risk of directly inhaling particles with PBA remains high. In bacteriological and microbiological laboratories, both coarsely and finely dispersed aerosols are likely to occur and a probability of their formation can be considered the same. This is due to peculiarities of various working processes in a laboratory. Thus, centrifuging and manipulations with PCR-devices involve higher risks that a finely dispersed aerosol with PBA particles would occur whereas using pipettes, pouring liquids from one vessel to another, stirring or any other non-automated manipulations with a biomaterial more often result in formation of a coarsely dispersed aerosol. Given

[3] Sistema infektsionnogo kontrolya v protivotuberkuleznykh uchrezhdeniyakh: rukovodstvo [The infection control system in anti-tuberculosis institutions: guide]. In: L.S. Fedorova ed. Moscow – Tver, Izd-vo "Triada" LLC, 2013, 192 p. (in Russian).

that, we took a probability of each aerosol out of these two types as equal to 0.5.

The A1 path. In case there is an emergency with a finely dispersed aerosol, a negative outcome of most such emergencies is assumed to be prevented by individual and collective protection systems (from gloves and a facemask to an ultraviolet bactericide device). Multiple statistical studies have proven that such an outcome when an emergency is detected in due time and all the safety precautions are taken properly occurs in not more than 80 % of actual cases [16]. The remaining 20 % of cases involve primary infection of an expert; therefore, we assume that a probability of infection is 0.1 (80 % from 0.5) and a probability of its absence is 0.4 accordingly.

Such a fact as a person becoming infected with microbacteria is assessed in a peculiar way. This peculiarity is that primary infection is often latent for a long period; this does not allow detecting it in a short time and results produced by diagnostic examinations might not be objective. Hence, a probability that infection is established early will be significantly lower at the 3rd bifurcation stage than a probability of it being established rather late, 0.02 against 0.08.

The next stage involved considering whether effective measures were taken or not and treatment methods that were applied would produce positive effects practically in any situation in future. Hence:

– measures are taken (effective) in 98 % – 0.0196;

– measures are not taken (human factor, not effective, a treatment scheme is improper) in 2 % – 0.0004.

Measures that have been taken directly after infection was established produce a positive effect in treatment and lead to:

– recovery with its probability being 0.95 – 0.01862;

– disease (0.0499) – 0.00097804;

– fatal outcome (0.0001) – 0.00000196.

In case relevant measures have not been taken, we can assume only 2 ultimate outcomes, disease (0.00038) and fatal outcome (0.00002).

Similarly, if we consider a scenario when infection with a biological agent was established late, we get the following figures. Recovery is achieved due to proper immune prevention and express treatment (0.0392) whereas a developed disease (0.0384) will require additional treatment procedures and more time. We cannot exclude a fatal outcome completely with its probability being 0.000784. In case of refusal from treatment or selecting improper treatment, we cannot speak about early recovery just as in the first case. Disease development is equal to 0.00158 and a probability of a fatal outcome is equal to 0.000016. The quantification results as per outcomes of probable events are provided in the Table.

We checked the validity as follows. All the end probabilities of outcomes resulting from the bifurcation stages as per the path related to formation of a finely dispersed aerosol should be equal to 0.5: $P(A_1) = (0.01862 + 0.00097804 + 0.00000196 + 0.000396 + 0.000004 + 0.0392 + 0.03919216 + 0.00000784 + 0.001584 + 0.000016) + 0.4 = 0.1 + 0.4 = 0.5$.

Depending on a situation, a probability of a fatal outcome $P(F_{fda})$ can have the following values 0.00000196, 0.00002, 0.00000784, 0.000016. The most unfavorable scenario occurs when infection has been established too late and effective prevention activities and treatment procedures have been neglected. Its value is 0.00002.

Similarly, we determined probabilities as per the A2 path when a coarsely dispersed aerosol occurred.

Validity as per this path was checked as well.

$$P(A_2) = (0.014896 + 0.000782432 + 0.000001568 + 0.0003168 + 0.0000032 + 0.03136 + 0.0311353728 + 0.000006272 + 0.0012672 + 0.0000128) + 0.42 = 0.8 + 0.42 = 0.5.$$

The probability of a fatal outcome varies within 0.000001568–0.000016 on this path. When assessing biological factors, it is most difficult to make any assessments as per the disease path since we have to consider all the peculiarities of biological factors, how contagious a specific bacterium is, multiple drug resistance and in future it is also necessary to consider a risk that closed relatives or friends of an infected person may become infected as well.

Quantification as per outcomes

Conditions		A_1 path			A_2 path		
		Outcome	Notation	Value	Outcome	Notation	Value
Infection established early	Measures taken	Recovery	$P(R_1)$	0.01862	Recovery	$P(R_3)$	0.014896
		Disease	$P(D_1)$	0.00097804	Disease	$P(D_5)$	0.000782432
		Fatal outcome	$P(F_1)$	0.00000196	Fatal outcome	$P(F_5)$	0.000001568
	Measures not taken	Recovery	–	–	Recovery	–	–
		Disease	$P(D_2)$	0.000396	Disease	$P(D_6)$	0.0003168
		Fatal outcome	$P(F_2)$	0.000004	Fatal outcome	$P(F_6)$	0.0000032
Infection established late	Measures taken	Recovery	$P(R_2)$	0.0392	Recovery	$P(R_4)$	0.03136
		Disease	$P(D_3)$	0.03919216	Disease	$P(D_7)$	0.0311353728
		Fatal outcome	$P(F_3)$	0.00000784	Fatal outcome	$P(F_7)$	0.000006272
	Measures not taken	Recovery	–	–	Recovery	–	–
		Disease	$P(D_4)$	0.001584	Disease	$P(D_8)$	0.0012672
		Fatal outcome	$P(F_4)$	0.000016	Fatal outcome	$P(F_8)$	0.0000128

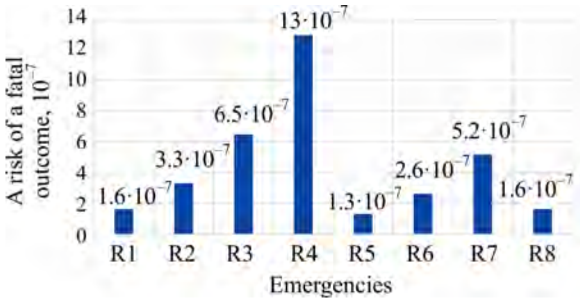

Figure 4. The results produced by calculating a risk of a fatal outcome for an expert depending on development of a situation involving splashing of a tested biomaterial with PBA

The most unfavorable scenario. A probability of emergencies during laboratory tests is equal to $8.3 \cdot 10^{-2}$ a year.

We calculated a risk (R) of a fatal outcome for an expert depending on how a situation developed. This risk was calculated by multiplying its probability by an annual probability of emergencies. Figure 4 provides the results.

The analysis revealed that the highest risk in a situation when immune prevention and treatment were neglected and infection was established late as well amounted to $1.3 \cdot 10^{-6}$ in case of an emergency involving occurrence of an aerosol.

Eventually, having calculated all the probabilities, we moved on to achieving the basic goal of creating the reason tree, which was to determine how probable the main event was. Having estimated all the combinations of preconditions, we determined a range for a probability / risk of an end event I. If we consider a combined implementation of single reasons as per the path A that is represented by biological peculiarities, then we can see that a probability of a person becoming infected, together with other reasons, will vary within $0.9 \cdot 10^{-4}$–$0.9 \cdot 10^{-3}$. This describes the most unfavorable outcome that can occur in a laboratory dealing with determining microbacteria drug resistance. Therefore, laboratory personnel who deal with examining bacterial drug resistance and multiple drug resistance are an occupational group with the highest risks of infection. If we consider a situation when only one biological factor works, a probability of such an event varies within a range from $2 \cdot 10^{-3}$–$7 \cdot 10^{-3}$ to $9 \cdot 10^{-2}$.

We determined all probable outcomes and united them in a logical sequence. This made it possible to detect potential emergency scenarios. By analyzing the event tree, we determined the most dangerous variants of how an emergency would develop; knots, which, in our opinion, would make the greatest contribution to a risk due to being very probable or due to potential damage caused by them.

Discussion. This methodology for assessing infection hazard for laboratory personnel relies on risk-based approaches meaning that absence of any hazard is provided by excluding impermissible risks. Permissible risks rates recommended by the WHO, for example, when it comes down to drinking water quality amount to 10^{-5}.

Risk assessment provides an insight into possible hazardous events, their reasons and outcomes, probability of their occurrence and making various relevant decisions. If we analyze concepts available in literature, we can conclude that ultimately a risk rate is determined by a possible damage even in cases when nothing indicates it directly [17]. Multiple risk analysis techniques are applied in world practice for emergencies, for example:

- ETA (Event Tree Analysis), which is a graphic method for representing mutually exclusive sequences of events that follow the initial one in accordance with functioning and not functioning of systems created to mitigate consequences of a hazardous event. This method can be applied to perform qualitative and / or quantitative assessment. A sequence of events can easily be depicted as an event tree; therefore, ETA makes it easy to establish what events aggravate or alleviate consequences bearing in mind additional systems, functions or barriers;
- "Bow tie" analysis is a schematic way to describe and analyze how a hazardous event develops, starting from its reasons and up to its consequences. This method combines examining reasons for an event by using a fault tree and analyzing consequences by using an event tree. However, the focus of bow tie analysis is on barriers between reasons and hazardous events and consequences. "Bow tie" diagrams can be built based on detected faults and event trees but they are more often created directly by performing a brainstorm. "Bow tie" analysis is used to examine risks by showing a range of possible reasons and consequences. This method should be applied in a situation when it is too difficult to perform full-scale analysis of a fault tree or when examination is mostly aimed at creating barriers or management techniques for each fault path. "Bow tie" analysis is often much simpler to understand than event tree analysis or fault tree analysis. Consequently, it can be quite useful for information exchange when more complicated analysis techniques are applied. Initial data for the method include information about reasons and consequences of hazardous events, risk, barriers and management techniques that can either prevent, mitigate or stimulate them;
- Bayesian analysis and Bayes net. Bayesian analysis is alleged to be created by Thomas Bayes. He suggested combining prior and posterior data to assess the complete probability. Events that reflect effects produced by "reasons" are called hypotheses in this case since they are probable events leading to this one. Unconditional probability that a hypothesis is valid is called prior (how probable a reason is in general); conditional probability, an occurred event considered, is called posterior (how probable a reason turned out to be considering data about an event)[4];
- Analytic network process (ANP) is a more general form of analytic hierarchy process (AHP), which considers dependence and feedbacks between elements. ANP has certain peculiarities including structurization of all the elements that describe a problem in a network, use of relative techniques to measure preferences by making pair comparisons (provides a universal way to solve an issue related to measuring criteria in different scales) and a possibility to consider and assess mutual influence exerted by criteria and selected alternatives (other methods do not provide this opportunity). Many issues in decision-making cannot be depicted as hierarchical structures due to existing dependences and interrelations between elements located at different levels in a hierarchy. Besides, there are tasks where not only significance of specific criteria influences priorities of alternatives but also significance of alternatives influences priorities of criteria [18];
- Decision tree represents a decision-making process graphically showing possible decisions, state of nature, probability of their occurrence, as well as costs (gains or losses) under different combinations of states of nature and possible decisions. Creating a decision tree based on tasking at a meaningful level requires differentiation between available decisions and probable accidental events that should be formulated as a whole group of events with known probabilities of their occurrence[5].

Having analyzed all the aforementioned methods, we selected decision tree since we consider this method to provide the best possible solutions to the research tasks set in the present study.

[4] Crouhy M., Galai D., Mark R. The essentials of risk management. USA, McGraw Hill, 2014, 2nd ed., 672 p.
[5] Lantz B. Machine Learning with R. Birmingham–Mumbai, Packt Publishing, 2013, 396 p.

Methodologies of risk-based approaches that differ as per their specificity have been described in research works by contemporary scientists from many countries [19–22]. However, developing methodical support for the established risk factors and creating local regulatory and technical documentation for clinical and diagnostic laboratories requires further improvement.

Conclusion. Quantitative risk analysis has revealed that a probability of a person becoming infected is going to be within $0.9 \cdot 10^{-4}$–$0.9 \cdot 10^{-3}$ in case of the most unfavorable outcome. In case only one biological factor works, a probability of infection decreases.

Creating an event tree makes it possible to analyze an emergency involving PBA splashing in a laboratory and to establish the most unfavorable scenario of its development. Analysis of paths and development variants allows making changes in a system and influencing factors of its functioning. Therefore, developing recommendations on how to mitigate a risk is the last stage in logical-probabilistic approach to risk assessment and analysis. It is advisable to focus on developing safety measures aimed at preventing emergencies. A system of activities aimed at reducing a probability of an emergency involving PBA occurrence at a workplace includes the following: regular training in biologically safe work procedures; making overstrain and emotional loads of personnel as small as it is only possible; use of reliable equipment; tracing of defects; selecting proper protective equipment and biological safety boxes; keeping proper ventilation and disinfection; intelligent design of spaces where laboratory tests are accomplished; etc. It is advisable to select several safety measures and measures aimed at preventing emergencies involving PBA splashing out of all the suggested ones concentrating on those that require minimal costs and can still provide risk reduction down to its acceptable levels or those that can provide maximum risk reduction within laboratory spaces given the available means.

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Research article

RISKS OF BECOMING INFECTED WITH SARS-COV-2 FOR MEDICAL PERSONNEL IN A LARGE INDUSTRIAL CITY DURING THE PANDEMIC: COMPARATIVE ASSESSMENT

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The COVID-19 pandemic has produced its effects on functioning of all the state institutions, the public healthcare system being a peculiar one among them. Medical personnel have become an unprotected population group that was actively involved into the epidemic process. Results produced by several studies indicate that relative risks to become infected with COVID-19 are by up to 11.6 times higher for medical personnel than in population at large. A share of medical personnel among patients with COVID-19 varies in different countries, from 4.2 % in China to 17.8 % in the USA. According to official statistics, in 2020 a share of medical personnel who became infected with COVID-19 in in-hospital foci amounted to 68.6 % in the RF regions located in the Urals and Siberian Federal Districts.

High epidemic potential of the virus and intensive mass contacts between medical personnel and their patients make for rapid SARS-CoV-2 spread and infection among them. It is vital to examine all the range of risk factors that cause SARS-CoV-2 infection among medical personnel.

The present study involved using "The map of epidemiological investigation focused on the incidence of the new coronavirus infection (COVID-19) in medical personnel". The map was located on Google Cloud Platform. Overall, 613 medical workers from different medical organizations took part in the research. We applied sociological, epidemiological and statistical research techniques.

We established that work in an infectious diseases hospital increased a relative risk of SARS-CoV-2 infection by 1.8 times (RR = 1.78; 95 % CI [1.65–1.93]). The total risk of SARS-CoV-2 infection was insignificant for workers employed at a medical organization that provided scheduled medical assistance to population (RR = 1.02; 95 % CI [1.00–1.04]). However, certain factors created elevated risks of infection. Any contacts with COVID-19 patients who were close relatives, friends or neighbors were established to be significant (RR = 1.13; 95 % CI [1.04–1.228]).

The research results should be used when organizing work procedures and anti-epidemic activities in infectious diseases hospitals and medical organizations providing scheduled assistance to population. The focus should be on providing medical personnel with personal protective equipment as well as on calculating relevant duration of a work shift relying on the risk-based approach.

Keywords: *pandemic, COVID-19, SARS-COV-2, medical personnel, risk factors of infection, risk-based approach.*

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Pandemic spread of the SARS-CoV-2 virus has influenced functioning of all the state institutions. Public healthcare systems have faced extreme loads in all countries, the Russian Federation included. As of March 01, 2022, more than 438.5 million cases of the infection were registered all over the world; 432.5 million people recovered and 5.9 million died. In the Russian Federation, approximately 16.5 million people became infected and 352.4 thousand of them died. In Sverdlovsk region, 355.3 thousand infection cases and 10.3 thousand fatal outcomes were registered[1].

Medical personnel are exposed to impacts exerted by variable biological factors due to their occupational activities. The SARS-CoV-2 virus is no exception, since it can be considered, among other things, a healthcare-associated infection (HAI). Medical personnel have been at the forefront of fighting against COVID-19 from the very beginning and have become the most unprotected population group that is involved into the epidemic process the most actively [1–3].

There is no sufficient information on COVID-19 incidence among medical personnel; however, some official data highlight that the SARS-CoV-2 infection spreads among the examined occupational group much more actively. Thus, according to official data on registered HAIs cases in the regions included into the Ural and Siberian Federal Districts in 2020, medical personnel accounted for 68.8 % among those who became infected with SARS-CoV-2 in hospital; COVID-19 incidence among them reached 90.4–151.48 per 1000 workers in some regions[2].

Results produced by some research works indicate that medical personnel who have contacts with patients releasing SARS-CoV-2 face by 11.6 times higher risks of infection than population at large [4]. Most researchers work with data on a share of infected medical personnel in the overall structure of COVID-19 patients. Thus, for example, in China a share of infected medical workers amounted to 4.2 % (in particular, 11.9 % in Wuhan); in Italy, 9.0 %, and in the USA, 17.8 %. A study that concentrated on COVID-19 incidence among medical personnel in Italy mentioned 20 % of infected workers among personnel [5–7].

High epidemic potential of the virus as well as close contacts with both co-workers and patients contribute to SARS-CoV-2 infection among medical personnel [3, 8]. In its turn, there are no sufficient data on risks of the infection spread among medical personnel working in different healthcare organizations, for example, infectious diseases hospitals for treating COVID-19 patients or medical organizations that provide scheduled medical aid to population. It is vital to examine the whole range of risk factors causing SARS-CoV-2 infection in detail depending on conditions at workplaces.

Our research goal was to comparatively assess risks of SARS-CoV-2 infection for medical personnel working in different healthcare organizations in a large city during the COVID-19 pandemic.

Materials and methods. The study was accomplished by experts from the Ural-Siberian Scientific Methodical Center for healthcare-Associated Infections Prevention of Rospotrebnadzor’s State Research Center of Virology and Biotechnology VECTOR together with experts from the Center for Public Health and Medical Prevention (Ekaterinburg).

The present study involved using “The map of epidemiological investigation focused on the incidence of the new coronavirus infection (COVID-19) in medical personnel” to examine risk factors of infection (hereinafter the Map). It was developed by experts from the Rospotrebnadzor’s State Research Center of

[1] Koronavirus: statistika [Coronavirus: statistics]. Available at: https://yandex.ru/covid19/stat/ (March 01, 2022) (in Russian).

[2] Smirnova S.S., Vyatkina L.G., Zhuikov N.N., Egorov I.A. Analiz vyyavleniya i registratsii infektsii, svyazannykh s okazaniem meditsinskoi pomoshchi v Ural'skom i Sibirskom federal'nykh okrugakh v 2020 godu: informatsionnyi byulleten' [Analyzing detection and registration of healthcare-associated infections in the Ural and Siberian Federal Districts in 2020: information bulletin]. Ekaterinburg, Yunika, 2021, 56 p. (in Russian).

Virology and Biotechnology VECTOR[3]. The Map consisted of seven sections and contained both open and close-ended questions. It was located on Google Cloud Platform and the link to it (URL) was distributed among medical personnel by corporate email and messengers.

We applied sociological, epidemiological (descriptive-estimative and analytical) and statistical procedures in our study.

We estimated whether respondents were equipped with full sets of relevant personal protective equipment (PPE) and used them properly; the estimates relied on the following criteria:

– a full PPE set included protective overall, hat, shoe covers, two pairs of gloves, FFP2 or FFP3 respirator, safety goggles that formed a complete seal around the eyes or a mask that covered the face completely;

– a PPE set without complete protection of the eyes lacked safety goggles with a complete seal or a mask covering the face completely;

– a PPE set without complete protection of the respiratory organs lacked FFP2 or FFP3 respirators (only facemasks or shields were applied etc.).

We estimated whether PPE was replaced with proper regularity using the following criteria: a PPE set should not be used for longer than 4 hours and a mask, longer than 2–3 hours[4]. Contacts a medical worker had with people infected with COVID-19 (relatives, friends, neighbors, co-workers or patients) were established by analyzing a respondent's epidemiological case history taken from the Map.

The obtained data were given as absolute and relative values (%) and were analyzed using conventional statistical procedures. To compare likelihood of an outcome, depending on various risk factors, we created a fourfold contingency table, calculated a relative risk (*RR*) and its 95 % confidence interval (CI).

The differences were considered authentic at $p \leq 0.05$. All the data were statistically analyzed with Microsoft Office 2010, WinPEPI 11.65 software package and "Medical statistics"[5].

Results. Overall, 613 medical workers employed by 18 medical organizations in Yekaterinburg took part in the questioning. They all had previously had COVID-19 (confirmed by laboratory tests); 28 of them (4.6 %) were supervisors at medical organizations (MO), 161 (26.3 %) doctors, 345 (56.3 %) nurses and 26 (4.2 %) medical assistants, 8 (1.3 %) administrative staff, and 45 (7.3 %) other staff of various sex, age and with different work records. Personnel employed at infectious diseases hospitals accounted for 19.1 % (117 people) of the respondents; the remaining 80.9 % (496 people) were employed at MO that provided scheduled medical aid to population. People of employable age (20–55 years) prevailed among infected medical workers and accounted for 79.8 % (489 people). Respondents of both sexes took part in the questioning; however, women prevailed among them (84.2 %) and this was quite typical for public healthcare.

Our study established certain differences in risk factors causing infection spread among

[3] Smirnova S.S., Stepanova E.A., Yuzhanina T.S. Karta epidemiologicheskogo rassledovaniya zabolevaniya novoi koronavirusnoi infektsiei (COVID-19) u meditsinskogo rabotnika [The map of epidemiological investigation focused on the incidence of the new coronavirus infection (COVID-19) in medical personnel]. *Rospotrebnadzor's State Research Center of Virology and Biotechnology VECTOR*. Available at: http://eniivi.vector.na4u.ru/wp-content/uploads/2020/05/karta-epid-rassled-covid19-05-2020.pdf (March 03, 2022) (in Russian).

[4] MR 3.1.0229-21. Profilaktika infektsionnykh boleznei. Rekomendatsii po organizatsii protivoepidemicheskikh meropriyatii v meditsinskikh organizatsiyakh, osushchestvlyayushchikh okazanie meditsinskoi pomoshchi patsientam s novoi koronavirusnoi infektsiei (COVID-19) (podozreniem na zabolevanie) v statsionarnykh usloviyakh (utv. Rukovoditelem Federal'noi sluzhby po nadzoru v sfere zashchity prav potrebitelei i blagopoluchiya cheloveka, Glavnym gosudarstvennym sanitarnym vrachom RF A.Yu. Popovoi 18 yanvarya 2021 g.) [Methodical guidelines MR 3.1.0229-21. Prevention of communicable diseases. Recommendations on how to organize anti-epidemic activities in medical institutions for treating patients with the new coronavirus infection (COVID-19) (suspected infection) in in-patient departments (approved by A.Yu Popova, the RF Chief Sanitary Inspector and the Head of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing on January 18, 2021)]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/573382386 (February 03, 2022) (in Russian).

[5] Meditsinskaya statistika: internet-portal [Medical statistics: Internet-portal]. Available at: https://medstatistic.ru/ (February 04, 2022) (in Russian).

medical personnel depending on working conditions.

Women accounted for 83.9 % (98 people) among medical personnel employed at infectious diseases hospitals; men, 16.2 % (19 people). We did not detect and significant sex-dependent risks of SARS-CoV-2 infection among medical personnel (Table 1).

The age structure of medical personnel employed at infectious diseases hospitals was as follows: 25 workers were aged 20–29 years (21.4 %); 17 workers, 30–39 years (14.5 %); 38 workers, 40–49 years (32.5 %); 19 workers, 50–54 years (16.2 %); 12 workers, 55–59 years (10.3 %); 5 workers, 60–64 years (4.2 %), one workers was aged 65 and older (0.9 %).

We analyzed the occupational structure of medical workers from infectious diseases hospitals and established that MO supervisors accounted for 3.4 % (4 workers); doctors, 18.8 % (22 workers); nurses, 59.8 % (70 workers); medical assistance and janitors, 11.1 % (13 workers); administrative staff, 0.9 % (1 worker); other staff, 6.0 % (7 workers). We detected a significant risk of SARS-CoV-2 infection for those workers employed at infectious diseases hospitals who dealt with cleaning (*RR* = 2.822, 95 % CI [1.85–4.304]).

Medical personnel employed at infectious diseases hospitals had certain hazardous occupational contacts typical for medical care. These contacts involved risky aerosol-generating procedures such as trachea intubation, artificial ventilation (AV), oxygenation with high precision, inhalations, tracheabronchial tree sanitation, taking sputum/smears from the nasopharynx, tracheostomy, bronchoscopy, and cardiopulmonary resuscitation (CPR). Forty-four workers (37.6 %) participated in them. Overall, 92 workers (78.6 %) provided medical aid to COVID-19 patients. Eighty-eight workers (75.2 %) had direct contacts with the environment influenced by an infected patient (personal things, bed linen, a bed, a bedside table etc.). We established a significant risk of infection for all the aforementioned types of contacts. Thus, when a medical worker was present during an aerosol-generating procedure provided to a COVID-19 patient, it increased a risk of infection by 3.1 times (*RR* = 3.129, 95 % CI [2.304–4.25]). When a medical worker directly provided medical aid to a COVID-19 patient, a risk of infection grew by 4.1 times (*RR* = 4.072, 95 % CI [2.695–6.152]). Contacts with the environment influenced by COVID-19 patients (for example, objects they touched or used) resulted in 3.9 times higher risks of infection (*RR* = 3.881, 95 % CI [2.632–5.721]).

One worker (0.9 %) employed at an infectious diseases hospital did not use PPE when contacting COVID-19 patients. Seventy-five workers (64.1 %) used full PPE sets that protected the respiratory organs and eyes and included protective overalls, FFP2/FFP3 respirators, and safety goggles with a complete seal around the eyes. Fifteen workers (12.8 %) employed at infectious diseases hospitals used PPE sets without proper protection for the eyes or respiratory organs. Twenty-three workers (19.7 %) employed at infectious diseases hospitals mentioned not having safety goggles with a complete seal or a mask that covered the whole face in their PPE sets. Protection of the respiratory organs (FFP2 or FFP3 respirators) was absent in PPE sets used by four workers (3.4 %). Only 70.9 % of the workers replaced their PPE sets as regularly as it was stipulated by the existing standards. Use of PPE sets without full protection provided for the eyes and with full protection provided for the respiratory organs increased risks of SARS-CoV-2 infection for medical personnel at infectious diseases hospitals by 1.7 times (*RR* = 1.678, 95 % CI [1.137–2.477]). Failure to replace PPE sets according to the standardized regularity also influenced risks of infection (*RR* = 2.761, 95 % CI [1.923–3.964]).

Thirty-eight workers (33.0 %) had to work in a "red zone" for 6 hours; 5 workers (4.3 %), from 6 to 8 hours; 27 workers (23.5 %), from 8 to 12 hours; and 44 workers (38.3 %), from 12 to 24 hours. One worker (0.9 %) employed at an infectious diseases hospital had a work shift that exceeded 24 hours. We established a risk of SARS-CoV-2 infection to grow as a work shift became

Table 1

Risks of SARS-CoV-2 infection for workers employed at infectious diseases hospitals treating COVID-19 patients

No.	Indicator	Number of healthcare workers with laboratory-confirmed COVID-19	*RR* (relative risk)	95 % CI
sex				
1	men	19	1.031	0.664–1.603
2	women	98	0.97	0.624–1.507
age				
3	20–29 years	25	1.03	0.692–1.531
4	30–39 years	17	0.842	0.527–1.345
5	40–49 years	38	1.214	0.86–1.713
6	50–54 years	19	1.221	0.791–1.885
7	55–59 years	12	1.034	0.605–1.767
8	60–64 years	5	0.607	0.262–1.405
9	65 years and older	1	0.243	0.036–1.657
position				
10	supervisors	4	0.74	0.294–1.86
11	doctors	22	0.65	0.424–0.997
12	nurses	70	1.157	0.829–1.615
13	medical assistants, janitors	13	2.822	1.85–4.304
14	administrative staff	1	0.652	0.103–4.108
15	other staff	7	0.803	0.398–1.619
types of contacts in medical care provision (from the number of answers)				
16	treatment of COVID-19 patient	92	4.072	2.695–6.152
17	presence during aerosol-generating procedures provided to a COVID-19 patient	44	3.129	2.304–4.25
18	having a direct contact with objects influenced by a COVID-19 patient	88	3.881	2.632–5.721
use of PPE, completeness of their sets and replacement (from the number of answers)				
19	not using PPE during contacts with a COVID-19 patient	1	0.302	0.045–2.038
20	using PPE without complete protection of the eyes and respiratory organs	15	0.132	0.079–0.222
21	using PPE without complete protection of the eyes but with complete protection of the respiratory organs	23	1.678	1.137–2.477
22	using PPE with complete protection of the eyes but without complete protection of the respiratory organs	4	0.869	0.35–2.158
23	PPE (incomplete set and non-use when providing medical care to a COVID-19 patient)	43	0.244	0.175–0.341
24	Failure to replace PPE regularly	21	2.761	1.923–3.964
duration of a work shift (from the number of answers)				
25	shift duration up to 6 hours	38	1.618	1.154–2.269
26	shift duration from 6 to 8 hours	5	0.047	0.019–0.113
27	shift duration from 8 to 12 hours	27	2.173	1.526–3.095
28	shift duration from 12 to 24 hours	44	3.946	2.947–5.283
29	shift duration over 24 hours	1	0.629	0.1–3.966
adherence to hand sanitation (from the number of answers)				
30	non-compliance with hands sanitizing standards during medical procedures	1	0.746	0.121–4.615
contacts with COVID-19 patients (from the number of answers)				
31	COVID-19 among relatives, friends, or neighbors	9	0.497	0.262–0.944
32	COVID-19 among co-workers	58	8.896	6.943–11.397
33	**total *RR***		**1.78**	**1.65–1.93**

longer. Thus, a 6-hour work shift increased a risk of SARS-CoV-2 infection by 1.6 times (*RR* = 1.618, 95 % CI [1.154–2.269]); a shift lasting from 8 to 12 hours, by 2.2 times (*RR* = 2.173, 95 % CI [1.526–3.095]); from 12 to 24 hours, by 4.0 times (*RR* = 3.946, 95 % CI [2.947–5.283]).

Adherence to hand sanitation standards is a vital component in infection prevention, medical personnel included. In our study, only one worker (0.9 %) did not adhere to these standards when performing variable medical procedures. Although it was objectively rather difficult to accomplish this procedure in a "red" zone in an infectious diseases hospital, 40 workers (34.2 %) sanitized their hands prior to and after each aseptic procedure and 58 workers (49.6 %) did it after a direct contact with a COVID-19 patient or any objects inside a hospital. We did not detect any significant influence exerted by this factor on probable SARS-CoV-2 infection in this occupational group; however, this fact needs further investigation.

We analyzed epidemiological case histories of workers employed at infectious diseases hospitals. The analysis revealed that nine workers had contacts with COVID-19 patients beyond their MO (close relatives, friends or neighbors) and a share of such contacts equaled 7.7 %. Much more workers employed at infectious diseases hospitals mentioned their contacts with infected colleagues, namely, 59 workers (49.6 %) and this increased risks of SARS-CoV-2 infection by 8.9 times (*RR* = 8.896, 95 % CI [6.943–11.397]).

Risk factors of SARS-CoV-2 infection had certain peculiarities for medical personnel employed at MO that did not treat infectious diseases (Table 2).

Table 2

Risks of SARS-CoV-2 infection for workers employed at medical organizations providing scheduled medical aid to population

No.	Indicator	Number of healthcare workers with laboratory-confirmed COVID-19	*RR* (relative risk)	95 % CI
sex				
1	men	78	0.993	0.892–1.104
2	women	418	1.007	0.905–1.121
age				
3	20–29 years	103	0.993	0.903–1.093
4	30–39 years	86	1.039	0.944–1.143
5	40–49 years	136	0.953	0.871–1.043
6	50–54 years	65	0.95	0.84–1.074
7	55–59 years	49	0.992	0.871–1.13
8	60–64 years	37	1.096	0.974–1.234
9	65 years and older	20	1.184	1.068–1.314
position				
10	supervisors	24	1.062	0.909–1.242
11	doctors	139	1.093	1.011–1.181
12	nurses	275	0.967	0.895–1.044
13	medical assistants, janitors	13	0.608	0.413–0.894
14	administrative staff	7	1.083	0.831–1.411
15	other staff	38	1.047	0.918–1.195
types of contacts in medical care provision (from the number of answers)				
16	treatment of COVID-19 patient	199	0.741	0.681–0.807
17	presence during aerosol-generating procedures provided for a COVID-19 patient	55	0.648	0.541–0.775
18	having a direct contact with objects influenced by a COVID-19 patient	181	0.735	0.672–0.803

Continuation of the Table 2

No.	Indicator	Number of healthcare workers with laboratory-confirmed COVID-19	*RR* (relative risk)	95 % CI
use of PPE, completeness of their sets and replacement (from the number of answers)				
19	not using PPE during contacts with a COVID-19 patient	16	1.169	1.031–1.325
20	using PPE without complete protection of the eyes and respiratory organs	308	1.471	1.347–1.606
21	using PPE without complete protection of the eyes but complete protection of the respiratory organs	55	0.855	0.737–0.993
22	using PPE with complete protection of the eyes but without complete protection of the respiratory organs	20	1.031	0.859–1.238
23	PPE (incomplete set and non-use when providing medical care to a COVID-19 patient)	399	1.502	1.331–1.694
24	Failure to replace PPE regularly	24	0.642	0.487–0.846
duration of the work shift (from the number of answers)				
25	shift duration up to 6 hours	136	0.871	0.778–0.975
26	shift duration from 6 to 8 hours	287	1.567	1.433–1.713
27	shift duration from 8 to 12 hours	72	0.755	0.629–0.907
28	shift duration from 12 to 24 hours	79	0.516	0.402–0.662
29	shift duration over 24 hours	7	1.092	0.838–1.423
adherence to hand sanitation (from the number of answers)				
30	non-compliance with hands sanitizing standards during medical procedures	7	1.06	0.781–1.438
contacts with COVID-19 patients (from the number of answers)				
31	COVID-19 among relatives, friends, or neighbors	88	1.13	1.04–1.228
32	COVID-19 among co-workers	61	0.055	0.018–0.166
33	**total *RR***		**1.02**	**1–1.04**

Women accounted for 84.3 % in these MO (496 people); men, 15.7 % (78 people). Our study did not reveal any sex-dependent risk factors of SARS-CoV-2 infection for medical personnel who provided scheduled medical aid to population.

The age structure in this group was as follows: 103 workers were aged 20–29 years (20.7 %); 86 workers, 30–39 years (17.3 %); 1365 workers, 40–49 years (27.4 %); 65 workers, 50–54 years (13.1 %); 49 workers, 55–59 years (9.9 %); 37 workers, 60–64 years (7.5 %); 20 workers were aged 65 years and older (4.1 %). We established that older workers aged 65 years and more had higher risks of SARS-CoV-2 infection against their younger co-workers (*RR* = 1.184, 95 % CI [1.068–1.314]).

We examined the occupational structure in the group of workers employed at MO providing scheduled medical aid to population. The group included 24 MO supervisors (4.8 %), 139 doctors (28.0 %), 275 nurses (55.5 %), 13 medical assistants and janitors (2.6 %), 7 administrative workers (1.4 %), and 38 other staff (7.7 %). Risks of infection were by 1.1 times higher for doctors due to their specific occupational tasks (*RR* = 1.093, 95 % CI [1.011–1.181]).

Medical personnel dealing with providing scheduled medical aid to population turned out to be not ready to contacts with COVID-19. This resulted in security measures not being observed properly by them when they treated patients with infectious diseases. Yet, COVID-19 was lately diagnosed in many patients treated at those MO and 40.1 % of the respondents (199 people) participated in their treatment, including aerosol-generating procedures with 27.6 % (55 people) of the respondents accomplishing them. Direct contacts with the environment influenced by an infected patient (personal things, bed linen, a bed, a bedside table etc.) were mentioned by 181 workers (36.5 %).

Sixteen workers (3.2 %) employed at MO providing scheduled medical aid to population did not use PPE when contacting COVID-19 patients. Only 113 workers (22.8 %) used full sets with complete protection of the respiratory organs and eyes that included overalls, FFP2/FFP3 respirators, and safety goggles with a complete seal around the eyes. PPE sets with either incomplete protection of the eyes or respiratory organs were used by 308 workers (62.1 %). Other fifty-five workers (11.1 %) mentioned absence of safety goggles with a complete seal or a mask covering the whole face. Twenty workers (4.0 %) did not have protection of the respiratory organs (FFP2 or FFP3 respirators in a PPE set). Eighty-four point seven percent of the respondents replaced their PPE with standardized regularity. Failure to use PPE when contacting COVID-19 patients and use of PPE with incomplete protection of the eyes and respiratory organs increased risks of infection by 1.2 (*RR* = 1.169, 95 % CI [1.031–1.325]) and 1.5 times (*RR* = 1.471, 95 % CI [1.347–1.606]) accordingly.

Ninety-eight workers (21 %) in MO providing scheduled medical aid to population had work shifts that lasted up to 6 hours; 282 workers (60.4 %) had to work from 6 to 8 hours; 45 workers (9.6 %), from 8 to 12 hours; 35 workers (7.5 %), from 12 to 24 hours; and 7 workers (1.5 %) had a shift longer than 24 hours. A working shift from 6 to 8 hours long increased risks of infection by 1.6 times (*RR* = 1.567, 95 % CI [1.433–1.713]).

Six respondents (1.2 %) working in MO that provided scheduled medical aid to population failed to sanitize their hands in conformity with the established regulations. One hundred and sixty-three workers (32.9 %) sanitized their hands prior to each aseptic procedure and after it; 169 workers (34.1 %) did it after touching a COVID-19 patient or after contacts with objects influenced by such a patient. We did not establish any elevated risks of infection associated with failure to follow hand sanitation regulations when accomplishing medical procedures. However, this fact requires further investigation.

Workers employed at MO providing scheduled medical aid to population, just as their counterparts working in infectious diseases hospitals, had contacts with COVID-19 patients beyond their workplaces. Thus, 79 respondents (15.9 %) had contacts with relatives, friends or neighbors who were infected with COVID-19; three respondents (0.6 %) contacted infected coworkers. This increased risks of SARS-CoV-2 infection (*RR* = 1.13, 95 % CI [1.04–1.228]). Table 2 provides the complete results produced by analyzing this occupational group.

Discussion. Medical personnel become infected with pathogenic biological agents to a greater or lesser extent regardless of a MO type and what medical aid it provides. However, risks of infection grow significantly during epidemic or pandemic spreads of viruses with high epidemic potential, SARS-CoV-2[6] virus being among them.

Over the last 20 years, the world has faced several epidemics of viral communicable diseases: severe acute respiratory syndrome (SARS) in 2002, A (H1N1) virus flu from 2009 to 2010, Ebola Virus Disease (a major outbreak occurred in West Africa in 2014–2016), and Middle East respiratory syndrome (MERS) in 2015. Every time, health workers have been at the forefront in fighting against these diseases and they have always had high occupational risks of infection, severe disease and fatal outcomes[7] [9]. Undoubtedly, COVID-19 pandemic has already become the most significant event in the 21st century. Starting from the first day of

[6] Prevention, identification and management of health worker infection in the context of COVID-19: Interim guidance. *WHO*, 2020. Available at: https://apps.who.int/iris/bitstream/handle/10665/336265/WHO-2019-nCoV-HW_infection-2020.1-eng.pdf?sequence=1&isAllowed=y (March 01, 2022).

[7] Novaya koronavirusnaya infektsiya COVID-19: professional'nye aspekty sokhraneniya zdorov'ya i bezopasnosti meditsinskikh rabotnikov: metodicheskie rekomendatsii [New coronavirus infection COVID-19: occupational aspects related to preserving health and providing safety for medical personnel: methodical guidelines]. In: I.V. Bukhtiyarov, Yu.Yu. Gorblyanskii eds. Moscow, AMT, Scientific Research Institute for Occupational Medicine, 2021, 132 p. (in Russian).

SARS-CoV-2 spread, medical personnel have been a population group that is the most actively involved into the epidemic process. Public healthcare systems in every country, the Russian Federation included, have been facing extreme loads since the pandemic started. Thus, in China (in Wuhan in particular) during the early stage in SARS-CoV-2 spread from December 2019 to February 2020 a number of COVID-19 cases was by 3.5 times higher among health workers than among population at large[7]. When it comes down to fatal outcomes, we should mention that, according to the WHO report, approximately 115.5 thousand health workers died during the period from January 2020 to May 2021.

High incidence among medical personnel and hospital maintenance staff produces negative effects on quality of emergency and scheduled medical aid provided to population as well as on implementation of prescribed anti-epidemic activities[8]. Given the ongoing pandemic, it is still necessary to examine risk factors of SARS-CoV-2 infection for medical personnel and to use the result of these studies as grounds for developing occupational safety programs both in a specific MO and at the national level as well[9] [10–12].

By now, the basic risk factors of infection have been established. They include providing medical aid to patients with COVID-19 given a significant growth in a number of patients needing hospitalization, incomplete PPE sets or failure to provide all medical workers with them, as well as low adherence to antiseptic hand sanitation among health workers[8] [7, 13].

According to the results of analytical studies accomplished by experts from Denmark and Sweden, infection was the most frequent among male health workers aged younger than 30 [14, 15]. In this study, we did not establish sex to be a significant risk factor of SARS-CoV-2 infection. As for an age of infected medical personnel, we detected a high share of infected workers aged 65 years and older among those employed at MO providing scheduled medical aid to population (RR = 1.184, 95 % CI [1.068–1.314]). Those elderly workers were engaged in providing scheduled medical aid due to redistribution of health workers when younger ones had to be transferred to infectious diseases hospitals [16].

Some studies established that in many countries health workers who were involved in providing medical aid at different stages and levels had different risks of SARS-CoV-2 infection. For example, in Italy paramedics and nurses had higher (by 1.5 times) risks of becoming infected with SARS-CoV-2 virus than other medical personnel. In its turn, in Great Britain COVID-19 prevalence turned out to be the highest among workers with non-medical specialties (janitors and cleaners) [17]. The World Health Organization (WHO) also detected high risks for workers who cleaned wards where patients infected with SARS-CoV-2 were treated[8]. Our study also confirms that workers responsible for cleaning hospital wards account for a significant share of infected personnel of infectious diseases hospitals (RR = 2.822, 95 % CI [1.85–4.304]). At the same time, doctors working in MO that provided scheduled medical aid to population also had elevated risks of infection since they had to perform primary examinations of patients with unknown infectious status. Still, these risks were a bit less significant (RR = 1.093, 95 % CI [1.011–1.181]).

Provision with PPE in sufficient quantities and its proper use as well as relevant quality of this equipment are necessary conditions for reducing risks of infection, especially when it comes down to a global spread of a droplet infection [18, 19]. Thus, Gómez-Ochoa with colleagues (2021) detected a high risk of infection for health workers who used PPE with incomplete protection of the eyes or did not use any PPE at all. The risk grew from 2.82 to 3.72 times [1]. In Great Britain and the USA

[8] COVID-19: Occupational health and safety for health workers: Interim guidance. ILO, WHO, 2021. Available at: https://hlh.who.int/docs/librariesprovider4/hlh-documents/covid-19---occupational-health-and-safety-for-health-workers.pdf?sfvrsn=581e60c6_5 (March 01, 2022).

[9] Caring for those who care: guide for the development and implementation of occupational health and safety programmes for health workers. Geneva, WHO, ILO, 2022, 124 p.

experts also revealed that if health workers who treated patients with COVID-19 did not use a full PPE set or failed to replace it regularly, they had elevated risks of infection that were from 1.31 to 1.46 times higher [4].

We also established in our study that incorrect use of PPE or using incomplete sets made a significant contribution to growing risks of infection, by 1.6 times a (*RR* = 1.678, 95 % CI [1.137–2.477]) when using an incomplete PPE set that did not protect the eyes and up to 2.8 times (*RR* = 2.761, 95 % CI [1.923–3.964]) when workers failed to replace their PPE sets regularly. Medical personnel at MO that provided scheduled medical aid to population did not have enough PPE sets at the first stages in fighting against the infection. This meant they were not ready to interact with COVID-19 patients and, as a result, risks of infection grew for them.

Loads on medical organizations grew drastically due to a significant increase in a number of patients infected with SARS-CoV-2. This resulted in longer work shifts and, consequently, longer contacts between medical personnel and infected patients. The situation was aggravated further by improper PPE use[7]. Chou and others (2020) established that a growth in work shift duration became a significant risk factor of SARS-CoV-2 infection for health workers. This risk grew by 2.2 times (*RR* = 2.173, 95 % CI [1.526–3.095]) for workers employed at infectious diseases hospitals when their work shift lasted 8–12 hours and by up to 4.0 times (*RR* = 3.946, 95 % CI [2.947–5.283]) when it lasted 12–24 hours. However, workers employed at MO that provided scheduled medical aid to population had a risk of infection even if they worked in their usual shifts lasting from 6 to 8 hours (*RR* = 1.567, 95 % CI [1.433–1.713]). This might be due to using an incomplete PPE set [20].

Adherence to hand sanitation regulations when accomplishing medical procedures is a key issue influencing risks of infection[10]. When workers employed at infectious diseases hospitals in China failed to sanitize their hands properly, this created by 3.1 times higher risks of SARS-CoV-2 infection [20]. Some data also indicate that failure to sanitize the hands with skin antiseptic together with irregular hygienic washing was by 2.2–3.0 times more frequent among health workers who had already had laboratory-confirmed COVID-19 [13]. In this study, we did not establish any effects produced by failure to adhere to hand sanitation regulations when accomplishing medical procedures on likelihood of SARS-CoV-2 infection; however, this fact requires further investigation.

Conclusion. We established that working in an infectious diseases hospital created by 1.8 times higher risks of SARS-CoV-2 infection for medical personnel (*RR* = 1.78, 95 % CI [1.65–1.93]). Major risks of infection among medical personnel at infectious diseases hospitals occurred due to the following: treating a patient with COVID-19 (*RR* = 4.072, 95 % CI [2.695–6.152]), accomplishing aerosol-generating procedures (*RR* = 3.129, 95 % CI [2.304–4.25]), direct contacts with the environment influenced by a COVID-19 patient (*RR* = 3.881, 95 % CI [2.632–5.721]), cleaning hospital wards (*RR* = 2.822, 95 % CI [1.85–4.304]), failure to regularly replace PPE (*RR* = 2.761, 95 % CI [1.923–3.964]), use of PPE with incomplete protection provided for the eyes (*RR* = 1.678, 95 % CI [1.137–2.477]). We detected that as a work shift in a "red" zone became longer, risks of SARS-CoV-2 infection for medical personnel grew from 1.6 to 3.9 times (*RR* = 1.618, 95 % CI [1.154–2.269]; *RR* = 3.946, 95 % CI [2.947–5.283]).

The total risks of SARS-CoV-2 infection were insignificant (*RR* = 1.02, 95 % CI

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[10] SanPiN 3.3686-21. Sanitarno-epidemiologicheskie trebovaniya po profilaktike infektsionnykh boleznei (utv. postanovleniem Glavnogo gosudarstvennogo sanitarnogo vracha RF ot 28 yanvarya 2021 goda № 4) [SanPiN 3.3686-21. Sanitary-epidemiological requirements to communicable diseases prevention (approved by the RF Chief Sanitary Inspector on January 28, 2021 No. 4)]. Razdel XLIV. Profilaktika infektsii, svyazannykh s okazaniem meditsinskoi pomoshchi [Section XLIV. Prevention of healthcare-associated infections]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/573660140 (February 03, 2022) (in Russian).

[1.00–1.04]) in medical organizations that provided scheduled medical aid to population. At the same time, some specific risk factors were rather significant, including, for example, a work shift lasting from 6 to 8 hours (*RR* = 1.567, 95 % CI [1.433–1.713]), use of PPE with incomplete protection provided for the eyes and respiratory organs (*RR* = 1.471, 95 % CI [1.347–1.606]), workers' age being 65 years and older (*RR* = 1.184, 95 % CI [1.068–1.314]), failure to use PPE when treating a patient infected with COVID-19 (*RR* = 1.169, 95 % CI [1.031–1.325]). Some non-occupational factors also exerted their influence on risks of SARS-CoV-2 infection for this occupational group, in particular, contacts with close friends or relatives as well as neighbors who were infected with COVID-19 (*RR* = 1.13, 95 % CI [1.04–1.228]).

Global SARS-CoV-2 spread has again highlighted that it is vital to protect health workers when they have to deal with both new and returning infectious agents able to induce an epidemic or even a pandemic.

Our research results should be considered when organizing work and anti-epidemic activities in infectious diseases hospitals and medical organizations providing scheduled medical aid to population. It specifically concerns providing health workers with PPE in these medical institutions and duration of their work shifts. Prevention of infection spread among medical personnel should rely on the risk-based approach and consider risks of exposure to not only known pathogens given the ongoing COVID-19 pandemic but also probable new epidemic threats in future.

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ANALYSIS OF RISK FACTORS CAUSING HEALTH DEFICIENCY AND ITS INDICATORS IN CHILDREN WITH CONGENITAL HEART DISEASES TWO YEARS AFTER RADICAL SURGERY

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Our research goal was to analyze risk factors that could cause health disorders in children two years after a radical heart surgery. It is vital for optimizing diagnostics and predicting negative outcomes of surgical treatment for congenital heart diseases (CHD) using data taken from anamnesis vitae and genetic indicators.

We performed prospective cohort monitoring of 89 children with CHD during two years starting from the moment they had a radical heart surgery. The study design included the following stages: quality of life assessment using "Cardiac Module" in the Pediatric Quality of Life Questionnaire (USA, 2001); collecting data to create anamnesis vitae by questioning; identifying types of polymorphisms of xenobiotic biotransformation genes, inborn and adaptive immunity genes participating in embryogenesis of the cardiovascular system; logistic regression incremental multifactorial analysis of independent variables in anamnesis vitae, peculiarities of a radical surgery, health indicators prior to an operation, as well as polymorph variants of the examined genes with dependent variants: types of functioning and the complex integral health indicator two years after surgical treatment.

*The complex integral health indicator and indicators of physical functioning were significant ones in 2-year dynamics of patients' health after surgical treatment for CHD. These indicators reflected children's quality of life long time after a radical heart surgery. Health deficiency and impaired quality of life two years after a radical heart surgery was associated with HLADRB1*04, HLADRB1*11, HLADRB1*12, HLADRB1*13 alleles and the major allele T in the polymorph variant of CYP1A1 T/C (rs1048943) gene. Influence exerted by these alleles on quality of life long time after a radical heart surgery is determined by long-term toxic inflammation in an operated heart. CHD severity, an age when a radical surgery was performed, as well as unsatisfactory material benefits and living conditions are common medical and social risk factors that cause health deficiency and impaired quality of life long time after a radical heart surgery.*

Keywords: *CYP1A1, HLADRB1, congenital heart diseases, quality of life, risk factors, radical heart surgery, complex integral health indicator, indicators of physical functioning.*

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Over the last decade, considerable changes have occurred in both domestic and world cardiac surgery. They make it possible to perform surgical treatment of congenital heart diseases (CHD) during the first year of a child's life; critical and severe CHD can be treated even in the neonatal period[1]. Advanced surgery technologies applied in the early postnatal period gave an opportunity to achieve a substantial decrease in neonatal mortality including deaths due to severe and critical CHD. An open-heart surgery involving artificial circulation remains the gold standard of surgical treatment for CHD. A radical heart surgery is what complex CHD treatment is based on since it corrects anatomic defects in the cardiovascular system most effectively. At the same time, a following drug therapy and rehabilitation provided to children with CHD compensate for residual hemodynamic and functional disorders in the cardiovascular system. Many studies have established that it is impossible to reach full compensation regarding the cardiovascular system functioning in children who have undergone a radical heart surgery [1]. This influences other health indicators, for example, retarded physical development [2]. Mussato with colleagues showed that speech disorders developed in 56 % of children with CHD after surgical intervention and 21 % of them had certain cognitive disorders [3].

We should remember that *Health* is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity[2]. Therefore, we can state that children have certain health deficiency after a radical heart surgery in a remote post-operation period. If we return to how the World Health Organization defines health, we can speak about physical, emotional, social and mental functioning as integral components of an individual's health. Accordingly, each of these functioning types can be impaired and this requires specific rehabilitation impacts. A vital task that should be solved within individual rehabilitation after a radical heart surgery to treat CHD is to detect disorders in a certain type of functioning.

Another important issue is to create an individual rehabilitation program after a radical heart surgery performed to treat CHD. To do that, it is necessary to predict risks of health deficiency, both in general and as per specific types of functioning in particular, in a remote post-operation period. Health deficiency can have several predictors; they can be both constitutional (genetic) markers and anamnesis vitae indicators (social factors related to a patient's family and individual medical factors) since their associations with CHD have been described in many studies [4–6].

We would like to pay special attention to immune response genes (*HLA-DRB1*) and signaling membrane receptors of inborn immunity (*TREM1*) that can participate in CHD induction, both as inflammatory embryopathies and maintaining inflammation in the cardiovascular system prior to and after the pathology has been treated surgically [7].

Health deficiency in a remote period after a radical heart surgery can occur due to a long-term immune-inflammatory process in the cardiovascular system or, on the contrary, due to frequent respiratory infections as signs of immune deficiency.

Given all the aforementioned, we set our research goal as optimizing diagnostics and predicting negative health outcomes in children two years after a radical heart surgery that was performed to treat CHD. This goal should be achieved by analyzing risk factors with the use of anamnesis vitae indicators and genetic markers.

Materials and methods. To solve the set tasks, we performed a prospect cohort study at the Research Institute for Complex Issues of Cardiovascular Diseases and the Kemerovo Regional Clinical Cardiology Dispensary named after academician L.S. Barbarash. A test group was created in the children division of the latter healthcare institution in 2019–2020 by overall inclusion

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[1] Bokeriya L.A., Gudkova R.G. Serdechno-sosudistaya khirurgiya – 2014. Bolezni i vrozhdennye anomalii sistemy krovoobrashcheniya: ezhegodnyi stat. sbornik [Cardiovascular surgery – 2014. Diseases and congenital anomalies of the circulatory system: annual statistical collection]. Moscow, 2015, 226 p. (in Russian).

[2] Constitution of the World Health Organization. *WHO*, 2006, 45th ed., 20 p. Available at: https://www.afro.who.int/sites/default/files/pdf/generic/who_constitution_en.pdf (October 15, 2021).

of all patients who had a radical heart surgery with artificial circulation in their case history.

We applied the following criteria to include patients into the test group within our prospect study:

- a patient was aged from 0 to 15 years inclusively at the moment of a surgery;
- a patient suffered from a congenital heart disease that required radical surgical intervention with artificial circulation;
- an entry was made into the CHD register as per anamnesis vitae and instrumental research methods.

We used the following criteria for excluding a patient:

- a congenital heart disease that required an x-ray endovascular surgery;
- a congenital heart disease that required palliative surgical intervention with artificial circulation;
- genetic chromosome diseases;
- no entry into the CHD register.

Our prospective study group consisted of 89 children (44 girls and 45 boys). CHD were distributed as per nosologic groupings in the way shown in Table 1.

Our analysis of the children's anamnesis vitae established that one third of them were born by cesarean section; more than a half of the children received formula feeding instead of breast milk; each fifth child had neonatal pneumonia and conjugated jaundice (Table 2). Approximately 80 % of the children did not receive all the necessary vaccinations. More than a half of the children were assigned into the category "get sick too often with illnesses lasting for a long time" according to the criteria developed by V.Yu. Albitskii and A.A. Baranov (1985). Each fifth child had concomitant diseases of the central nervous system and on average approximately 8 % of the patients with CHD had concomitant diseases of the genitourinary system and gastrointestinal tract as well as atopic dermatitis.

Infectious exacerbations occurred in 35 children (39.33 %) in the early period after a radical heart surgery and eight children (8.99 %) had non-infections exacerbations. Infectious exacerbations included long-term (more than 5 days) fever, pneumonia, hydrothorax, hydropericardium, pericarditis, and some septic symptoms. Non-infectious exacerbations that developed after CHD surgical treatment included heart rhythm and conduction disorders accompanied with lower ejection function, convulsions, and diaphragmatic cupula paresis.

Complex health assessment. We assessed health of all the examined patients concerning their physical, psychoemotional, social and mental functioning. We also estimated their intelligence quotient (IQ) and language development prior to surgical treatment for CHD and 2 years after it.

Table 1

CHD distributed as per nosologies

CHD nosology	An absolute number of children	Specific weight, %
Congenital malformations of cardiac septa	31	34.83
Ventricular septal defect	14	15.73
Septal defects	4	4.5
Atrioventricular septal defect	3	3.37
Tetralogy of Fallot, congenital malformations of great arteries	15	16.9
Single ventricle heart	6	6.74
Coarctation of the aorta	5	5.62
Congenital stenosis of aortic valve	3	3.37
Coarctation of the aorta and ventricular septal defects combined, hyperplasia of aorta	3	3.37
Total anomalous pulmonary venous connection	2	2.25
Partial anomalous pulmonary venous connection	1	1.12
Atresia of pulmonary artery type I	1	1.12
Ebstein anomaly	1	1.12
Total	89	100

Table 2

The group profile of the examined children

Data from anamnesis vitae	Absolute number	Specific weight, %
Born by cesarean section	29	32.58
Breast-fed only up to 6 months of age	60	67.42
Early neonatal diseases:		
Pneumonia	17	19.1
Conjugated jaundice	19	21.3
Vaccination:		
Complete	18	20.2
Incomplete	71	79.8
Frequency of respiratory infections during the first year of life (more than 2 times)	29	32.58
Frequency of respiratory infections during the second and third year of life (ARI, otitis, bronchitis, pneumonia)	74	83.15
Allergic dermatitis	5	5.6
GIT diseases* after the first year of life (GERD**, gastritis, duodenitis)	5	5.6
GUS diseases*** (UTI****)	8	8.9
Diseases of the nervous system	22	24.7
Conduction defeats in anamnesis (transitoryAB-blockade, 1–2 degree)	12	13.48

Note: *GIT is the gastrointestinal tract, **GERD is gastroesophageal reflux disease, ***GUS is the genitourinary system, ****UTI is urinary tract infection.

Quality of life is a significant indicator in assessing a patient's health. We estimated it as per questioning results produced by using psychometric tests and certain questionnaires such as Pediatric Quality of Life Questionnaire, PEDsQL 4.0 (J.W. Varni et al., USA, 2001). They are aimed at estimating physical functioning (PH), emotional functioning (EF), social functioning (SF), school functioning (ScF), mental health and the complex integral health indicator [8, 9].

We used "Cardiac Module" of the PEDsQL 4.0 in our study. Two parallel forms of the questionnaire, one filled in by a child (self-report) and the other filled in by a parent (proxy-report), made it possible to objectively estimate the children's quality of life.

The testing completed, all the data were coded into Quality of Life scores as per the copyrighted procedures (Multinational Center for Quality of Life Research) provided by the authors of the applied questionnaire. We applied the invert correlation meaning the lower a score was, the higher a percent of functioning was. We accepted the following scale. One score corresponded to 100–76 % or perfect functioning; 2 scores were equal to 75–51 % or good functioning; 3 scores were equal to 50–26 % or satisfactory functioning; and 4 scores were equal to 25–0 % or poor functioning. The estimates were made for each type of functioning, physical, psychoemotional, social and mental; all these types were estimated by a parent, a patient (child) and a doctor.

The children's physical, psychoemotional, social and mental functioning as well as their intelligence quotient (IQ) and language development were estimated starting from a certain age. Table 3 provides data on an age when estimates of a specific functioning type started as well as on a number of children who participated in these estimates.

Samples of peripheral blood were taken from all the examined children to determine their immune genetic types.

We identified types of polymorphisms of xenobiotic biotransformation genes, inborn and adaptive immunity genes two years after surgical treatment for CHD. It was done to analyze a role played by constitutional factors in determining health deficiency in the examined children.

Molecular and genetic research. We examined genome DNA extracted from peripheral blood leukocytes. Genome DNA was obtained by using phenol-chloroform extraction according

Table 3

Age limits and children samplings to estimate their physical, psychoemotional, social and mental functioning as well as intelligence quotient (IQ) and language development

Estimate	Age	A number of children participating in estimations
Physical functioning	Older than 2 years	76
Psychoemotional functioning	Older than 5 years	51
Social functioning		
Mental functioning		
Intelligence quotient (IQ)		
Language development		

to the conventional procedure. Blood samples were taken from all the participants prior to a heart surgery. Blood was taken from the ulnar vein into a tube with Ethylenediaminetetraacetic acid (EDTA, Becton Dickinson Vacutainer, USA). Next, blood aliquots of 700 µl were put into 1.5-ml eppendorf tubes (Axygen, USA) with tightly locking caps. All the samples of biological materials were marked properly and then stored under -80ºC until the research started. Concentrations of extracted DNA were estimated using NanoDrop ND-2000C spectrophotometer (Thermo, USA). Our choice on single-nucleotide polymorphic sites for molecular genotyping was determined by localization in the following genes: those coding enzymes of xenobiotics biotransformation (*GSTP, CYP1A2, CYP1A1*), participating in determination of heart development (*CRELD1, GATA6*), signaling membrane (*TREM1*) and intracellular (*NOTCH1*) receptors of inborn immunity and a classic immune response gene (*HLADRB1*). Minor allele frequency for SNP did not exceed 5 % in the population according to data provided by HapMap.

We resorted to open research data[3] to estimate expected or proven molecular outcomes in determining CHD occurrence for selected SNP. Overall, we selected 20 gene polymorphisms that are given in Table 4.

Genotyping was performed by using PCR with TaqMan probes (Thermo Fisher Scientific, USA) on ViiA™ 7 Real-Time PCR System (Life Technologies, USA).

We analyzed *HLA-DRB1* by the polymerase chain reaction method considering the results in real time. The analysis was accomplished with kits manufactured by "DNA-technologies" company (Russia) and with DT-96 detector amplifier manufactured by the same company according to the procedures established by the manufacturer. Genotyping quality control was performed by repeated genotyping of 10 % of randomly selected samples. We focused on analyzing frequencies of 14 *HLA-DRB1* gene alleles.

Statistical analysis. We analyzed our research results with Statistica for Windows software package produced by StatSoft Inc., Version 10.0, and MedCalc 17.5.3.

Within the present study, distribution of each quantitative indicator was examined by using Kolmogorov – Smirnov test and Shapiro – Wilkes test. Quantitative data were given as median values (Me) as well as the 25th and 75th quartiles (Q25 – UQ and Q75 – LQ). We compared non-parametric indicators by using Wilcoxon test; pair comparisons were accomplished by using Mann – Whitney test. Statistical significance of differences between qualitative indicators was determined by using chi-square (χ^2) with Yates' correction. We used Spearman's correlation coefficient to determine how strong correlations were between the examined indicators. Those indicators with *p*-level not exceeding 0.05 were considered statistically significant; that is, a zero hypothesis was abandoned when an

[3] SNPedia. Available at: https://www.snpedia.com/index.php/Rs (October 20, 2021); dbSNP. *National Library of Medicine*. Available at: https://www.ncbi.nlm.nih.gov/snp/rs (October 20, 2021).

Table 4

Characteristics of the examined gene polymorphisms

Gene	SNP type	SNP ID	Amino acid replacement	Localization on a chromosome as per GRCh.p12*	Nucleotide replacement
GSTP1	Upstream variant	rs6591256	-	Chr11.67582428	A/G
GSTP1	Upstream variant	rs17593068	-	Chr11.67583461	G/T
GSTP1	Intron variant	rs1871042	-	Chr11.67586373	C/T
GSTP1	Missense variant	Rs1695	Missense mutation Ile105Val	Chr11.67585218	A/G
CYP1A1	Missense variant	rs1048943	Missense mutation Ile462Val	Chr15.74720644	T/C
CYP1A2	Intron variant	rs762551	-	Chr15.74749576	C/A
CRELD-1	Missense variant	rs73118372	Missense mutation Met383Arg	Chr3.9943989	T/C
CRELD-1	Intron variant	rs9878047	-	Chr3.9943773	T/C
CRELD-1	Synonymous variant	rs3774207	Amino acid codon H [CAC] > H [CAT]	Chr3.9943972	C/T
GATA6	Intron variant	rs10454095	-	Chr18.22197478	T/C
NOTCH1	Intron variant	rs13290979	-	Chr9.136531182	A/G
TREM1	Intron variant	rs1817537	-	Chr6:41276829	C/G
TREM1	Intron variant	rs3804277	-	Chr6.41277434	C/T
TREM1	Intron variant	rs6910730	-	Chr6.6:41278895	A/G
TREM1	Upstream variant	rs7768162	-	Chr6.41276829	A/G
TREM1	Downstream Variant	rs2234246	-	Chr6.41276002	C/T
TREM1	Downstream transcript variant	rs4711668	-	Chr6.41278735	C/T
TREM1	Upstream variant	rs9471535	-	Chr6.41287752	C/T
TREM1	Missense variant	rs2234237	Missense mutation Thr25Ser	Chr6.41282728	A/T

Note: *GRCh38.p12 is the Genome Reference Consortium for checking SNP localizations.

error was less than 5 %. This fully conforms to the conventional standards applied in biomedical research[4].

We created mathematical models to predict how probable risks of health deficiency were two years after surgical treatment for CHD and to classify these risks. To do that, we applied multiple logistic regressions, including a stepwise variant for four-score categories of a dependent variable; classification trees; ROC-analysis. Classification trees made it possible to identify significant predictors and rank them. ROC-analysis enabled estimating significance of an obtained equation that was used to calculate probability of health deficiency two years after surgical treatment for CHD. This analysis included the following parameters: AUC (area under curve) described diagnostic value of an indicator (0.9–1.0, perfect; 0.8–0.9, very good; 0.7–0.8, good; 0.6–0.7, average; 0.6 and lower, unsatisfactory)), factor sensitivity (Se) and specificity (Sp).

Results and discussion. Table 5 provides data on distribution of scores that estimated functioning (PD) as per different types of health estimates made by a doctor, a patient, and a parent.

We did not detect any significant differences between estimates made by a doctor, a patient, and a parent. We additionally performed a correlation analysis between estimates of various functioning types made by parents, patients, and doctors two years after a radical heart surgery. The analysis revealed highly authentic correlations (Table 6).

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[4] Lakin G.F. Biometriya: uch. posobie dlya biol. spets. vuzov, 4-e izd., pererab. i dop. [Biometry: the manual for biological specialties in higher education, the 4th edition, revised and supplemented]. Moscow, Vysshaya shkola Publ., 1990, 352 p. (in Russian).

Table 5

Distribution of functioning scores (PD) as per different types of health estimates given by a doctor, a patient, and a parent

Indicators	1– Doctor			2 – Patient			3 – Parent			*p* 1,2	*p* 1,3	*p* 2,3
	Me	25 % PQ	75 % PQ	*Me*	25 % PQ	75 % PQ	*Me*	25 % PQ	75 % PQ			
PD phys.	2.66	1.75	3.56	2.67	1.66	3.69	2.64	1.65	3.63	-0.04	0.04	0.08
PD emot.	2.51	1.70	3.31	2.46	1.61	3.31	2.49	1.69	3.30	0.13	0.04	-0.09
PD soc.	2.44	1.55	3.33	2.57	1.73	3.42	2.48	1.63	3.32	-0.34	-0.09	0.26
PD mental	2.39	1.32	3.46	2.41	1.53	3.29	2.46	1.57	3.35	-0.04	-0.16	-0.13

Note: PD is a functioning score: phys means physical; soc, social, emot, emotional; p is the significance level.

Table 6

Correlations between score estimates made by doctors, children, and parents two years after a radical heart surgery

Indicators	Spearman *R*	*t* ·(*n*-2)	*p*-value
PD phys. doctor & PD phys. patient	0.967	29.948	0.000
PD emot. patient & PD emot. parent	0.848	12.574	0.000
PD soc. doctor & PD soc. patient	0.927	19.449	0.000
PD mental doctor & PD mental patient	0.916	17.928	0.000
PD phys. patient & PD phys. parent	0.964	28.646	0.000
PD emot. patient & PD emot. parent	0.840	12.200	0.000
PD soc. patient & PD soc. parent	0.837	12.045	0.000
PD mental patient & PD mental parent	0.849	12.656	0.000
PD phys. doctor & PD phys. parent	0.933	20.475	0.000
PD emot. doctor & PD emot. parent	0.836	11.985	0.000
PD soc. doctor & PD soc. parent	0.832	11.828	0.000
PD mental doctor & PD mental parent	0.769	9.469	0.000

Note: PD is a functioning score: phys. means physical; soc., social, emot., emotional; *p* is the significance level, *R* is Spearman's correlation coefficient.

Given that, we applied integral indicators in our logistic regressions (a simple mean of estimates made by parents, children, and doctors) for each type of functioning (physical, emotional, social and mental) as well as for the complex integral health indicator.

We searched for associations between independent factors including anamnesis vitae, circulatory disorders prior to surgical treatment, peculiarities of a radical heart surgery, health indicators prior to a radical heart surgery as well as polymorphisms of the examined genes, on one hand, and dependent variables including integral indicators of various functioning types and the complex integral health indicators, on the other hand. This done, we established several significant associations shown in Tables 7 and 8.

Table 7 provides data on statistically significant associations between independent variables related to anamnesis vitae, circulatory disorders prior to surgical treatment, peculiarities of a radical heart surgery, health indicators prior to a radical heart surgery as well as polymorphisms of the examined genes and the integral indicator of physical functioning two years after surgical treatment for CHD.

Obviously, statistically significant associations occurred only for the genetic markers (*HLA-DRB1*11* and *HLA-DRB1*12)*. Both these alleles code the same serological specificity, HLA-DR5, and this indicates that HLA II class molecules as antigen-representing receptors have a special role in determining physical functioning two years after surgical treatment for CHD.

We can assume that an immune phenotype determines phenotypic manifestations of one's health. We established a positive association with immune-inflammatory diseases, such as unspecified spondyloarthritis, juvenile arthritis and antiphospholipid syndrome both for HLA-DR5 antigen and *HLA-DRB1*12* allele [10, 11]; and simultaneously a positive association was established between *HLA-DRB1*11* allele and autoimmune thyroid disease [12]. Possibly, subclinical immune inflammation in children with *HLA-DRB1*11* and *HLA-DRB1*12* could become apparent through inhibited physical functioning. Accordingly, high frequency of *HLA-DRB1*12* among children with CHD can result in its higher relative frequency among children with poor physical functioning. In any case, HLA-DR5 phenotype has positive associations with poor physical functioning two years after a radical heart surgery.

We did not establish any significant associations with any other independent variables for other types of functioning estimated two years after a radical heart surgery.

We estimated the complex integral health indicator as a simple mean of all the integral indicators of various types of functioning (physical, emotional, social and mental) two years after a radical heart surgery. We similarly examined associations between the complex integral heath indicator and independent variables related to anamnesis vitae, circulatory disorders prior to surgical treatment, peculiarities of a radical heart surgery, health prior to a radical heart surgery as well as polymorphisms of the examined genes. Table 8 provides the results.

Obviously, the complex integral health indicator had a positive association with CHD score as per its severity and criticality, family structure and *HLA-DRB1*13* allele two years after a radical heart surgery. A negative statistically significant association was established for material benefits. These associations indicate that the more critical a CHD is, the poorer results are produced by two-year rehabilitation with a higher complex integral indicator that describes poor quality of one's health.

When it comes down to family structure, we should note that one score was assigned to a two-parent family; two scores, a large two-parent family; three scores, a single-parent family; four scores were assigned to children who did not have parents or family (and lived in an orphanage). Given this scoring system, the association with this variable indicates that the higher the score describing family issues is, the higher the score is that describes poor quality of one's health. Accordingly, children from orphanages had the poorest quality of life two years after surgical treatment for CHD.

Table 7

Results produced by the logistic regression stepwise multifactorial analysis

Indicators	β-coefficient	Standard error of β-coefficient	B-coefficient	Standard error of B-coefficient	*p*-value
Intercept			1.969	0.143	0.000
*HLA-DRB1*12*	0.343	0.146	0.874	0.372	0.025
*HLA-DRB1*11*	0.329	0.147	0.399	0.178	0.032

Note: Intercept is a free coefficient in logistic regression.

Table 8

Logistic regression stepwise multifactorial analysis of independent variables

Indicators	β-coefficient	Standard error of β-coefficient	B-coefficient	Standard error of B-coefficient	*p*-value
Intercept			1.711	0.206	0.000
CHD score as per severity and criticality	0.633	0.123	0.065	0.013	0.000
Material benefits	-0.531	0.120	-0.559	0.127	0.000
*HLA-DRB1*13*	0.605	0.133	0.722	0.159	0.000
Family structure	0.428	0.132	0.450	0.138	0.003

Note: Intercept is a free coefficient in logistic regression.

Table 9

Descriptive statistical characteristics and boundaries of "poor" and "good" score estimates for the complex integral health indicator two years after CHD surgical treatment

Indicator	Average	Median	25-th percentile	75-th percentile
The complex integral health indicator two years after surgical treatment for CHD	2.276	2.125	2.000	2.500
Indicator	Below or equal to	Result (a score for regression)	Above or equal to	Result (a score for regression)
The complex integral health indicator two years after surgical treatment for CHD	2.000	"good" (0 scores)	2.250	"poor" (1 score)

The score estimate given to material benefits was linked to the official Russia's Minimum Wage (RMW) per each family member. If wages per one family member were lower than RMW, then such a family was considered poor (0 scores); if the indicator was equal to RRMW or higher, a family was considered wealthy (1 score). Accordingly, the established negative association with material benefits indicates that the lower family incomes are, the higher the score is that describes poor quality of one's health two years after surgical treatment for CHD.

Other mechanism can be associated with HLA-DR6 molecular itself that is coded by *HLA-DRB1*13* allele. The molecule was found to have weal antigen properties as far back as in 80ties last century. They can become apparent through an ineffective immune response to environmental antigens. That is, this allele and a membrane receptor with HLA-DR6 isotype are associated with functional Ir-associated immune deficiency [13]. General poor quality of health can become obvious exactly due to weak immunity phenomenon.

Our next step was to develop methodical approaches to complex diagnostics and prediction of health disorders in children who had a radical heart surgery due to CHD. To do that, we used a multiple logistic regression with its major dependent variable being occurrence or absence of health deficiency in children two years after surgical treatment for CHD.

All the aforementioned data indicate that the complex integral health indicator describes children's health in a remote post-operation period. We calculated a simple mean and median value of the complex integral health indicator as well as its percentile and standard deviations. These descriptive statistical indicators gave grounds for determining a boundary between "poor" and "good" estimates for the complex integral health indicator in a remote post-operation period. The data are provided in Table 9.

Therefore, we introduced boundaries of "poor" and "good" results of the complex health assessment two years after a radical heart surgery to treat CHD. This made it possible to create a multiple logistic regression with a binary dependent variable ("either a "good" or a "poor" complex integral health indicator) that was subsequently used to build a logarithmic equation for predicting a risk of a certain event. Accordingly, "a poor" complex integral health indicator was taken as health deficiency two years after surgical treatment for CHD.

Table 10 provides results produced by the logistic regression for the complex integral health indicator two years after surgical treatment for CHD.

Obviously, we established many significant associations for the complex integral health indicator that described good health or its deficiency two years after surgical treatment for CHD with simultaneous significant dimensionality of a free coefficient in logistic regression (intercept). This indicates an expected event can be predicted quite effectively.

We should note that β-coefficients show relative influence exerted by a predictor on the dependent variable whereas B-coefficients show prognostic value of a predictor.

Table 10

Results produced by the logistic regression for the complex integral health indicator

Regression of the dependent variable: "poor" complex integral health indicator – 1 / "good" – 0	β-coefficient	Standard error of β-coefficient	B-coefficient	Standard error of B-coefficient	*p*-value
Intercept			-0.759	0.350	0.041
Family structure	0.524	0.108	0.541	0.112	0.000
Material benefits	-0.615	0.103	-0.634	0.106	0.000
CHD score as per severity and criticality	0.705	0.127	0.071	0.013	0.000
An age when a radical heart surgery was performed	0.424	0.099	0.072	0.017	0.000
*CYP1A1 T/C rs1048943*T*	0.215	0.094	0.396	0.174	0.033
*HLA-DRB1*04*	0.303	0.095	0.334	0.105	0.004
Living conditions	0.443	0.112	0.465	0.117	0.001
*HLA-DRB1*13*	0.457	0.113	0.534	0.132	0.001
*HLA-DRB1*01*	-0.223	0.098	-0.258	0.113	0.033

Note: Intercept is a free coefficient in logistic regression.

Given that, we can see that logistic regression analysis made it possible to estimate how probable a risk of a certain event was. In our case, this event was health deficiency that occurred two years after surgical treatment for CHD. B-coefficients of each significant predictor were included into a formula used for calculating this risk.

In this case, the analyzed risk of health deficiency two years after surgical treatment for CHD is calculated as per the following equation:

$$Y = (\mathrm{EXP}\ (Z) / (1 + \mathrm{EXP}\ (Z))) \cdot 100\ \%,$$

where

$$Z = (-0.759 + (X_1 \cdot 0.541) - (X_2 \cdot 0.634) + (X_3 \cdot 0.071) + (X_4 \cdot 0.072) + (X_5 \cdot 0.396) + (X_6 \cdot 0.334) + (X_7 \cdot 0.465) + (X_8 \cdot 0.534) - (X_9 \cdot 0.258)),$$

where

Y is a probable risk of health deficiency two years after CHD surgical treatment (the coefficient showing a probable risk of health deficiency, %);

-0.759 is a free coefficient in logistic regression;

X_1 is family structure (two-parent family, 1; large two-parent family, 2; one-parent family, 3; children from orphanages, 4);

X_2 is material benefits (poor families with incomes lower than RMW per one family member, 0; wealthy families with incomes per one family member being equal to RMW or higher, 1);

X_3 is a CHD score as per its severity, criticality and frequency (scores are given in Table 11);

X_4 is an age when a radical heart surgery was performed (years);

X_5 is allele T presence in CYP1A1 T/C, rs1048943 gene polymorphism (absence, 0; presence in heterozygote, 1; presence in homozygote, 2);

X_6 is allele 04 presence in HLADRB1 gene polymorphism (absence, 0; presence in heterozygote, 1; presence in homozygote, 2);

X_7 is living conditions (excellent, 1; good, 2; bad, 3; exceptionally bad, 4);

X_8 is allele 13 presence in HLADRB1 gene polymorphism (absence, 0; presence in heterozygote, 1; presence in homozygote, 2);

X_9 is allele 01 presence in HLADRB1 gene polymorphism (absence, 0; presence in heterozygote, 1; presence in homozygote, 2).

Scores for various nosologies within the CHD grouping were assigned considering three criteria, namely, their severity, criticality and frequency that made a radical heart surgery necessary (Table 11).

The equation based on the logistic regression for calculating Y (a probability of health deficiency two years after surgical treatment for CHD) has a logarithmic nature. This means risk rates fall within the range from 0 to 100 %. Thus, if Y tends to 50 %, then a risk of

Table 11

CHD scores for logistic regression considering their severity, criticality and frequency

Nosology	Score for logistic regression
Septal defects and their combination	1
Coarctation of the aorta	2
Heart valve disease (MV, TV)	2
Anomalies of great arteries	3
Coarctation of the aorta and ventricular septal defects combined, hyperplasia of aorta	4
Congenital stenosis of aortic valve	4
Tetralogy of Fallot, congenital malformations of great arteries	5
Atrioventricular septal defect	5
Partial anomalous pulmonary venous connection	5
Ebstein anomaly	6
Total anomalous pulmonary venous connection	7
Atresia of pulmonary artery type I	8
Single ventricle heart	9

Note: TV is tricuspid valve; MV is mitral valve.

this expected event is equally probable; if *Y* tends to zero, then a risk is unlikely; and on the contrary, if *Y* tends to 100 %, then health deficiency two years after surgical treatment for CHD is highly likely. Contributions made by all the predictors to health deficiency two years after a radical heart surgery were statistically significant ($p < 0.001$).

All the predictors for likelihood of health deficiency two years after surgical treatment for CHD can be estimated in a period prior to and after a surgery thereby establishing how probable this health deficiency is as well as creating an individual rehabilitation program for a specific patient to be applied during a post-operation period.

CHD severity and criticality (Table 11) and an age when a radical heart surgery required to treat it was performed were two basic predictors of health deficiency in a remote post-operation period. The established positive association indicated that the more severe and more critical a CHD was, the poorer quality of life would be expected in a remote post-operation period.

On the other hand, the positive association with an age when a radical heart surgery was performed indicated that the older a patient was, the poorer quality of life would be expected in a remote post-operation period. An age when a radical heart surgery should be performed on children with septal CHD remains disputable and requires separate research. Within this study, most patients had septal CHD and an age when a surgery was performed became a predictor of health deficiency two years after surgical treatment for CHD. Therefore, we can assume that septal sporadic non-syndromic CHD should be treated with a radical surgery at a younger age. This will help not only treat CHD more effectively but also rehabilitate a patient better after a radical heart surgery. At the same time, it is necessary to determine the youngest possible age for such surgeries bearing implantation materials in mind.

A role that belongs to each identified genetic predictor of health deficiency in a remote post-operation period is associated with its influence on CHD occurrence and effects that prolong immune inflammation in the heart after a surgery. In particular, *HLA-DRB1*04* allele that has strong correlations with systemic and organ-specific autoimmune and autoinflammatory diseases can determine elevated inflammation potential in such children [14]. On the contrary, *HLA-DRB1*13* allele that is associated with immune deficiency determines immune paresis to macro- and microenvironment antigens [15]. As we have already mentioned, immune deficiency associated with *HLA-DRB1*13* (HLA-DR6) can become obvious through frequent respiratory diseases and this will lead to deteriorating children's quality of life in a remote period after surgical treatment for CHD.

The established negative association with *HLA-DRB1*01* allele indicates that the more frequent this allele is, the less frequent health deficiency is two years after surgical treatment for CHD. That is, this allele is a predictor of health deficiency and poor quality of life in a remote period after surgical treatment for CHD. *HLA-DRB1*01* allele is a dominant one in populations across the world [13] with its share reaching 25 %. This outlines its property to determine people's immune resistance to macro- and micro-environmental factors. In this case, this allele is a marker showing children's good adaptation capabilities after a radical heart surgery.

Homozygosis as per major (wild type) allele T in *CYP1A1 T/C* (rs1048943) gene polymorphism determines elevated oxidation of xenobiotics and endobiotics with occurring adducts [16]. They stimulate an immune response and autoinflammatory reactions due to, among other things, arachidonic acid participating in metabolism [17]. Thereby a toxic-inflammatory process is activated also through this gene polymorphism. Overall, these gene polymorphisms will make for manifestation of a prolonged inflammatory response against the background of effector immune reactions being in deficiency. Frequent respiratory diseases in such children, which we mentioned earlier [18], result from immune genetic determination. Health deficiency develops in such children due to, among other things, prolonged subclinical inflammation [19, 20].

Contribution made by social factors to health deficiency in a remote post-operation period is associated with direct and indirect effects produced by them on effectiveness of rehabilitation and compliance-therapy. Poor living conditions and material benefits are major adverse factors that impose certain limitations on successful outpatient rehabilitation. Bearing this in mind, children from poor families should be provided with additional inpatient rehabilitation.

We performed ROC-analysis to establish the threshold value of the complex integral health indicator that described risks of health deficiency two years after surgical treatment for CHD and to test the quality of the derived regression equation. The analysis covered a qualitative indicator showing whether health deficiency was present (1) or absent (0) two years after a radical heart surgery, on one hand, and data on *Y* (the coefficient showing likelihood of health deficiency) calculated for each patient. The performed ROC-analysis established a cutoff score for likelihood of health deficiency two years after surgical treatment for CHD. This score equaled 57.66 ($p < 0.001$). The results are shown in Figure 1.

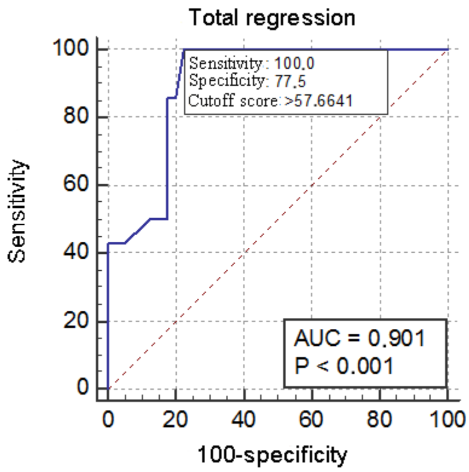

Figure 1. ROC-analysis to establish the threshold value of the complex integral health indicator that described risks of health deficiency two years after surgical treatment for CHD and to determine its diagnostic significance, sensitivity and specificity regarding calculated risks of this expected event

Obviously, the ROC-analysis established that the value of the complex integral health indicator two years after surgical treatment for CHD equal to 57.66 was the boundary between absence and presence of health deficiency. According to this criterion, the derived equation has excellent diagnostic value (AUC = 0.901), specificity (100.0 %) and sensitivity (77.5 %). That is, if we use it to calculate likelihood of health deficiency two years after surgical treatment for CHD, we can determine whether it will or will not occur with precision close to 90 %. Health deficiency will develop in children with the complex integral health indicator calculated for them being equal to or higher than 58 %. Children with this calculated indicator not exceeding 58 % do not have risks of health deficiency in future.

Significance of predictors for health deficiency occurrence two years after surgical treatment for CHD is also proven by estimating them with such a mathematical analysis method as "classification tree". We performed "classification tree" analysis and established two significant classification factors shown in Figure 2.

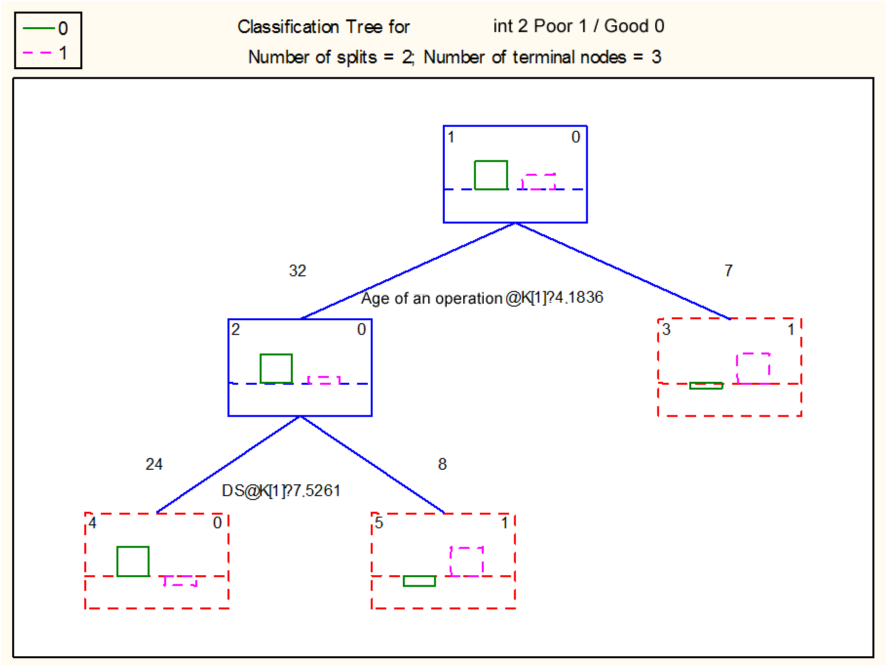

Figure 2. Classification trees of the complex integral health indicator in the second enacted period (qualitative estimate is as follows: 0 scores means "good" and 1 score means "poor") depending on factors related to anamnesis vitae, circulatory disorders prior to surgical treatment, peculiarities of a radical surgery, health prior to a radical surgery, as all as polymorphisms of the analyzed genes: DS is CHD score as per its severity, criticality and frequency (Table 11), @K[1]? is a cutoff score: it equals 4.1836 for an age when an operation was performed and 7.5261 for a CHD score

The primary step in classifying a risk of health deficiency two years after surgical treatment for CHD relies on an age when a radical surgery was performed. The dividing factor is an age of 4 years and 2 months. In case an operation has been performed at an older age, a risk of health deficiency grows; and if it has been performed at a younger age, it decreases. A CHD score (Table 11) as per its severity, criticality and frequency is the next classification factor. A cutoff score equals 7.5. If a CHD score is higher than this value, health deficiency two years after surgical treatment for CHD is highly likely. Accordingly, children who had Tetralogy of Fallot and had an operation at an age younger than 4 years should recover completely two years after a radical heart surgery, as their complex integral health indicator shows.

We ranked the analyzed predictors by using "classification trees' procedure for mathematical analysis as per their significance for occurrence of health deficiency two years after surgical treatment for CHD. Figure 3 provides the results.

It is obvious that a CHD score as per its severity, criticality and frequency (Table 11) is the most significant predictor of health deficiency two years after CHD surgical treatment. Its influence on the dependent variable (presence or absence of health deficiency two years after surgical treatment for CHD) reached 99 %. The second rank place belongs to an age when a radical heart surgery was performed. Accordingly, a functional category (FC) prior to surgical treatment for CHD holds the third rank place. Therefore, the most significant influence on health deficiency in a remote post-operation period was exerted by factors related to a CHD itself (its severity and criticality, a child's age when a radical surgery took place and a functional category during that period). Genetic markers made the smallest contributions according to this rank scale, from 35 to 20 %.

The overall practical conclusion results from calculating the complex integral health indicator two years after surgical treatment for CHD. If this indicator calculated for a child is higher than 58 % in a post-operation period, this child needs mandatory additional inpatient rehabilitation during the first two years after a radical heart surgery.

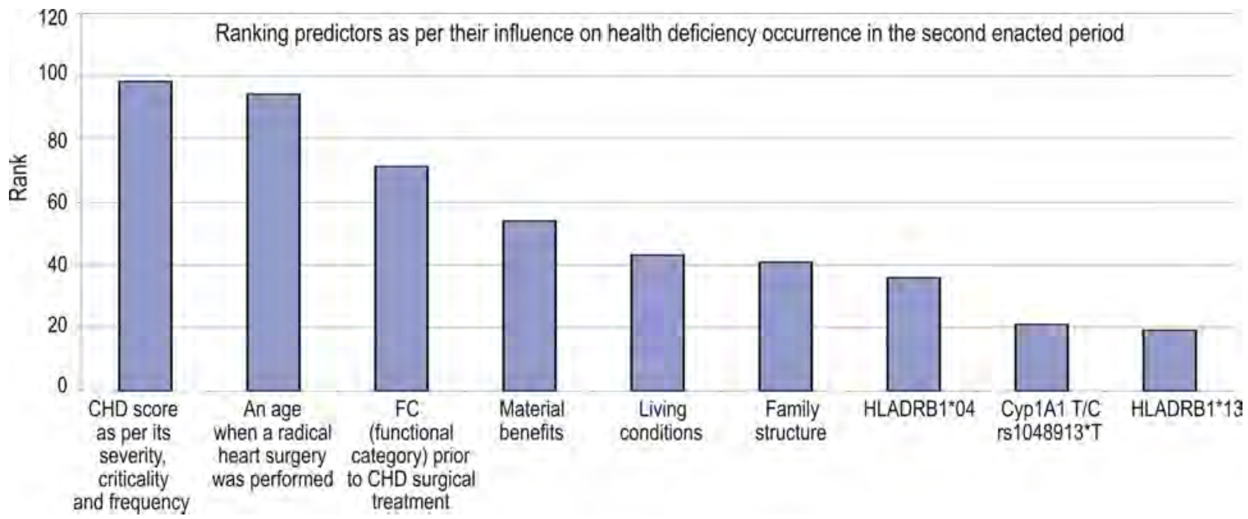

Figure 3. Ranks assigned to the significant predictors of the dependent variable showing health deficiency or its absence (1 / 0) two years after surgical treatment for CHD produced by using “classification trees” procedure for mathematical analysis

Conclusion. Therefore, this study has established that indicators of physical functioning and the complex integral health indicator are among most significant predictors of health deficiency two years after surgical treatment for CHD. These indicators describe children’s quality of life in a remote period after a radical heart surgery.

Health deficiency and impaired quality of life two years after a radical heart surgery are associated with alleles *HLA-DRB1*04, HLA-DRB1*11, HLA-DRB1*12, HLA-DRB1*13* and major allele *T* in *CYP1A1 T/C* (rs1048943) gene polymorphism. Effects produced by these alleles on quality of life in a remote period after a radical heart surgery can occur due to their capability to induce prolonged toxic-inflammatory process in the great after a surgery.

Certain medical and social risk factors also can induce health deficiency and lead to impaired quality of life in a remote period after a radical heart surgery. Among them, we should primarily mention severity and criticality of a CHD itself, an age when a radical operation was performed, as well as poor material benefits and unsatisfactory living conditions. Additional inpatient rehabilitation might become a solution to the problem. It is necessary to provide better rehabilitation for children after surgical treatment for CHD considering the complex integral health indicator with its threshold value being 58 %.

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Competing interests. The authors declare no competing interests.

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Research article

RISK FACTORS OF OCCUPATIONAL BURNOUT IN DENTISTS EMPLOYED BY STATE CHILDREN'S DENTAL POLYCLINICS

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Recently occupational burnout has become more frequent among dentists. Exposure to stress is especially typical for those dentists who work with children.

We identified risk factors that caused developing occupational burnout among dentists employed by state children's dental polyclinics.

We performed comprehensive questioning with 120 dentists participating in it. They all were employed by state children's dental polyclinics in Saint Petersburg. Totally, there were 8 male participants and 112 female ones; their average age was 47.2 ± 11.34 years; average working experience as a dentist, 19.2 ± 13.6 years. The dentists filled in standardized questionnaires including Maslach Burnout Inventory (MBI), RAND SF-36 for assessing quality of life and Work Ability Index. Our study was designed as a "case – control" one. Based on the data of MBI, two groups were created: respondents with occupational burnout by two and three MBI scales (case) and respondents without any occupational burnout (control). To analyze risk factors of occupational burnout, we compared frequency of signs in the groups and calculated odds ratio and their statistical significance.

Several significant risk factors of occupational burnout were identified for this group. They included age >40 years; working experience as a dentist >10 years; presence of chronic diseases and diseases of the musculoskeletal system; impaired physical functioning, general health, and emotional role functioning, as well as the integral quality of life index. Dentists aged 40–49 years have the highest risk of occupational burnout. Working experience that is longer than 20 years creates significantly elevated risks of occupational burnout. Chronic diseases and diseases of the musculoskeletal system as well as impaired quality of life multiply risks of occupational burnout.

These research results can be used to develop activities aimed at preventing occupational burnout among dentists working with children.

Keywords: *dentist, state children's dental polyclinics, children, occupational burnout, Maslach Burnout Inventory, risk factors, quality of life, case–control study.*

Dentists are exposed to various harmful occupational factors including nervous and mental overloads that make for occupational stress development [1–6]. Occupational burnout (OB) is a possible outcome of occupational stress. The conventional model of occupational burnout includes three basic components: emotional exhaustion (EE), depersonalization (DP) and reduced personal accomplishment (RPA)[1].

Occupational burnout is rather widespread among dentists. When dentists suffer from it, it leads to their inability to accomplish work tasks and to be active in life. Instead, dentists with burnout experience apathy and are indifferent to not only occupational performance but also other life values. All this produces negative effects on their mental, physical and social functioning, their work ability (WA), professional relationships with

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colleagues and patients as well as their personal life [7, 8]. Age, working experience, specialization, employment (by a state or a private clinic), chronic diseases as well as such mental qualities as anxiety, sensitivity and introversion are among established risk factors of developing OB in dentists who work with adults [9–12]. Exposure to stress is rather typical for doctors with this specialty and it is especially true for those who work with children [13, 14]. In most cases, specific behavioral reactions a child tends to have and the necessity to communicate with parents result in growing emotional and mental loads a dentist has to bear. Several authors [15, 16] noted that a probability of OB was very high among dentists employed by state children's dental polyclinics. It is necessary to examine risk factors of OB in this occupational group in order to develop relevant activities aimed at timely detection and prevention of this syndrome. There are extremely few works available in scientific literature with their focus on analyzing risk factors of OB development among dentists.

Our research goal was to identify risk factors that caused developing occupational burnout among dentists employed by state children's dental polyclinics.

Materials and methods. Our research concentrated on examining risk factors causing OB development in dentists who worked in state children's dental polyclinics. We questioned 120 dentists with various specialties (children dentists, orthodontists and dental surgeons) from eight state dental polyclinics for children in Saint Petersburg. The sampling was made up of 8 men and 112 women aged from 23 to 72 years (their average age was 47.2 ± 11.34 years) with working experience in the sphere from 1 to 49 years (average working experience was 19.2 ± 13.6 years).

The participants filled in several standardized questionnaires: Maslach Burnout Inventory (MBI) developed by Maslach & Jackson [17] and adapted by N.E. Vodopyanova[2], RAND SF-36[3] survey for assessing quality of life and Work Ability Index (WAI)[4]. The questioning was anonymous; the participating dentists filled in the forms during breaks in a work shift. MBI contains 22 statements regarding feelings and emotions associated with occupational activities, relationships with colleagues and patients. It allows estimating basic OB components, namely EE, DP and RPA; the latter is sometimes called "loss of motivation". RAND SF-36 is a common instrument to measure quality of life. It contains 36 questions that create eight scales: physical functioning (PF), role physical (RP), bodily pains (BP), general health (GH), vitality (V), social functioning (SF), role emotional (RE), and mental health (MH). The survey scales give grounds for calculating the integral quality of life index. We determined whether quality of life was impaired as per each scale in the survey by comparing its value for each respondent with a relevant population standard [18]. WAI was applied to assess changes in the participants' work ability (WA).

Our study was designed as a "case – control" one. Two groups were formed based on the results produced by MBI. The first one was made of respondents who had occupational burnout by two or three MBI scales (case); the second one included respondents without any signs of OB (control). To analyze risk factors of OB, we compared frequencies of signs in the case and control groups and calculated odds ratio [19]. Qualitative signs were analyzed by using Pearson's χ^2 test. Differences were considered authentic at the significance level being $p < 0.05$. We calculated odds ratio (OR and 95 % confidence interval

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(CI)) to assess risk factors of OB development. We considered the following possible risk factors: sex, age, working experience in the sphere, specialization, existing chronic diseases, diseases of the musculoskeletal system, poorer quality of life (as per specific scales and as per the integral index as well) and lower WA.

All the data were statistically analyzed in SPSS 17.0 and MedCalc software packages.

Results and discussion. The Figure shows how the participating dentists were distributed as per OB intensity.

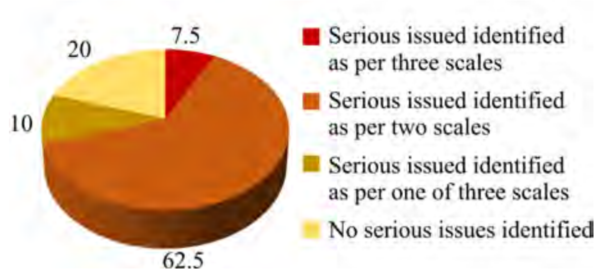

Figure. Distribution of the participating dentists as per OB intensity, %

High scores by the EE and DP scales and low scores by the RPA scale indicate occupational burnout is already developing. Three levels in its development are determined depending on the total scores. The EE scale has the following gradations: 25 scores or more means emotional exhaustion is high; 16–24 scores, average; 0–15 scores, low. The DP scale gradations are as follows: 11 scores or more, depersonalization is high; 6–10 scores, average; 0–5 scores, low. According to the RPA scale, 30 scores or lower, reduced personal accomplishment is apparent; 31–36 scores, average; 37 scores or more, low[2].

Eighty-four respondents out of 120 dentists participating in the study (70 %) had occupational burnout by two or three scales in the MBI questionnaire. Serious issues were identified by all three scales (EE, DP and RPA) in nine (7.5 %) people and 75 dentists (62.5 %) had serious issues identified by the EE and DP scales. Serious issues were identified by only one scale in 12 (10 %) respondents. We did not identify occupational burnout by any scale in 24 (20 %) respondents.

This distribution made it possible to create two groups. The first one included dentists with OB identified by two or three scales in the MBI questionnaire ("case"). The second group was made of dentists without any signs of occupational burnout ("control"). Twelve respondents who had OB identified by only one scale in the MBI questionnaire were excluded from the further analysis.

Table 1 provides profiles of the examined groups depending on risk factors of OB development.

Having analyzed the results provided in Table 1, we established that the compared groups had significant differences as per age ($p < 0.001$). Thus, 52.4 % of the respondents with occupational burnout were aged 50 years and older and another 28.4 % were aged 40–49 years; as for the respondents without occupational burnout, 66.7 % of them were younger than 40 years. Then, there were significant differences between the groups as per working experience in the sphere ($p < 0.001$): most respondents with occupational burnout (71.4 %) had been working in the sphere for more than 20 years and only 7.2 % of them had working experience shorter than 10 %. Half of the respondents without occupational burnout (50 %) had working experience shorter than 10 years and another 25 % had been working in the sphere for less than 20 years. Significant differences were also detected depending on already existing chronic diseases and diseases of the musculoskeletal system ($p < 0.05$). The overwhelming majority of the dentists with occupational burnout had chronic diseases and diseases of the musculoskeletal system, 97 % and 90 % accordingly. We did not detect these diseases in any respondent from the control group. We did not detect any significant sex-related differences or differences related to specialization between the groups.

Statistically significant differences were detected between the groups depending on lower value of indicators showing quality of life as per six out of eight SF-36 scales and the integral quality of life index ($p < 0.05$). Most dentists with occupational burnout had impaired PF (34.5 % against 8.3 % in the control), RP (19 % against 0 %), GH (29.8 % against 0 %), V (26.2 % against 0 %), RE (33 % against 0 %) and MH (17.9 % against 0 %). The integral quality of life index had lower values in 34.5 % of cases among the respondents from the case group whereas there were no such cases in the control one. Our assessment of work ability (WA) established that 22.6 % of the respondents with occupational burnout had moderate WA; the remaining had good and very good WA. All the respondents without occupational burnout had good or very good WA.

Table 2 provides the results produced by analyzing odds ratio for occupational burnout.

Table 1

Profiles of the examined groups depending on risk factors of OB development

Factors	Group with OB, "case"		Group without OB, "control"		(*p*)
	n	%	*n*	%	
Sex					
Male	6	7.1	2	8.3	>0.05
Female	78	92.9	22	91.7	
Age					
< 40 years	16	19.0	16	66.7	<0.001
40–49 years	24	28.6	1	4.2	
≥ 50 years	44	52.4	7	29.2	
Working experience					
< 10 years	6	7.2	12	50	<0.001
10–20 years	18	21.4	6	25	
> 20 years	60	71.4	6	25	
Specialization					
Children's dentist	56	66.7	16	66.7	0.454
Dental surgeon	10	11.9	1	4.2	
Orthodontist	18	21.4	7	29.2	
Chronic diseases					
Yes	67	97	0	-	<0.05
No	2	3	6	100	
Diseases of the musculoskeletal system					
Yes	67	90	0	0	<0.05
No	2	10	9	100	
Impaired physical functioning					
Yes	29	34.5	2	8.3	<0.05
No	58	65.5	22	91.7	
Impaired role physical					
Yes	16	19.0	0	0	<0.05
No	68	81.0	24	100	
Apparent bodily pains					
Yes	2	2.4	0	0	>0.05
No	82	97.6	24	100	
Impaired general health					
Yes	25	29.8	0	0	<0.05
No	59	70.2	24	100	
Lower vitality					
Yes	22	26.2	0	0	<0.05
No	62	73.8	24	100	
Impaired social functioning					
Yes	17	20.2	0	0	>0.05
No	67	79.8	24	100	
Impaired role emotional					
Yes	28	33.3	0	0	<0.05
No	56	66.7	24	100	

Continuation of the Table 1

Factors	Group with OB, "case"		Group without OB, "control"		(*p*)
	n	%	*n*	%	
Impaired mental health					
Yes	15	17.9	0	0	<0.05
No	69	82.1	24	100	
Lower integral quality of life index					
Yes	30	22.6	0	0	<0.05
No	54	77.4	24	100	
Work ability index					
Moderate	19	22.6	0	0	>0.05
Good and very good	65	77.4	24	100	

Table 2

Analysis of odds ratio for occupational burnout among dentists

Risk factors	Odds ratio OR (95 % CI)	Validity of differences (*p*)
Age		
≥ 50 years	6.29 (2.19–18.08)	0.006
40–49 years	24.00 (2.89–199.36)	0.0033
< 40 years	Control	–
Working experience		
> 20 years	20.00 (5.50–72.67)	< 0.0001
10–20 years	6.00 (1.56–23.07)	0.009
< 10 years	Control	–
Impaired physical functioning		
Yes	5.80 (1.27–26.41)	0.023
No	Control	–
Impaired vitality		
Yes	1.63 (0.92–2.87)	0.093
No	Control	–
Chronic diseases		
Yes	351.00 (15.17–8120.01)	0.0003
No	Control	–
Diseases of the musculoskeletal system		
Yes	158.33 (8.35–3004.01)	0.0007
No	Control	–
Impaired role physical		
Yes	11.81 (0.68–204.28)	0.0897
No	Control	–
Impaired general health		
Yes	21.00 (1.23–358.77)	0.0355
No	Control	–
Impaired role emotional		
Yes	24.72 (1.45–421.35)	0.0266
No	Control	–
Impaired mental health		
Yes	10.93 (0.63–189.61)	0.1005
No	Control	–
Lower integral quality of life index		
Yes	27.42(1.61–466.94)	0.0221
No	Control	–
Work ability		
Moderate	16.37 (0.95–280.49)	0.054
Good and very good	Control	–

Significant risk factors that could cause occupational burnout in this occupational group of doctors included age > 40 years, working experience in the sphere > 10 years, chronic diseases, diseases of the musculoskeletal system, impaired physical functioning, general health, role emotional, as well as lower integral quality of life index. Such factors as impaired vitality, role physical, mental health or moderate work ability do not have significant influence on developing occupational burnout. The results provided in Table 2 indicate that risks of occupational burnout grow with age. Dentists aged 40–49 years and those who are 50 years or older have by 24 and 6.3 times higher risks of OB accordingly than their colleagues who are younger than 40 years. Consequently, people aged 40–49 have the highest risks of OB.

Dentists with long working experience have higher risks of OB. The respondents with their working experience being 10–20 years have by 6 times higher risks of OB than their colleagues with working experience shorter than 10 years; those with working experience exceeding 20 years, have by 20 times higher risks of occupational burnout. Chronic diseases and diseases of the musculoskeletal system increase risks of OB development by 351 and 158 times accordingly.

The results produced in this "case – control" study are in general consistent with data produced by correlation analysis of risks causing OB development among dentists who work with adults. According to them, risk factors of OB development include age, working experience, specialization, chronic diseases, and dentists' psychological qualities [9–12, 20, 21]. Additional risk factors of OB detected for dentists who work with children are quality of life indicators related to physical and emotional functioning.

Therefore, our research results indicate that there are several significant risk factors causing OB among dentists working with children in state dental polyclinics. These risk factors include age older than 40 years; working experience longer than 10 years; chronic diseases; diseases of the musculoskeletal system; impaired general health, role physical and role emotional functioning as well as integral quality of life index. This study is the first to reveal significant risk factors of OB development among dentists working with children. We have established that dentists aged 40–49 years have the highest risks of OB development. Working experience exceeding 20 years also raises chances of OB development rather significantly. Existing chronic diseases and diseases of the musculoskeletal system increase chances of OB development by multiple times. Impaired quality of life indicators are another significant factor that makes for OB development in this occupational group.

Conclusion. Since occupational burnout is widely spread among dentists who work with children, it is necessary to analyze OB factors in this occupational group for developing relevant activities aimed at detecting and preventing it. The results of the present study show that OB occurs in 70 % of doctors in this occupational group. Significant risk factors that cause OB include age older than 40 years; working experience in the sphere exceeding 10 years; chronic diseases and diseases of the musculoskeletal system; impaired physical functioning, general health, role emotional functioning, as well as lower integral quality of life index.

These results make it possible not only to get better insight into factors making for OB development in dentists working with children but also to give grounds for developing a prevention program aimed at mitigating risks of occupational burnout. The detected risk factors can be used for developing relevant activities aimed at OB prevention among dentists.

It is advisable to include Maslach Burnout Inventory into periodical medical examinations since this questionnaire allows timely detection of relevant OB signs. Prevention activities should involve creating a special room in a polyclinic where dentists could get necessary relief from workloads. There should also be specific activities aimed at removal of emotional overstrain and recovery of work ability.

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Research article

CREATING BIOINFORMATICS MATRIX OF MOLECULAR MARKERS TO PREDICT RISK-ASSOCIATED HEALTH DISORDERS

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Long-term or permanent chemical ambient air pollution in residential areas is among priority factors that cause medical and demographic losses. It is necessary to achieve greater precision when assessing risks of changes in homeostasis at their early reversible stage (molecular level). These changes are highly likely to transform into pathological processes at an older age in case the exposure persists.

Our research goal was to create a bioinformatics matrix of molecular markers to predict risk-associated health disorders (exemplified by a marker of exposure). We introduced a stepwise research algorithm that involved using the proteome technology to identify expressed proteins and cause-effect relations between them and influencing factors; revealing molecular-cellular and functional relationships within the "exposure factor – gene – protein – negative outcome" system to predict risk-associated health disorders. The algorithm was implemented to examine the proteomic blood plasma profile of children aged 3–6 years living under long-term aerogenic exposure to fluoride-containing compounds.

We established certain changes in the proteomic profiles of the exposed children in comparison with non-exposed ones as per 27 identified proteins. A bioinformatics matrix was created on the example of cathepsin L1; we established that changes in the level of this protein had a cause-effect relationship with fluoride ion concentrations in urine. Qualitative synthesis of molecular-cellular localization, functional and tissue belonging showed that cathepsin L1 expression caused by elevated fluoride ion levels in urine could affect extracellular matrix remodeling, degradation and post-translation modification of proteins in cells of the lungs, large intestine, and pancreas, in cardiomyocytes and in glomerular podocytes. It also mediated proteolysis of the subunits of the SARS-CoV-2 S1 protein necessary for the virus penetration into a cell and its replication. This created bioinformatics matrix exemplified by cathepsin L1 made it possible to predict risk-associated negative outcomes in exposed people including cardiomyopathy, colitis, glomerulonephritis, diabetes mellitus, atherosclerosis, and coronavirus infection. These predictive estimates raise effectiveness of early detection and development of preventive measures aimed at minimizing possible negative outcomes.

Keywords: *proteomic profile, children, cellular-molecular and tissue belonging, molecular markers, gene expression, negative effects, fluoride ion in urine, cathepsin L1, bioinformatics resources.*

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Health preservation and improvement, a growth in population life expectancy, and a decrease in mortality caused by variable diseases, including diseases of the cardiovascular system, malignant neoplasms and chronic respiratory diseases, are established as national priorities within the state policy in the sphere of socioeconomic and demographic development in the Russian Federation for the period up to 2024.

According to the WHO experts, long-term or permanent exposure to chemical pollution in ambient air, water and soils is among leading risk factors causing additional adverse health outcomes[1] [1]. Overall, the burden of diseases caused by complex chemical loads is estimated to account for 15–35 %. If we want to reduce health losses among people who are exposed to chemical pollution (first of all, the most sensitive population groups such as children, teenagers, and young people), we should achieve greater precision when trying to predict risks of changes in homeostasis. It is especially vital when it comes down to early reversible stages in such changes (at the molecular level) since they are very likely to transform into pathological processes at an older age if exogenous introduction of chemicals persists.

The highly informative proteome technology can be a useful tool for searching for potential molecular markers indicating the dynamic balance has been impaired. This technology involves examining protein compositions and thereby makes it possible to identify changes resulting from expression of genes that code target proteins (DNA-RNA-protein relations) under exposure to harmful factors, including chemical ones [2–5]. It is most advisable to use this approach since proteins bear the major functional loads when a living organism interacts with the environment (either directly or through their enzymatic activities). Identification of molecular protein and peptide targets, determination of their structure, functions, tissue belonging, and their involvement into pathogenesis of functional disorders should be accomplished by using up-to-date bioinformatics and toxicogenetic resources [6–10]. When done, this guarantees effective predictions of expected negative health outcomes. Identifying associative pathogenetic relations between effects produced by exposure factors and expression of protein molecular markers makes it possible to predict risk-associated negative outcomes. It is especially vital for achieving greater effectiveness of early (cellular and molecular) detection of health disorders in exposed population.

Given all the above-stated, it seems advisable to elaborate on approaches to performing studies with their focus on identifying expressed proteins associated with exposure to chemical factors. It is also important to perform biological and biochemical interpretation of their cellular and functional belonging since it helps examine molecular-cellular mechanisms in detail and achieve more precision in estimating probable negative health outcomes participating in pathogenesis of risk-associated noncommunicable diseases. All this gave grounds for determining the goal of the present research.

Our research goal was to create a bioinformatics matrix of molecular markers to predict risk-associated health disorders (exemplified by a marker of exposure).

Materials and methods. It is possible to create a bioinformatics matrix of molecular markers to predict risk-associated health disorders by using the following stepwise research algorithm:

– creating samplings made of exposed and non-exposed people from population groups that are the most sensitive to negative effects produced by chemical factors (a test group and a control group);

– establishing actual exposure by determining elevated contents of chemicals in biological media that are proven to be associated with this exposure (identifying markers of exposure);

[1] O sostoyanii sanitarno-epidemiologicheskogo blagopoluchiya naseleniya v Rossiiskoi Federatsii v 2020 godu: Gosudarstvennyi doklad [On sanitary-epidemiological welfare of the population in the Russian Federation in 2020: The State Report]. Moscow, The Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing, 2021, 256 p. (in Russian).

– creating a proteomic profile, identification, comparative analysis and spotting out protein strains that differ in their intensity in a test group against a control one and these differences are statistically significant;

– establishing cause-effect relations between identified expressed proteins and exposure factors (as per contents of markers of exposure in biological media);

– qualitative synthesis and creation of a phylogenetic tree that reflects molecular-cellular and functional relations within the "exposure factor – gene – protein – negative outcome" system to predict risk-associated health disorders.

The suggested algorithm was implemented in a study that focused on proteomic blood plasma profiles of children aged 3–6 years who lived under long-term aerogenic exposure to gaseous and solid fluoride compounds. This exposure created non-carcinogenic health risks that were by 1.5–2 times higher than their acceptable levels. We made our test group by including children with elevated fluoride-ion contents in urine that were by 1.5 or more times higher than the reference value[2]. This indicator was selected due to being the marker of exposure to fluoride compounds according to the previously established cause-effect relations. Children from the control group had the examined chemical in their urine in contents not exceeding the reference value or being close to it. The children were examined in full conformity with the ethical principles stated in the WMA Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects, 2013). The study was approved by the Committee on Biomedical Ethics of the Federal Scientific Center for Medical and Preventive Health Risk Management Technologies; it was mandatory to obtain an informed voluntary consent from legal representatives of all the examined children prior to any examination.

Proteomic profiles were examined by using two-dimensional gel electrophoresis in polyacrylamide gel. The resulting blood plasma electrophoretograms were visualized by dyeing with silver and documented with a gel documentation system (BioRad, USA). The obtained proteomic maps were comparatively analyzed with PDQuest software package (BioRad, USA); we spotted out significant protein stains as per their intensity and performed subsequent analysis with liquid chromatography together with mass-spectral analysis (with UltiMate 3000 chromatograph (Germany) and AB Sciex 4000 QTRAP tandem mass spectrometer with Nanospray 3 ionization source (Canada)). Data produced by tandem examinations were analyzed with ProteinPilot, verison 4.5 (AB Sciex) and identified according to UniProt_sprot_fasta database (as of November 24, 2017), with sampling as per Homo Sapience taxon (peptide fingerprint). Major part of the information about the obtained protein was extracted from two databases, Gene Ontology Resource and UniProt[3]. We established genes that coded expression of the identified proteins by using HGNC database of human gene name[4].

All the obtained data were statistically analyzed with Statistica 10 software package. We comparatively assessed relative volumes of protein stains in the test group against the same parameters in the control one. The study results are given as the mean value ($\bar{X}$) and the standard error of the mean (*SEM*). Statistical significance of differences in variables between the groups was determined as per Mann – Whitney test ($U \leq Ucr$) with the significance level set at $p \leq 0.05$.

We detected cause-effect relations between changes in statistically significantly different protein strains and fluoride-ion concentrations and assessed them by building a mathematical logistic regression model. The built models were estimated to test their au-

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[3] Gene Ontology Resource. Available at: http://geneontology.org/ (April 08, 2022); UniProt. Available at: http://www.uniprot.org (April 08, 2022).

[4] HGNC database of human gene name. Available at: https://www.genenames.org (April 12, 2022).

thenticity and relevance; the estimation was based on dispersion analysis with using Fischer's F-test, determination coefficient (*R2*), and Student's t-test at the statistical significance level being $p \leq 0.05$.

Proteins were classified as per classes, biological and molecular functions by using Panther Classification System and Gene Ontology and GO Annotations databases[5]. To establish expression of proteins in various tissues in a body, we used data provided by Tissue expression database and The Human Protein Atlas[6]. Relationships within the "exposure factor (marker of exposure) – gene – protein – disease" system were described with the use of Comparative Toxicogenomics as a source of information[7].

Results and discussion. We comparatively analyzed the results produced by densitometry of proteomic blood plasma profiles of the examined children. The analysis revealed authentic differences in relative volumes of 27 protein stains between the children from the test and control groups (Table 1).

Approximately 75 % of the detected protein stains were by 1.4–37.6 greater in volumes in children from the test group than in their counterparts from the control one; the remaining 25 % had by 1.5–36.6 times smaller volumes ($p = 0.0001–0.009$).

Figure 1 shows a fragment of a two-dimensional electrophoretogram used for detecting quantitative differences in cathepsin L1 in blood plasma of the examined children.

We performed bioinformatics analysis to detect how the identified proteins were localized; to do that, we used Panther classification. The analysis established that most of them (57.7 %) were localized in cellular structures (GO:0110165) and 15.4 % of the proteins were localized in protein complexes (GO:00032991). The proteins were classified as follows depending on their participation in the life cycle: 22.7 % proteins were signal transfers/carriers (PC00219), 13.6 % metabolite interconversion enzymes (PC00262), and also three groups each containing 9.1 % of the proteins were protein modifying enzymes (PC00260), cytoskeletal proteins (PC00085) and adaptor proteins (PC00226) (Table 2 and Figure 2).

We analyzed class properties as per molecular processes and established that most proteins were responsible for binding with other molecules (GO:0005488; 44.8 %) and catalytic activity (GO:0003824; 31.3 %) (Table 3 and Figure 3).

We examined and classified biological functions performed by the identified proteins. The results showed that most of them were responsible for cellular (GO:0009987; 30 %) and metabolic processes (GO:0008152; 15 %) as well as biological regulation (GO:0065007; 12 %) (Table 4 and Figure 4).

The established class properties (localization, participation in the life cycle, and biological functions) of the identified proteins were identical in the children from the both groups, the test and control.

We analyzed cause-effect relations between changes in contents of 27 expressed proteins and fluoride-ion concentrations in urine. The analysis established an authentic direct correlation only for cathepsin L1 ($R^2 = 0.45$; $b_0 = 764.23$; $b_1 = 51.47$; $p = 0.016$) and this was in line with experimental data indicating that exposure to fluoride compounds led to elevated cathepsin L1 expression [11].

We took cathepsin L1 as an example protein to create a bioinformatics matrix showing functional belonging (Figure 5) using Gene Ontology and GO Annotations bioinformatics platform[8].

[5] Panther Classification System. Available at: http://www.pantherdb.org (March 23, 2022); Gene Ontology and GO Annotations. Available at: https://www.ebi.ac.uk/QuickGO (March 23, 2022).

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[8] Gene Ontology and GO Annotations. Available at: https://www.ebi.ac.uk/QuickGO/ (March 19, 2022).

Table 1

Proteins detected in children proteomic blood plasma profiles that are authentically different from the control group

No.	Protein	UniProt identifier	Coding gene	An average protein stain volume, $\bar{X} \pm SEM$	
				Test	Control
1	Keratin, type I cytoskeletal 9	P35527	KRT9	1406.3 ± 148.7*	2232.5 ± 272.2
2	Band 4.1-like protein 3	Q9Y2J2	EPB41L3	1890.6 ± 56.2*	2833.8 ± 135.7
3	Inositol 1,4,5-triphosphate receptor interacting protein-like 1	Q6GPH6	ITPRIPL1	1736.9 ± 56.2*	2743.4 ± 304.4
4	Hemoglobin subunit beta	P68871	HBB	2350.7 ± 161.6*	1447.9 ± 253.0
5	Laminin subunit alpha-3	Q16787	LAMA3	2435.4 ± 148.4*	66.5 ± 61.5
6	Apolipoprotein A-I	P02647	APOA1	66.5 ± 12.5*	2435.4 ± 148.4
7	Eukaryotic peptide chain release factor GTP-binding subunit ERF3B	Q8IYD1	GSPT2	2547.5 ± 118.0*	94.0 ± 81.0
8	Immunoglobulin J chain	P01591	JCHAIN	1785.0 ± 86.0*	101.0±34.0
9	THO complex subunit 2	Q8NI27	THOC2	3157.56 ± 65.4*	2983.4 ± 61.1
10	NCK-associated protein 5-like	Q9HCH0	NCKAP5L	2586.6 ± 105.1*	2840.3 ± 92.5
11	GRB10-interacting GYF protein 1	O75420	GIGYF1	2340.7 ± 183.3*	95.4 ± 61.4
12	Kelch-like protein 4	Q9C0H6	KLHL4	1806.6 ± 78.0*	100.5 ± 76.9
13	Prothrombin	P00734	F2	1893.7 ± 117.3*	1724.6 ± 47.4
14	Nucleophosmin	P06748	NPM1	469.0 ± 120.0*	94.0 ± 26.0
15	Complement C4-B	P0C0L5	C4B	2749.8 ± 56.0**	1821.2 ± 259.7
16	Cathepsin L1	P07711	CTSL	1712. 0 ± 123.7*	518.5 ± 125.5
17	Ankyrin-1	P16157	ANK1	1765.6 ± 91.0*	454.2 ± 505.1
18	Choline transporter-like protein 3	Q8N4M1	SLC44A3	1715.2 ± 123.0*	72.7 ± 71.0
19	Olfactory receptor 8A1	Q8NGG7	OR8A1	1712.1 ± 123.7*	518.5 ± 248.0
20	Transthyretin	P02766	TTR	3966.9 ± 189.3*	2344.4 ± 300.2
21	Vitronectin	P04004	VTN	3568.8 ± 233.2*	1844.1 ± 142.6
22	Tyrosine-protein phosphatase non-receptor type 14	Q15678	PTPN14	1639.1 ± 156.8*	99.5 ± 95.63
23	Transcription termination factor 1	Q15361	TTF1	3109.5 ± 75.2*	3342.2 ± 118.7
24	Apolipoprotein C-III	P02656	APOC3	4249.6 ± 250.1*	3027.4 ± 250.1
25	Myotubularin	Q13496	MTM1	4408.1 ± 263.9*	3228.0 ± 335.8
26	Apolipoprotein C-II	P02655	APOC2	3802.7 ± 272.0*	2326.7 ± 295.1
27	Serum amyloid protein A-1	P0DJI8	SAA1	2326.3 ± 154.1*	61.8 ± 5.9

Note: * means differences in mean values are authentic between the groups at p = 0.0001; ** means authentic differences in mean values between the groups at p = 0.009.

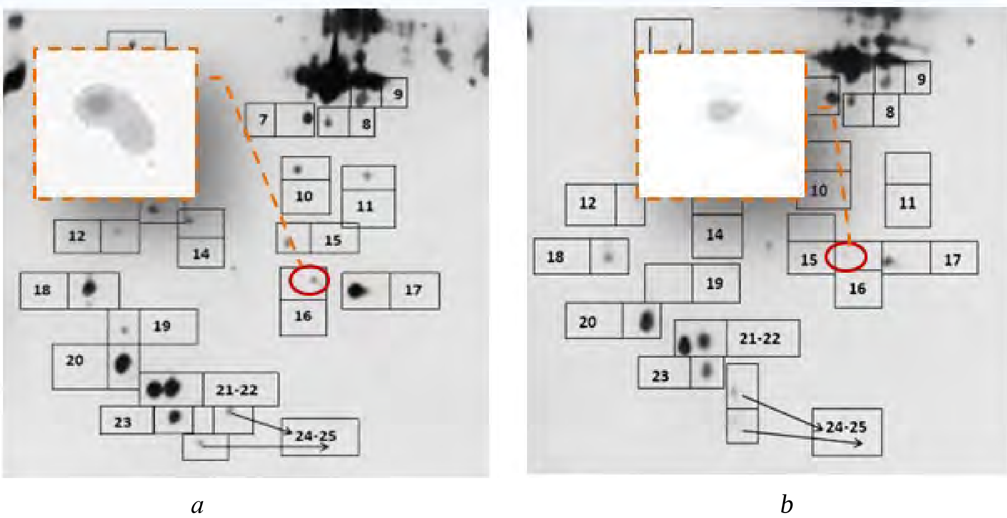

Figure 1. A fragment of a two-dimensional children blood plasma electrophoretogram: a, a child from the test group; b, a child from the control group

Table 2

Classes of proteins identified in children blood plasma depending on their participation in the life cycle

Protein class*	Protein
Protein modifying enzyme	Tyrosine-protein phosphatase non-receptor type 14, Prothrombin, Cathepsin L1
Adaptor	Ankyrin-1, Kelch-like protein 4
Transfer/carrier	Apolipoprotein A-I, Apolipoprotein C-II, Apolipoprotein C-III, Hemoglobin subunit beta
Cytoskeletal protein	Band4.1-like protein 3, Keratin 9
Metabolite interconversion enzyme	Transthyretin, Inositol 1,4,5-triphosphate receptor interacting protein-like 1, Myotubularin
Transporter	Choline transporter-like protein 3
Chaperone	Nucleophosmin
Cell adhesion molecule	Laminin subunit alpha-3
Protein-binding activity modulator	Complement C4-B
Transmembrane signaling receptor	Olfactory receptor 8A1
Defense protein	Immunoglobulin J chain
Gene-specific transcriptional regulator	THO complex subunit 2
Translation protein	Eukaryotic peptide chain release factor GTP-binding subunit ERF3B

Note: * according to The PANTHER Classification System[9].

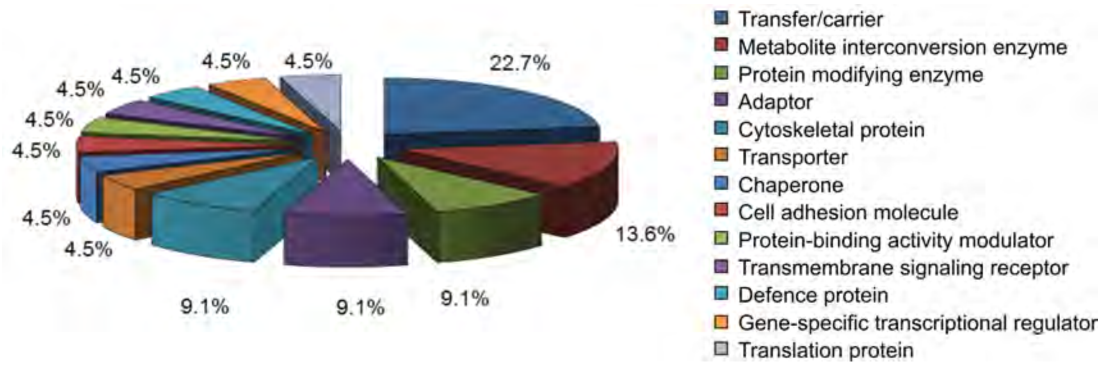

Figure 2. Classes of proteins identified in children blood plasma depending on their participation in the life cycle

Table 3

Molecular functions performed by the identified proteins in children blood plasma

Molecular function*	Protein
Molecular transducer activity	Olfactory receptor 8A1
Molecular adaptor activity	Ankyrin-1
Transporter activity	Choline transporter-like protein 3
Translation regulator activity	Eukaryotic peptide chain release factor GTP-binding subunit ERF3B
Binding	Olfactory receptor 8A1; THO complex subunit 2; Hemoglobin subunit beta; Eukaryotic peptide chain release factor GTP-binding subunit ERF3B; Nucleophosmin; Ankyrin-1; Vitornectin
Catalytic activity	Eukaryotic peptide chain release factor GTP-binding subunit ERF3B; Tyrosine-protein phosphatase non-receptor type 14; Prothrombin; Hemoglobin subunit beta; Myotubularin; Cathepsin L1

Note: * according to The PANTHER Classification System[9].

[9] The PANTHER Classification System. Available at: http://www.pantherdb.org/ (March 19, 2022).

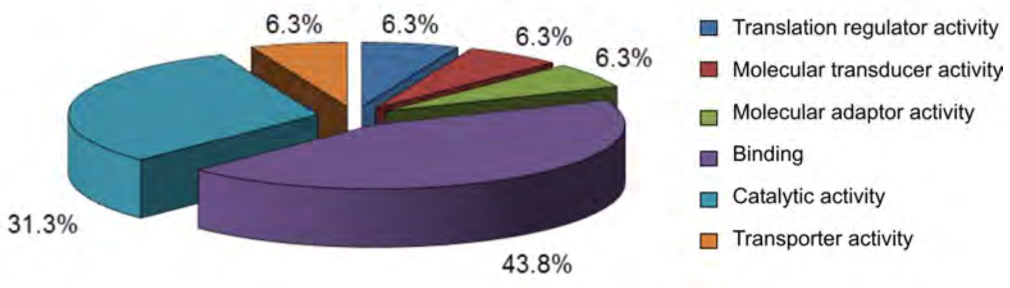

Figure 3. Molecular functions performed by the identified proteins in children blood plasma

Table 4

Biological functions performed by the identified proteins in children blood plasma

Biological function	Protein
Biological adhesion	Vitronectin
Growth	Prothrombin
Immune processes	Complement C4-B; Cathepsin L1
Biological regulation	Prothrombin; Olfactory receptor 8A1; Nucleophosmin; Complement C4-B; GRB10-interacting GYF protein 1; Myotubularin
Cellular processes	NCK-associated protein 5-like; Prothrombin; THO complex subunit 2; Olfactory receptor 8A1; Hemoglobin subunit beta; Choline transporter-like protein 3; Eukaryotic peptide chain release factor GTP-binding subunit ERF3B; Nucleophosmin; Ankyrin-1; Transthyretin; Myotubularin; Vitronectin; GRB10-interacting GYF protein 1; Cathepsin L1
Development processes	Tyrosine-protein phosphatase non-receptor type 14; Prothrombin; Myotubularin;
Localization	THO complex subunit 2; Choline transporter-like protein 3; Nucleophosmin; Ankyrin -1; Myotubularin
Metabolic processes	THO complex subunit 2; Hemoglobin subunit beta; Eukaryotic peptide chain release factor GTP-binding subunit ERF3B; Nucleophosmin; Transthyretin; Complement C4-B; Myotubularin; Cathepsin L1
Multicellular organismal process	Tyrosine-protein phosphatase non-receptor type 14; Prothrombin; Olfactory receptor 8A1
Response to stimulus	Prothrombin; Olfactory receptor 8A1; Complement C4-B; GRB10-interacting GYF protein 1; Cathepsin L1
Signaling	Olfactory receptor 8A1; GRB10-interacting GYF protein 1

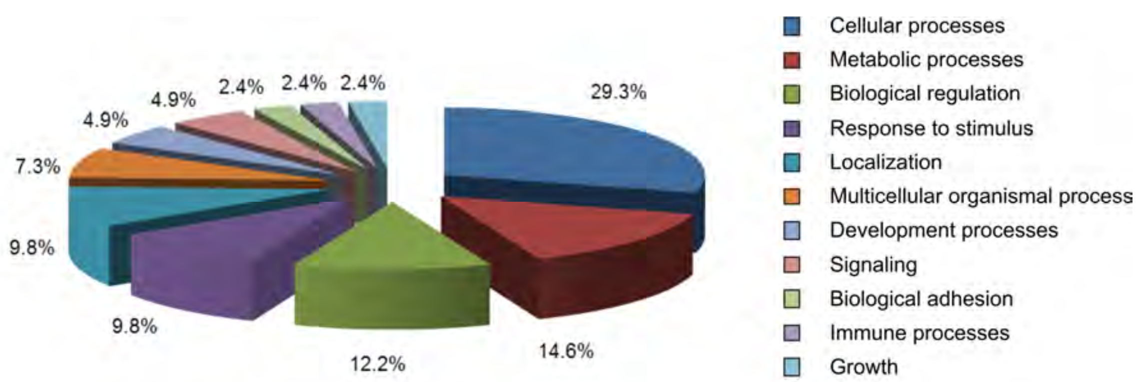

Figure 4. Biological processes provided by the identified proteins in children blood plasma

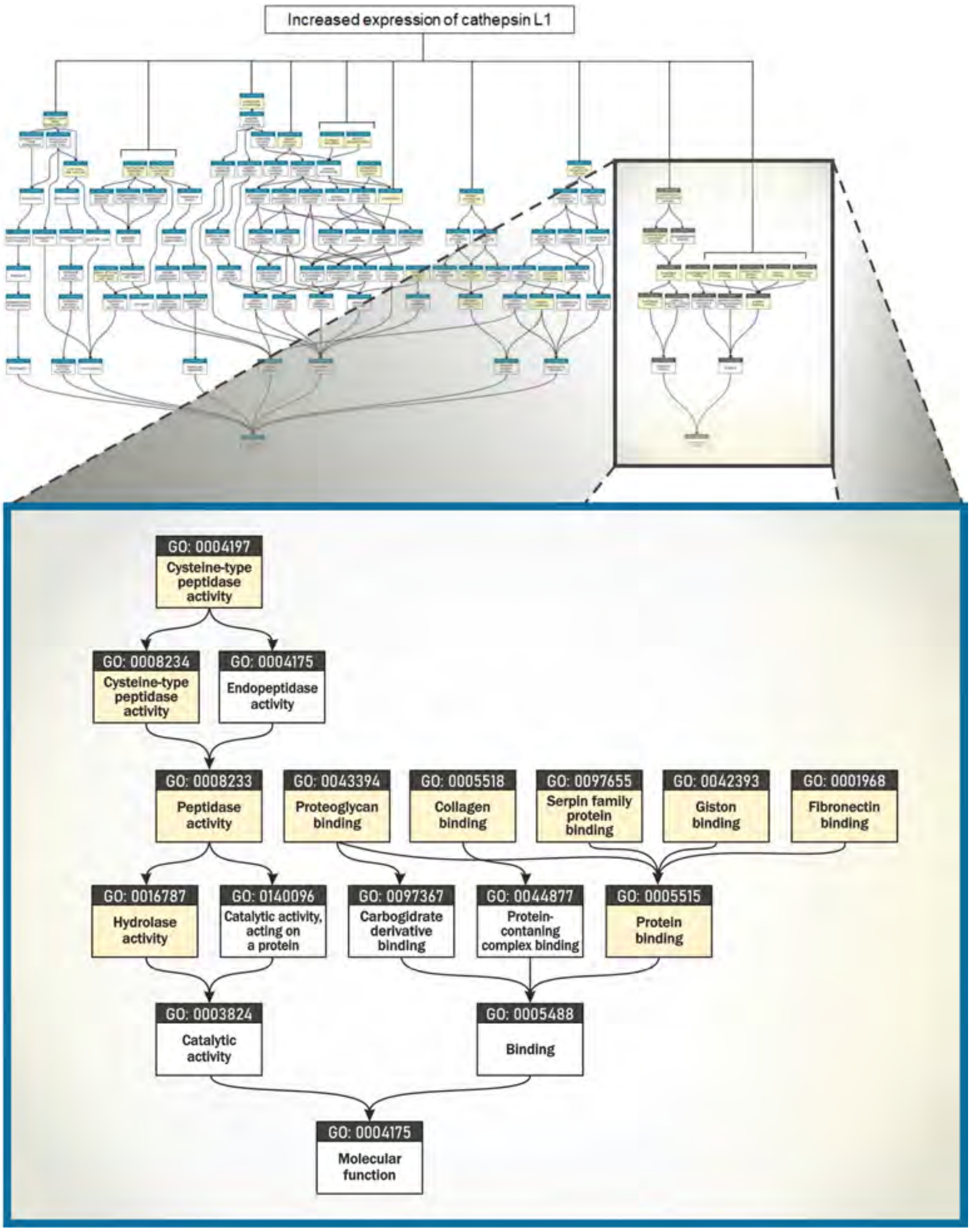

Figure 5. A scheme showing functional belonging of Cathepsin L1
(Gene Ontology and GO Annotations database, 2022)

Cathepsin L1 is expressed in tissues of the respiratory tract, endocrine system, gastrointestinal tract, pancreas, kidneys and muscular tissues. According to the phylogenetic tree, 477 orthologous proteins belong to this protein subfamily. They are from different taxons including Rattus norvegicus (rats) and Mus musculus (mice) (Figure 6).

Bioinformatics analysis of localization, functional and tissue belonging has revealed that proteins from cathepsin family are lysosomal cysteine proteases. They participate in processes involved in cell death, protein degradation and post-translation modification, extracellular matrix remodeling, autophagy and immune signals transfer. Some processes are specifically associated with elevated cathepsin L1 levels. They include degradation and impaired extracellular matrix remodeling in lung and large intestine macrophages; trypsinogen-trypsin imbalance with developing inflammation in pancreatic parenchyma; disrupted transfer of signals through mitogen-activated protein kinase (MAPK) pathways in cardiomyocytes;

Figure 6. A fragment of the phylogenetic tree showing orthologous genes of Cathepsin L1 (STRING Consortium database[10], 2022)

damage to glomerular podocytes [12–17]. In addition, cathepsin L1 mediates proteolysis of the subunits of the SARS-CoV-2 S1 protein necessary for the virus penetration into a cell and its subsequent replication [18–20]. If exposure to fluoride-containing compounds persists, this results in greater likelihood of risk-associated negative health outcomes including progressing dilated cardiomyopathy, atherosclerosis, pancreatitis and diabetes mellitus, glomerulonephritis, colitis, and coronavirus infection.

Conclusion. We implemented the suggested algorithm and comparatively analyzed proteomic blood plasma profiles of non-exposed children and children who were exposed to fluoride-containing compounds. As a result, 27 expressed proteins were identified. We took cathepsin L1 as an example since its expression correlated authentically with elevated fluoride-ion concentrations in urine (marker of exposure) and created a bioinformatics matrix. The matrix gave a possibility to predict likely risk-associated negative health outcomes in exposed children. These outcomes included cardiomyopathy, colitis, glomerulonephritis, diabetes mellitus, atherosclerosis, and coronavirus infection. The resulting predictive estimates raise effectiveness of early detection and allow developing preventive activities that are more effective for minimizing negative health outcomes.

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Competing interests. The authors declare no competing interests.

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Research article

EXPERIMENTAL MODELS OF ANIMAL CHRONIC PATHOLOGY IN ASSESSING HEALTH RISKS FOR SENSITIVE POPULATION GROUPS

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The methodology for health risk assessment and hygienic standardization of chemicals often neglects such a vulnerable population group as people with chronic non-communicable diseases. According to the data provided by the WHO, the prevalence of such pathologies is high in many European countries; therefore, when a disease burden in a certain population is unaccounted for, this may result in lower accuracy of accomplished assessments. On the other hand, introduction of too conservative safe factors when hygienic standards are being developed for chemicals in various media leads to high uncertainty and excessive limitations.

Our research goal was to provide scientific substantiation for a methodology for using experimental pathology models to improve reliability of hygienic standardization and accuracy of health risk assessments for sensitive population groups (people suffering from non-chronic communicable diseases) under exposure to naturally occurring chemicals. Another goal was to test this methodology by performing a case study on drinking water. The testing results indicate that a chronic 6-month exposure to model substances produced more apparent toxic effects on experimental animals with model pathologies (spontaneous hypertension and experimental gentamicin-induced nephropathy) in comparison with "healthy" animals.

This allowed us to recommend using experimental models of congenital and induced animal pathology bearing in mind target organs for toxic effects produced by the analyzed chemicals to substantiate hygienic standards, health risks taken into account. This should be done at the stage when dose-dependent reactions are identified (determination of no-effect and / or threshold levels) in addition to studies performed on "healthy" animals. It is most appropriate to use this approach when the following conditions are met: 1) a research object is naturally occurring chemicals that are widely spread in the environment due to its natural formation; 2) pathologies of organs (systems) that are targets for biological effects produced by the tested chemicals are widely spread in a population (circulatory diseases, diseases of the excretory system, etc.).

Keywords: *experimental pathology models, nephropathy, spontaneously hypertensive rats, risk assessment, hygienic standardization, sensitive population groups, methodological approaches, barium, total mineralization.*

It is a common practice to use an uncertainty factor when developing hygienic standards for chemicals in environmental objects. This factor is used to achieve proper transfer to standardized values from threshold or no-effect doses (concentrations) determined through experiments on laboratory animals, mathematical modeling, or epidemiological studies. Uncertainty factor is assumed to consider all basic uncertainties including intraspecies and interspecies variation as well as database deficiencies (availability or absence of data on chronic and specific toxicity, reproductive toxicity or other remote effects; scales of an experiment or an epidemiological study are also impor-

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tant). This approach is widely used in national, regional (the EAEU countries) and the best international practices [1, 2].

According to several researchers, when a conservative uncertainty factor equal to 10 is applied for intraspecific variation, this may guarantee covering only 80–95 % of variability inherent to human population if we remember about differences in metabolism of xenobiotics [3]. Later it was noted, that this analysis did not include certain population sub-groups (age-related effects or those produced by genetic polymorphism were neglected etc.). In addition, a large group of potentially vulnerable people was neglected although these people are much more sensitive than “an average healthy adult person” is, for example, due to pathologies or functional disorders of an organ or a system of organs participating in toxicant metabolism [4–9]. If we allow for all the aforementioned indicators, then uncertainty factor with its established value equal to 10 can “protect” only 60 % of population [10, 11]. Besides, if people have certain chronic pathologies, they tend to take drugs for a long-term period. These drugs can make substantial alterations into a direct or indirect response given by the body to chemical exposure[1] [12, 13]. Preexisting kidney diseases undoubtedly play a significant role in occurring nephrotoxic disorders. Experiments involving laboratory animals provided convincing evidence that common human diseases (hypertension, kidney failure and kidney ischemia) enhanced renal toxic effects produced by cyclosporine and bacterial endotoxins. However, there are rather scarce scientific data on actual predictive value of clinical observations and results produced by experiments involving laboratory animals. Chemical toxicity is usually examined in experiments on healthy laboratory animals. This does not allow extrapolating their results on such vulnerable population groups as people suffering from chronic non-communicable diseases and / or taking drugs constantly.

Recently, multiple research works have been accomplished with their focus on providing substantiation for methodical approaches to selecting the most optimal factors of intraspecific and interspecific uncertainty together with establishing the most relevant values of uncertainty factors. For example, so called chemical-specific adjustment factors (CSAFs) have been developed; they consider data on toxicokinetics and toxicodynamics of a chemical and its metabolites in the body [14, 15]. Use of CSAFs has already been formalized in international recommendations and implemented into risk assessment practices[2] [16]; however, this approach also covers only optimal conditions when all the organs are healthy and function properly.

Therefore, such a vulnerable population group as people with chronic diseases is neglected completely in assessing health risks caused by exposure to chemical factors and in hygienic standardizing. We should note that there are certain global trends in population health that are also typical for the Republic of Belarus and most countries in the WHO-Euro region. These trends include excessive prevalence of chronic non-communicable diseases that account for 86 % in mortality and 77 % in the overall disease burden. Diseases of the circulatory system and oncological diseases are priority ones; their etiology may be potentially associated with exposure to chemical factors [17].

When the disease burden in a given population is neglected, this undermines accuracy of health risk assessment and hygienic standardization based on the conventional approach. At the same time, introduction of too high uncertainty factors when establishing maximum permissible concentrations in various media leads to high uncertainty and

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[2] Chemical-specific adjustment factors for interspecies differences and human variability: guidance document for use of data in dose/concentration–response assessment. Geneva, World Health Organization, 2005, 96 p.

excessive limitations. A good example here can be impossibility to use water from certain sources in drinking water supply since it contains natural chemicals in concentrations higher than established in "strict" standards and its treatment requires significant costs (barium).

Given all the above-stated, we can conclude that it is vital to develop more reliable hygienic standards and to accomplish more accurate health risk assessment under exposure to chemicals allowing for sensitive population groups. The issue is especially interesting when it comes down to substantiating hygienic standards for natural chemicals that occur in environmental objects in elevated concentrations due to regional peculiarities.

In the present study, we suggest a new methodical approach to reduce uncertainties associated with neglected potentially higher sensitivity of a vulnerable population group (people suffering from chronic non-communicable diseases or taking certain drugs constantly) in assessing health risks caused by exposure to naturally occurring chemicals and in their hygienic standardization.

Obviously, experimental pathology models, including spontaneously hypertensive rats (SHR), have been used for quite a long time to assess pharmacological properties of drugs [18–24] and to examine influence exerted on a developing pathology by certain food products [25, 26]. Such models are also applied in some toxicological studies, for example, a hypertension model to assess small doses of pollutants in ambient air or acute exposure to ethanol in small doses [27, 28]. However, there is no available methodology for systemic use of pathology models in assessing health risks and substantiating hygienic standards for naturally occurring chemicals in the environment.

Our research goal was to provide scientific substantiation for a methodology for using experimental pathology models considering the most common target organs and biological effects produced by the analyzed chemicals and to test this methodology. Its main purpose is to improve reliability of hygienic standardization and accuracy of health risk assessments for sensitive population groups under exposure to naturally occurring chemicals.

To achieve the goal, the following tasks were set:

1) to examine the existing experimental pathology models (exemplified by hypertension models and nephropathy models) and to substantiate their selection for further experimental testing of their use in hygienic standardization and health risk assessment (on the example of drinking water and its model chemical indicators typical for hydrochemical conditions in the republic);

2) to analyze and comparatively assess biological effects produced by model chemical indicators under different levels of exposure on healthy animals (average or standardized models) and experimental pathology models (risk group models);

3) to substantiate methodical approaches to applying experimental pathology models in hygienic standardization of naturally occurring chemicals based on health risk assessment considering sensitive population groups.

Materials and methods. Within the present study, we selected two experimental pathology models, namely, hypertension (spontaneous) and nephropathy (experimental gentamicin-induced) to test the suggested methodical approaches. Our choice is well grounded by performed analysis considering a whole set of relevant criteria.

A model chemical (barium) and a generalized indicator (total mineralization) were selected based on the following criteria: 1) relevance for regional hygienic standardization is confirmed by their prevalence in drinking water in the republic due to natural peculiarities of underground water-bearing horizons; 2) the cardiovascular and excretory system are exposure targets for model chemicals; their biological effects have been proven by multiple experiments and their threshold effects were considered in providing substantiation for national and foreign safety standards and levels recommended by the WHO[3]; 3) non-communicable diseases of organs (systems) that are target ones for biological effects produced by the analyzed chemicals are widely spread in population.

The suggested models were tested in a 6-month chronic experiment on laboratory animals. The animals drank water containing the analyzed chemicals in different concentrations; they had free access to water during the whole experiment and no limitations were imposed on drinking. Chemical concentrations were substantiated allowing for toxicometric parameters used in establishing standards for the analyzed chemicals at the national and international levels. These parameters were non-effective concentrations and concentrations that would certainly produce biological effects on healthy laboratory animals: water with barium concentration 1.3 mg/l and 70 mg/l and total mineralization being 1500 and 10,000 mg/l accordingly.

To test experimental pathology models, we created five groups, 10 randomly bred white male rats in each. The control group had free access to drinking water without any limitations on its consumed amount and the remaining four test groups drank water with the relevant concentrations of analyzed model chemicals ("control", "Ba 1.3", "Ba 70", "M 1500" and "M 10,000" groups in the classical model).

To model nephropathy, we created five groups of rats, 10 animals in each. Prior to the experiment, gentamicin was administered intraperitoneally in a dose 70 mg/kg/day for 10 days. After nephropathy developed, one group ("control") had free access to water in unlimited quantities and the remaining four test groups drank water with the analyzed substances in relevant concentrations ("EINP control", "EINP Ba 1.3", "EINP Ba 70", "EINP M 1500", "EINP M 10,000" groups in the experimentally induced nephropathy (EINP) model).

To test the hypertension model, we created three groups, 10 male SHR (spontaneously hypertensive rats) in each. The animals had persistent elevated blood pressure. The control group and two test groups had free access to the initial water and water with barium concentrations being 1.3 and 70 mg/l accordingly ("SHR control", "SHR Ba 1.3", "SHR Ba 70" in the hypertension model).

All our experiments were performed on randomly bred male white rats from the vivarium of the Scientific and Practical Center for Hygiene and SHR from the vivarium of the Institute for Bioorganic Chemistry of the Belarus National Academy of Sciences. Prior to the experiments, animals underwent a two-week quarantine period. Experimental animals had to be active, with good appetite, smooth and shiny fur and proper coloring of visible mucosa. They also had to be accustomed to standard nutrition provided in the vivariums.

Water with relevant barium (Ba) concentration and mineralization (M) was prepared by dissolving powder 2-water barium chloride ("VEKTON" LLC, Russia, State Standard GOST 4108-72) and a powder mineral additive called "Severyanka" ("Eko-proekt" LLC, Russia) in required proportions accordingly.

The experimental animals were weighed daily during the whole 6-month experiment; we also assessed their daily water consumption and noted any clinical signs of intoxication or deaths. To determine whether hypertension as an analyzed critical effect was developing, we took systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) in all the rates prior to the experiment and after it was over. The indicators were measured by

[3] Guidelines for Drinking-water Quality (4th ed. with adds). Geneva, WHO, 2017, 631 p.; Barium in Drinking Water: Guideline Technical Document for Public Consultation. *Health Canada*, 2018, 52 p. Available at: https://www.canada.ca/content/dam/hc-sc/documents/programs/consultation-barium-drinking-water/document-eng.pdf (November 20, 2021); Barium in Drinking-water: Background document for development of WHO Guidelines for Drinking-water Quality. WHO, 2016, 21 p. Available at: https://cdn.who.int/media/docs/default-source/wash-documents/wash-chemicals/barium-background-jan17.pdf?sfvrsn=9a2355a1_4 (November 20, 2021); Toxicological profile for barium and barium compounds. US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 2007, 231 p. Available at: http://www.atsdr.cdc.gov/toxprofiles/tp24.pdf (November 20, 2021); Barium and Compounds. CASRN 7440-39-3. US Environmental Protection Agency, National Center for Environmental Assessment, 2005, 34 p. Available at: https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0010_summary.pdf (November 20, 2021).

using "Systola" system for non-invasive blood pressure measurement in rats and "Flogiston" platform manufactured by "Nuerobotiks" LLC, Russia.

White rats were taken from the experiment by decapitation followed by autopsy that involved determining relative mass coefficients (RMC) of internal organs. To examine morphofucntional state of experimental animals' bodies, we applied various analysis techniques. We assessed relevant biochemical indicators of blood serum including urea, lactate dehydrogenase (LDG), cholesterol, gamma-glutamyl transpeptidase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin, creatinine, total bilirubin and total protein, α-amylase, glucose, uric acid, high and low density lipoproteins (HDLP and LDLP), phosphor, iron and magnesium. These indicators as well as functional indicators of the urinary excretion system were examined with Accent 200 automated biochemical analyzer (Poland). We examined morphofucntional composition of peripheral blood by flow cytometry performed with Mythic 18 hematology analyzer (Switzerland); morphological structure of animals' internal organs was examined using conventional procedures.

Experimental animals were cared for in conformity with the ethical principles of good laboratory practice[4].

All the experimental data were statistically analyzed with parametric and non-parametric procedures that are conventionally applied in medical and biological research. The analysis was performed in Statistica 10 and MS Excel software packages. The critical significance level for testing statistical hypotheses was taken at $p < 0.05$.

Results and discussion. Functional changes detected in the rats from "EINP control" indicated that the model pathology (chronic nephropathy) was developing in them in contrast to white rates that were not given any gentamicin ("control"). We detected a statistically significant decrease in phosphor concentration in blood, by 13.5 %; LDLP, by 1.9 times; urea, by 2.3 times ($p < 0.001$); total protein, by 16.9 % ($p < 0.01$); albumin, by 18.1 % ($p < 0.003$). There was a growth in concentrations of uric acid (by 29.8 %) ($p < 0.04$); creatinine (by 25.4 %); glucose (by 22.9 %); AST (by 13.6 %) ($p < 0.001$); ALT, by 43.9 % ($p < 0.007$). We also detected a decline in daily diuresis by 19.1 % ($p < 0.004$) and multi-directional shifts in protein and mineral metabolism. Thus, we established that secretion of total protein was by 1.2 times higher ($p < 0.008$); phosphor concentration was by 2.3 times lower; magnesium concentration, by 2.6 times lower; urea and creatinine concentration in urine were by 1.4 and 1.3 times lower accordingly (at $p < 0.001$). We also detected that leukocyte levels were by 12.1 % higher in the animals with induced nephropathy in comparison with healthy animals, including neutrophils (by 20.0 %), monocytes (by 2.2 times), eosinophils (by 29.3 %) and basophils (by 1.4 times) ($p < 0.01$).

Research results under exposure to the model chemicals indicated absence of any significant changes in overall health of animals from all 13 experimental groups throughout the chronic experiment. Water consumption remained at reference levels. A daily dose for laboratory animals that were given barium solutions in concentrations equal to 1.3 and 70 mg/l amounted to 0.05 and 2.7–2.9 mg/kg accordingly (Table 1).

We examined functional indicators of laboratory animals after the experiment was over and established statistically significant disorders occurring in some organs and systems. Thus, chronic consumption of water with barium concentration being 70 mg/l made for a statistically significant rise in blood pressure (both systolic and diastolic) in all experimental groups. White rats had SBP by 5.5 % ($p < 0.003$) and DBP by 9.4 % ($p < 0.009$) higher; animals with induced neuropathy, SBP by 9.7 % ($p < 0.001$) and DBP by 9.3 % ($p < 0.005$) higher; hypertensive rats, SBP by 14.8 % ($p < 0.003$) and DBP by 18.6 % ($p < 0.02$) higher (Table 2). Hypertension developed most apparently under exposure to

[4] Guide for the care and use of laboratory animals. Washington, D.C., National Academies Press, 1996, 154 p.

Table 1

A consumed dose and water consumption by rats under exposure to solutions with different barium concentrations and mineralization levels in the chronic experiment, Me (P_{25}–P_{75})

Experiment groups		Indicators, measuring units	
Animals	Group	Water consumption, ml	Dose, mg/kg a day
White rats	“control”	84.6 (71.4–97.8)	–
	“Ba1.3”	84.8 (71.6–98.0)	0.05 (0.05–0.05)
	“Ba 70”	84.7 (71.5–97.9)	2.70(2.68–2.72)
	“M 1500”	84.6 (71.4–97.8)	–
	“M 10,000”	85.0 (71.8–98.2)	–
White rats with neuropathy (EINP)	“EINP control”	85.2 (71.9–98.3)	–
	“EINP Ba 1.3”	85.0 (71.7–98.0)	0.05 (0.05–0.05)
	“EINP Ba 70”	85.3 (72.0–98.3)	2.71 (2.57–2.75)
	“EINP M 1500”	91.6 (72.8–103.5)	–
	“EINP M 10,000”	84.5 (78.1–97.1)	–
SHR (spontaneously hypertensive rats)	“SHR control”	105.0 (91.7–120.7)	–
	“SHR Ba 1.3”	106.3 (93.0–119.3)	0.05(0.05–0.06)
	“SHR Ba 70”	107.4 (94.1–120.4)	2.91(2.68–3.17)

Table 2

Blood pressure and heart rate of SHR under exposure to solutions with different barium concentrations in the chronic experiment, Me (P_{25}–P_{75})

Experimental groups	Blood pressure, measuring units					
	Initial			After 6 months		
	SDP, mm Hg	DBP, mm Hg	Heart rate, str./min	SDP, mm Hg	DBP, mm Hg	Heart rate, str./min
“SHR control”	140 (138–144)	123 (118–125)	484 (471–490)	189 (177–201)	167 (160–190)	534 (520–556)
“SHR Ba 1.3”	142 (133–147)	122 (113–123)	483 (473–491)	189 (184–202)	175 (163–186)	544 (532–555)
“SHR Ba 70”	145 (139–148)	123 (111–129)	486 (479–491)	217 (210–226)*	198 (193–206)*	534 (528–545)

Note: * means statistically significant differences at $p < 0.02$.

barium in a concentration equal to 70 mg/l in SHR since their blood pressure on average grew by 30 mm Hg with DBP growth being the most apparent. Heart rate did not change in any experimental group.

We detected a statistically significant growth in rats’ body mass in the experiment that involved chronic exposure to barium in drinking water in a concentration equal to 70 mg/l. Body mass of white rats grew by 2.8 % ($p < 0.003$); rats with nephropathy, by 6.1 % ($p < 0.02$); and hypertensive rats, by 5.1 % ($p < 0.01$) whereas there was no growth in body mass of rats from all the other test groups against the control ones.

When animals with kidney failure and without any renal pathology were exposed to barium in a concentration equal to 70 mg/l, this made for developing leukocytosis. It became apparent via growing levels of leukocytes and neutrophils, by 19.9 and 32.0 % ($p < 0.003$) against the control groups and by 14.6 and 16.7 % ($p < 0.01$) accordingly against the control group with nephropathy (EINP control). We also detected a 10.9 % decrease in thrombocytes ($p < 0.006$) and lower hemoglobin contents in erythrocytes (by 7.2 %) ($p < 0.001$), which determined its level in the test animal being by 4.2 % ($p < 0.001$) lower than in the control animals with nephropathy.

Toxic effects produced by barium on animals with nephropathy became obvious due to a more apparent decline by 12.5 % in total protein contents in blood ($p < 0.006$), and a

5.0 % growth in creatinine concentration ($p < 0.001$). Changes detected in blood serum of experimental animals with model pathology that were exposed to solutions with mineralization equal to 10,000 mg/l became obvious since mineral metabolism was apparently impaired. It was confirmed by statistically significantly lower phosphor and magnesium concentrations, by 19.7 and 12.5 % accordingly, as well as a 2.2 time decrease in uric acid concentration against the control group of white rats that were given gentamicin.

Exposure to barium in a concentration equal to 70 mg/l initiated weak leukocytosis in SHR as well but there were no other statistically significant changes in morphofucntional indicators of SHR blood (Table 3).

We compared biochemical blood indicators under exposure to barium in a concentration equal to 70 mg/l in the white rats control and SHR. The comparison revealed lower contents of total protein, by 20.7 % ($p < 0.004$) and 16.2 % ($p < 0.001$); and a higher AST concentration, by 21.4 % ($p < 0.001$) and 10.6 % ($p < 0.003$) accordingly. We should note that there were multi-directional shifts in mineral metabolism of hypertensive rats exposed to barium in a concentration equal to 70 mg/l such as an increase in phosphor concentration in blood serum by 25.7 % ($p < 0.001$) and a decline in magnesium concentration by 7.8 % ($p < 0.02$).

Chronic exposure to barium in a concentration equal to 70 mg/l induced proteinuria and its signs were more apparent in animals with nephropathy. Spontaneously hypertensive rats, in contrast to other animals, had statistically significant disorders of mineral metabolism and nitrogen-containing products of protein metabolism in their urine under exposure to barium in a concentration equal to 70 mg/l (Table 4).

We did not detect any changes in functional state of white rats' kidneys after they were exposed to drinking water with mineralization being 1500 mg/l. Still, drinking water with mineralization being 10,000 mg/l induced functional disorders of the urinary excretion system. We detected a statistically significant decrease in phosphor and magnesium contents in urine, by 42.4 and 35.7 % accordingly together with elevated urea excretion; these signs were even more apparent in animals with chronic nephropathy. We should also note that α-amylase excretion with urine fell by 19.4 % ($p < 0.01$) in comparison with the control white rats with kidney pathology.

Table 3

Morphofunctional indicators of SHR blood under exposure to solutions with different barium concentrations in the chronic experiment, Me (P_{25}–P_{75})

Indicators, measuring units	Experimental groups, exposure levels, mg/l		
	Control	Ba 1.3	Ba 70
Leukocytes, $\times 10^9$ cells/l	14.2 (13.6–14.9)	14.5 (12.9–15.5)	16.7 (15.9–17.2)*
Neutrophils, $\times 10^9$ cells/l	2.7 (2.5–2.9)	2.6 (2.4–2.8)	3.2 (2.9–3.5)*
Lymphocytes, $\times 10^9$ cells/l	9.4 (8.5–10.2)	9.1 (8.4–9.9)	9.3 (8.3–9.9)
Monocytes, $\times 10^9$ cells/l	1.2 (0.9–1.6)	1.0 (0.7–1.5)	1.1 (0.9–1.3)
Eosinophils, $\times 10^9$ cells/l	0.87 (0.80–0.91)	0.87 (0.81–0.91)	0.89 (0.83–0.95)
Basophils, $\times 10^9$ cells/l	0.18 (0.11–0.19)	0.17 (0.16–0.20)	0.18 (0.15–0.21)
Erythrocytes, $\times 10^{12}$ cells/l	8.2 (8.0–8.4)	8.1 (8.0–8.3)	8.1 (7.9–8.6)
Hemoglobin concentration, g/l	142 (139–143)	140 (139–141)	143 (142–143)
Hematocrit, l/l	0.39 (0.37–0.41)	0.38 (0.37–0.39)	0.39 (0.39–0.40)
Average erythrocyte volume, fl	51.4 (51.0–51.8)	51.1 (50.2–51.7)	51.5 (49.8–52.1)
Average hemoglobin contents in erythrocytes, pg	18.3 (18.1–18.7)	18.3 (18.1–18.7)	18.5 (17.8–18.7)
Average hemoglobin concentration in erythrocyte, g/l	363 (362–364)	363 (362–364)	364 (362–368)
Thrombocytes, $\times 10^9$ cells/l	849 (823–935)	853 (729–1015)	863 (844–900)
Average thrombocyte volume, fl	6.2 (6.1–6.3)	6.2 (6.1–6.3)	6.3 (6.1–6.3)

Note: * means statistically significant differences at $p < 0.001$.

Table 4

Functional state of SH rats' kidneys under exposure to solutions with different barium concentrations in the chronic experiment, Me (P_{25}–P_{75})

Indicators, measuring units	Experimental groups, exposure levels, mg/l		
	Control	Ba 1.3	Ba 70
Total protein, g/l	5.4 (5.2–6.0)	5.6 (5.4–5.8)	6.6 (6.1–7.0)*
Phosphor, mmol/l	33.9 (22.5–43.0)	33.3 (28.7–38.3)	17.9 (14.8–20.0)*
Iron, µmol/l	17.4 (17.1–17.5)	17.3 (16.4–17.5)	17.3 (16.4–18.7)
Magnesium, mmol/l	0.87 (0.54–0.98)	0.92 (0.81–1.00)	0.51 (0.46–0.54)*
Urea, mmol/l	251 (230–329)	232 (213–258)	192 (177–224)*
Uric acid, µmol/l	3700 (3303–3706)	3568 (3310–3689)	2916 (2791–3048)*
α-amylase, units/l	1185 (986–1234)	1197 (1074–1293)	1134 (1026–1247)
Creatinine, µmol/l	5244 (3480–6476)	5305 (4848–5935)	2753 (2359–3073)*
Glucose, mmol/l	0.99 (0.83–1.05)	1.02 (0.97–1.07)	0.92 (0.82–0.98)
Diuresis, l^{-3}/days	13.8 (13.0–14.1)	14.4 (14.0–15.2)	13.6 (13.1–13.9)
pH, pH units	7.1 (7.0–7.2)	6.9 (6.7–7.0)	7.0 (6.7–7.2)

Note: * means statistically significant differences at $p < 0.01$.

We analyzed relative mass coefficients (RMC) of internal organs taken from the experimental animals 6 months after gentamicin was administered in them. The analysis revealed that the liver mass grew by 5.3 % ($p < 0.02$) and the stomach mass grew by 16.4 % ($p < 0.001$) whereas kidney RMC went down by 6.8 % ($p < 0.03$). The heart mass grew statistically significantly in all animal groups (SHR, rats with nephropathy, white rats without kidney pathology) under exposure to water solutions with mineralization being 10,000 mg/l and barium in a concentration equal to 70 mg/l. Barium in this concentration also made for a decrease in liver and stomach RMC by 6.8 % ($p < 0.04$) and 21.2 % ($p < 0.001$) accordingly in animals with nephropathy and mineralization equal to 10,000 mg/l induced a decrease in the stomach mass by 20.0 % at $p < 0.001$.

The aforementioned changes in relative mass components as well as functional disorders detected in internal organs of experimental animals are confirmed by morphological examinations. Thus, after white rates were chronically exposed to barium in a concentration equal to 70 mg/l, we detected slight focal diffuse dystrophic changes in their cardiac muscle, signs of myocarditis, focal chronic hepatitis with slight hepatocytes dystrophy (1/3 parts of the lobule periphery), pyelitis and moderate dystrophic and necrobiotic changes in the epithelium of the proximal renal tubules. Chronic exposure to water solutions with mineralization being 10,000 mg/l resulted in kidney, heart and liver lesions in experimental animals. We detected focal diffuse dystrophic changes in the cardiac muscle and myocarditis, focal chronic hepatitis with hepatocytes dystrophy (2/3 parts of the lobule periphery), pyelitis and focal dystrophic changes in the epithelium of the proximal renal tubules, chronic slight active atrophic-hyperplastic gastritis.

After gentamicin was administered into experimental animals from "EINP control" group, we detected the following changes in their internal organs: slight liver and kidney dystrophy, signs of pyelitis together with glomerule lesions and signs of hepatitis. We did not detect any pathological changes in the heart and stomach. However, after white rats were exposed to barium in a concentration equal to 1.3 mg/l, we detected slight disorders, such as changes in the kidneys together with pyelitis but there were no toxic effects produced on the heart or stomach. After exposure to barium in a concentration equal to 70 mg/l, the animals had apparent changes in the kidneys, cardiac muscle lesions with developing myocarditis, and slight hepatocytes dystrophy. There was also chronic active gastritis with signs of hyperplasia and gland epithelium atrophy. Mineralization equal to 1500 mg/l induced slight hepatocytes dystrophy, signs of hepatitis, and slight changes in the kidneys of the experimental animals with nephropathy without any toxic effects produced on the heart or stomach. However, after these animals were exposed to water solutions with mineralization being 10,000 mg/l, we established moderate lesions of the cardiac muscle and kidneys, signs of developing pyelitis and myocarditis, moderate hepatocytes dystrophy as well as chronic active gastritis with hyperplasia and gland atrophy together with epithelium hypersecretion.

After SH rats underwent chronic exposure to barium in water in a concentration being equal to 1.3 mg/l, we did not detect any signs of toxic effects produced on the heart, liver or stomach of the experimental animals. There were slight changes in the epithelium of proximal renal tubules typical for such laboratory animals. After hypertensive rats were exposed to barium in a concentration equal to 70 mg/l, they had apparent changes in the epithelium of the proximal renal tubules, developing glomerulonephritis and pyelitis; there were also moderate lesions of the liver and heart. We detected chronic active gastritis with signs of both hyperplasia and gland atrophy and epithelium hypersecretion and desquamation.

Therefore, our test results indicate that toxic effects produced by the model chemicals under chronic 6-month experimental exposure were more apparent in the animals with modeled experimental pathologies (spontaneous hypertension and experimentally gentamicin-induced nephropathy) than in the classical (healthy) animals. Morphofucntional disorders detected in the urinary excretion system, cardiovascular system and hepatobiliary system proved that pathologies were developing in the experimental animals under chronic exposure to the analyzed chemicals in certainly effective concentrations. Toxic effects produced by barium in a concentration equal to 70 mg/l became apparent through developing leukocytosis, impaired protein metabolism, elevated blood pressure, morphofucntional changes in the heart with its mass growing obviously, as well as signs of chronic hepatitis, pyelitis, and dystrophic changes in the epithelium of the proximal renal tubules. After white rats were exposed to water with mineralization being 10,000 mg/l, this led to impaired mineral and protein metabolism as well as developing slight lesions of the kidneys, heart and liver. Barium in a concentration equal to 1.3 mg/l and mineralization being 1500 mg/l can be considered no-effect doses in this chronic experiment on rats.

Conclusions. We have suggested methodical approaches to applying experimental pathology models to assess health risks and to establish hygienic standards for chemicals. The approaches consider sensitive population groups (people suffering from chronic non-communicable diseases or taking certain drugs constantly). The methodology was tested on drinking water in the chronic experiment on model animals with spontaneous hypertension and experimentally induced chronic nephropathy. The model chemical indicators (barium and total mineralization) were selected for the experiment since they are typical for water-bearing horizons in the Republic of Belarus. The results confirmed our assumption that pathology models were authentically more sensitive and susceptible to toxic effects produced by the analyzed chemicals than classical models ("healthy" animals).

This allowed us to recommend using experimental models of congenital and induced animal pathology bearing in mind target organs for toxic effects produced by the analyzed chemicals to substantiate hygienic standards, health risks taken into account. This should be done at the stage when dose-dependent reactions are identified (determination of no-effect and/or threshold exposure levels) in addition to conventional studies performed on "healthy" animals. It is most appropriate to use this approach when the following conditions are met: 1) a research object is naturally occurring chemicals that are widely spread in the environment due to its natural formation; 2) pathologies of organs (systems) that are targets for biological effects produced by the tested chemicals are widely spread in a population (circulatory diseases, diseases of the excretory system, etc.).

It is also quite appropriate to examine biological effects produced by chemicals to determine their no-effect concentrations (doses) for reference effects in a chronic experiment on animals with model pathologies. Model pathologies should be selected bearing in mind organs that are targets for toxic effects produced by analyzed chemicals. When such experiments are performed in addition to conventional ones on "healthy" animals, this allows achieving more precise health risk assessment and creating more reliable hygienic standards for chemical concentrations in the environmental objects. This gives an opportunity to consider sensitive population groups and can also "enhance" an evidence base when hygienic standards for chemicals in various media are being revised, regional peculiarities taken into account, to make them less "strict" (risk-based standardization).

The suggested methodical approaches have been formalized in the instructions "The procedure for hygienic standardization of chemicals in drinking water as per health risk".

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