PREVENTIVE HEALTHCARE: TOPICAL ISSUES OF HEALTH RISK ANALYSIS

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Review

DEVELOPMENT OF THE RISK ANALYSIS METHODOLOGY GIVEN THE CURRENT SAFETY CHALLENGES FOR PUBLIC HEALTH IN THE RUSSIAN FEDERATION: VITAL ISSUES AND PROSPECTS

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The contemporary socioeconomic situation creates multiple safety challenges in the Russian Federation including public health safety. These challenges cannot be ignored when formulating strategic tasks of health risk analysis within predictions of the socioeconomic development of the Russian Federation for the period up to 2030. Targeted development of the risk analysis methodology in the Russian Federation has provided solid grounds for successful solution of primary tasks related to providing sanitary-epidemiological wellbeing of the country population. It has created a platform for further improvement of activities performed by the Rospotrebnadzor in various spheres. This includes development and greater detailing of results obtained by examining how health risks occur under exposure to heterogeneous environmental factors and work-related ones considering their combined effects. Another significant trend is proactive development of methods for assessing and managing health risks associated with potentially hazardous factors of new technologies and products (nanotechnologies, new foods, etc.).

Several fundamental aspects of risk analysis can be considered vital at the moment. This includes investigating mechanisms of risk occurrence; establishing regularities of risks of negative health outcomes with various severities under ongoing integration of body systems dysfunctions and considering capabilities of the body to recover its proper functioning and its adaptive resources; finding solutions to an issue associated with assessing additive properties of effects produced by risk factors including heterogeneous ones. Fundamental aspects of health risks analysis development are closely connected with an issue associated with formulating fundamentals of an information platform eligible for this methodology. It is impossible to achieve any development in investigating mechanisms of health risks occurrence under exposure to heterogeneous environmental factors and work-related ones without applying up-to-date investigation techniques, digital ones included.

The existing safety challenges for public health in the Russian Federation include the necessity to protect public health in order to extend a period of economic activity of the population and to develop labor and economic potential of the country; high levels of adverse impacts on the public health exerted by chemical, physical, and biological environmental factors; insufficient 'digital maturity' of methods employed to predict threats and provide sanitary-epidemiological wellbeing of the population. Given all the aforementioned, it seems advisable to outline the following promising trends in the development of the health risk analysis methodology: developing the fundamentals the methodology is based on; enlarging practical use of health risk assessment results in everyday activities of the Rospotrebnadzor; creating an information platform and digitalizing health risk analysis; developing a methodology for substantiating effective preventive programs aimed at health risk management.

Keywords: *health risk, safety, risk analysis methodology, information platform, digitalization.*

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The current socioeconomic situation creates a lot of safety challenges in the Russian Federation including safety of population health [1]. These challenges include an unfavorable sociodemographic situation that hampers the development of the state labor and economic potential; persistently strong adverse effects produced on the population health by chemical, physical and biological environmental factors; insufficient 'digital maturity' of methods employed to predict hazards and provide sanitary-epidemiological safety of the population.

These challenges cannot be ignored when formulating strategic tasks of health risk analysis within predictions of the socioeconomic development of the Russian Federation for the period up to 2030. The Prediction made by the RF Ministry of Economic Development in 2013 stipulates spheres and expected results of the socioeconomic development of the Russian Federation in future. They include a growth in life expectancy at birth to 78 years in 2030; a reduction in pollutant emissions from stationary sources down to 0.22 tons per 1 million rubles of the country GDP; a reduction in a number of cities with high and extremely high ambient air pollution down to 34.

This Prediction also creates a unified platform for developing strategies and targeted programs as well as middle-term forecasts and plans fixed in relevant documents.

It is advisable to coordinate strategic tasks of health risk analysis within providing sanitary-epidemiological wellbeing with development targets fixed within National Projects of the Russian Federation. For example, the aim of the Demography National Project is to create such conditions for people that allow them to live as long as possible without any limitations due to ageing and chronic diseases. The aim of the Ecology National Project is to reduce the total volumes of pollutant emissions by 2 million tons. There are also other important aims fixed in the Healthcare, Housing and Urban Environment, and Digital Economy National Projects.

Safety is understood as absence of impermissible risks for life and health both in Russian and international legislation. Health risk analysis methodology is among the most effective instruments for identifying spheres of human activities with the highest likelihood of health impairments due to environmental exposures and the necessity to substantiate certain decisions able to minimize this likelihood. Underestimating risks and hazards can lead to substantial losses in future; risk overestimation results in unjustified labor and financial costs, which are highly undesirable, especially in a period when an economic situation is unstable. Given that, a basic conceptual challenge in health risk analysis should be development of the methodology for health risk analysis aimed at achieving greater precision of risk assessments and higher effectiveness of risk mitigation.

Development of the methodology for health risk analysis has been described in detail within the public management of the sanitary-epidemiological wellbeing of the population [2]. This article also points out that targeted development of the risk analysis methodology in the Russian Federation has provided solid grounds for successful solution of primary tasks related to providing sanitary-epidemiological wellbeing of the country population. It has created a platform for further improvement of activities performed by the Rospotrebnadzor in various spheres. This includes development and greater detailing of results obtained by examining how health risks occur under exposure to heterogeneous environmental factors and work-related ones considering their combined effects. Another significant trend is proactive development of methods for assessing and managing health risks associated with potentially hazardous factors of new technologies and products (nanotechnologies, new foods, etc.).

When identifying promising trends in this development, it is advisable to consider risk analysis as a synthetic methodology that integrates essentials of several sciences including hygiene, medicine, biology, chemistry, mathematics, sociology, social sciences, etc. to obtain necessary results in accordance with relevant research tasks [3]. These essentials provide solid grounds for fundamentals of health risk analysis and promising trends in the development of the risk analysis methodology. They primarily include examinations of risk occurrence mechanisms. As opposed to description how the body systems function and how pathologies occur in them, which can be found in fundamental medicine, description of risk occurrence mechanisms involves using complexes of deterministic and probabilistic characteristics. A time component is very important in risk occurrence; it is advisable to follow two directions when investigating its role. Firstly, it is necessary to study how the body functions change due to natural causes in order to isolate negative responses to environmental exposures. Secondly, any information on dynamics of mutual influences exerted by organs and systems in the body, which can be derived by special research, makes it possible to differentiate a risk of negative health outcomes associated with a set of hazard factors as per a time of its realization. This is important for developing a methodology for examining risk evolution and substantiating risk management activities.

Another extremely important component in tackling these challenges is to establish regularities of risks of adverse effects with different severity given the existing integration of disruptions in proper functioning of the body systems and considering possible functional recovery of the body and its adaptation reserves during periods when exposure is less intensive or not present at all. This trend in fundamental research can be considered a priority one for developing risk assessment methods under intermittent burdens that are typical, for example, for occupational exposures.

Studies on adaptation processes have a substantial role in assessing hazards posed by various effects. This can make a crucial contribution to clarifying perceptions of which changes in health should be considered harmful and which should not. A comprehensive study of this postulate will make it possible to achieve much more specific perceptions of threshold limits of risk factors and, consequently, to develop conceptual perceptions of risk assessment methods and use of 'exposure – effect' threshold models.

Fundamental aspects of studies that determine principal outlooks in the health risk assessment methodology include solving a task of assessing additive effects produced by health risk factors, heterogeneous ones included. Methodical approaches to integrating probabilities in the general risk theory assume that likelihood of a response to exposure to two risk factors simultaneously is always lower than a sum of likelihoods of responses to exposure to each of these two factors separately. Theoretical provisions in the contemporary toxicology assume both additivity and potentiation (synergy) and antagonisms of toxic effects. The existing methods for health risk assessment accept a hypothesis that factors may have additive effects. This is explained by a possibility to neglect essence of combined effects under rather low levels of exposure that typically occur in real conditions. Identification of a real picture would give grounds for improvement of methods for modeling an 'exposure – effect' relationship.

An issue associated with formulating basic provisions about an information platform for the health risk analysis methodology is also close to fundamental aspects of the methodology development. These provisions should cover collecting relevant data for risk assessment, a system for storing these data and rules of getting access to them, filling new data into information databases, and coordination with the existing information resources. The main target of creating a national information platform for risk analysis is to bring together subjects, who assess risks, manage them, and communicate about risks and ways to mitigate them, in a unified information space. An information platform is a powerful tool for providing risk transparency, which is one of the basic principles of risk analysis.

Creation and development of a national information platform for risk analysis involves three basic structural components in accordance with the structure of health risk analysis. They are aimed at providing risk assessment, risk management, and risk communications.

The component that provides risk assessment should include databases about health risk factors for general population, workers, and consumers; information about identified levels of exposure to these factors; data on types and parameters of 'exposure – effect' relationships as well as on scientific substantiation of these data; information about risk categories and scales together with data on recommended measures adequate to levels of established health risks. It is advisable to supplement this component with accompanying information about experience in health risk assessment and software employed in the process.

Information support as regards risk management means there should be an economic block to calculate costs of a risk with subsequent assessment of risk management effectiveness. Other important elements include a database with data on the most effective sanitary-technical and medical-preventive technologies; a system of criteria that describe permissibility of health risks and hygienic standards based on health risks; a system for assessing potential hazards of economic activities to be used when planning relevant activities including control and surveillance ones.

An information platform is an information system in its essence; that is, it is a set of technical and organization support and software as well as qualified personnel. This system should timely provide decision makers with objective data necessary for adequate health risk analysis. In its turn, an information system as support for health risk analysis should be considered a basic structural element of the Federal State Information System (FSIS) of sanitary-epidemiological data; this creates necessary preconditions for transforming it into a digital platform.

Digitalization is an exceptionally important trend in risk analysis able to transform analogue data and their processing into a digital format. The prospects of its implementation within the FSIS of sanitary-epidemiological data provide wide opportunities for using digital technologies to achieve automation of decision-making in risk analysis. They make it possible to consider how to use artificial intellect in health risk assessment using big data and optimizing decisions aimed at risk mitigation including control and surveillance activities. This implementation also provides easy electronic access to any relevant information about health risks and ways to prevent or mitigate them. Transformation of information databases into knowledge bases and use of up-to-date digital technologies for data analysis such as neural networks, dynamic evolution models, etc. gives new opportunities to make risk management more effective due to use of artificial intellect and reduction in labor and financial costs.

The FSIS of sanitary-epidemiological data as a unified digital system for activities performed by the Rospotrebnadzor organs and institutions can become an intellectual basis for improvement and wide implementation of the health risk assessment methodology into practice. Another important aspect here is provision of interactions between the Rospotrebnadzor and other public authorities, economic entities, civil society, and other parties involved in public administration in an electronic format.

Improvement of a fundamental and information base should be considered relevant trends able to provide necessary development of the risk analysis methodology. They give grounds for trends that are more applied in their essence.

This year, the regulatory and methodical basis for health risk assessment has been renewed substantially. By now, two Guides have been renewed and approved, namely, Human Health Risk Assessment from Environmental Chemicals and the Guide on Assessment of Occupational Risks for Workers' Health.

These documents have several conceptual distinctions now. First of all, they have approved a new health risk definition where health risk is defined as a combination (product) of likelihood (or frequency) of health harm and severity of this harm. Also, methods for health risk quantification have been developed and harmonized scales of risk categories have been provided.

Risk assessment parameters are being further developed based on fundamentals stated in these documents. Thus, a system of quantitative criteria has been introduced to assess non-carcinogenic health risks under chronic inhalation exposure to a chemical. In addition to reference concentrations, it includes some additional exposure criteria that describe negative health outcomes in organs and systems excluding the critical ones [4]. In future, such a system of criteria can be added with parameters of mathematical models that describe exposure – response relationships; these parameters allow quantifying non-carcinogenic health risks.

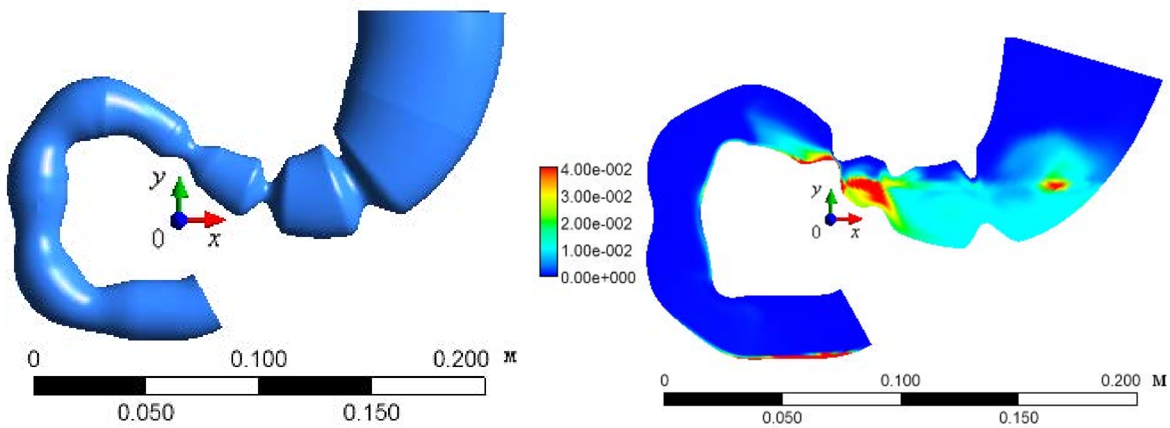
It is impossible to secure further development of methods for examining risk occurrence under exposure to heterogeneous environmental factors and work-related ones without employing up-to-date research techniques, digital ones included. Mathematical modeling is a promising way to investigate dysfunctions of the critical organs and systems under exposure to risk factors. Mathematical models are able to describe evolution of functional disorders in the body, to establish interrelations between organs and system, and to identify cause-effect relations between body responses and exposures.

Traditional experimental studies such as MRI, ultrasound scanning and endoscopy allow assessing some functional, morphological, and geometric parameters of internal organs. As opposed to them, mathematical modeling has greater accuracy in measuring and is significantly less time and labor-consuming.

Thus, a suggested mathematical model that describes how a multi-phase multi-component mixture flows in the three-dimensional antroduodenal section of the GIT (Figure 1) makes it possible to assess disorders of some basic functions, availability of mass sources due to interphase exchange, secretion and absorption of the mixture components. The authors examined influence of functional disorders and properties of different phases that describe food on the flow properties in the antroduodenal section of the GIT by conducting numeric experiments [5, 6].

Mathematical modeling is one of the most effective ways to find an optimal strategy for examining and predicting a course of viral infections. This approach allows saving time and resources necessary to solve the problem. Mathematical models make it possible to analyze effects produced by various factors and their combinations on the individual and population levels.

A structural scheme of a model that describes how the immune and neuroendocrine systems function in case of a viral infection consists of a set of interrelated elements of the immune and neuroendocrine system which are the most significant components in a bode response to a virus invasion [7]. The model allows for functional state of organs which are being considered. Factors influencing changes in their state include natural ageing and negative impacts exerted by various chemicals penetrating a body from the environment.



a *b*

Figure 1. *a*) Three-dimensional antroduodenal section of the GIT with peristaltic waves; *b*) volume fraction of food particles in the antroduodenal section of the GIT

The equation which defines how fast a number of healthy cells changes under virus invasion and immune response can be given as follows

$$\frac{dC_{HE}}{dt} = k_1 \left(C_{HE} + C_R \right) C_D + $$
$$+ k_2 C_R - k_3 C_{HE} C_{IFN} - k_4 C_{HE} C_V ,$$

where C_{HE} is a number of healthy non-resistant cells in a target organ;

C_R is a number of resistant cells in a target organ;

C_D is a number of dead cells in a target organ;

C_{IFN} is interferon concentration;

C_V is concentration of viruses.

Ambient air pollution is a widely spread and significant issue since it is a priority risk factor for human health affecting people throughout the life span. This makes it necessary to develop methods for predicting development of pathological states based on evolution mathematical models [8–10].

When airflow is modeled in the airways using computational aeromechanics, a complicated geometry of the hierarchical structure of the airways, starting from the trachea and large bronchi and further to the alveoli, is considered a continuous porous medium. Mathematical tasking is based on the basic mechanics laws, elasticity theory and filtration theory ratio. This approximation allows a substantial decrease in difficulties involved in mathematical description of how a gas and dust mixture moves along the huge volume of smaller airways and eases off the requirements to computational resources necessary to perform relevant computations [11, 12].

Mathematical description of particle trajectories in the airways was accomplished within modeling dust-carrying airflow (Figure 2). A series of computations was accomplished; they were then verified by an experiment on estimating changes in the disperse structure of a dust fraction in various sections of the respiratory system. This made it possible to identify probable levels of dust pollution in the respiratory area in order to model how deep dust particles would be able to penetrate into the lungs and into blood circulation from them.

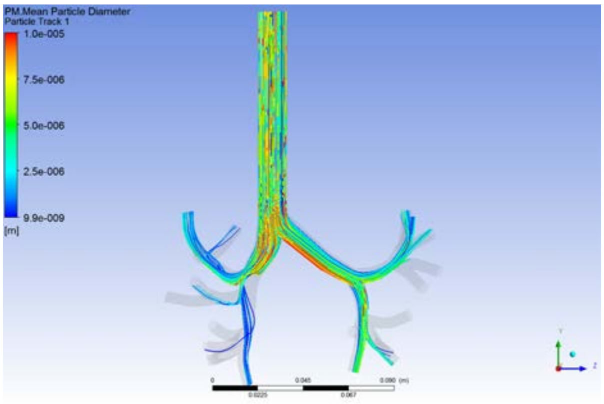


Figure 2. Particle trajectories in the airways (red color means large particles; blue color, smaller ones)

The suggested mathematical models that describe the human digestive, respiratory, immune and endocrine systems allow predicting changes in the functional state of these systems and their elements. Modeling results can then be used in evolution modeling of risk and predicting its levels under various environmental exposures.

Scientific and technological development constantly creates new challenges and facing them requires improvement of the conventional methodical approaches to health risk assessment. This is primarily due to emergence of new sources and types of factors that are potentially hazardous for human health.

Safety of new food products is now in the focus of the most heated discussion; this includes genetically modified organisms (GMO) with genotypes artificially modified by genetic engineering. As a rule, genetic modifications are made to achieve some research or economic goals. Nowadays, use of transgenes to create transgene organisms is the most common genetic modification[1].

[1] Zaid A., Hughes H.G., Porceddu E., Nicholas F. Glossary of biotechnology for food and agriculture: a revised and augmented edition of the glossary of biotechnology and genetic engineering. Rome, FAO, 2001.

Multiple research articles concentrate on examining possible risks associated with GMO creation [13].

At the same time, some experts believe that biotechnologies as such, GMO in particular, do not pose greater hazards than, for example, traditional selection technologies [13–19]. We should probably agree with an opinion stated in *Science* in 2000 [20] that there are very few data on health risks of GM-products but much more opinions [21]. This determines another trend in the development of the health risk assessment methodology, namely, assessing and managing health risks caused by GMO use considering both their direct and indirect effects.

Basic trends in the development of the system for GMO safety assessment in the Russian Federation have been outlined in studies by the Federal Research Center for Nutrition and Biotechnology [22].

Spread of new materials, including chemically synthesized ones, remains a serious threat for human health. Peculiarities of exposure to such materials, both separately to one of them or to their combination, and occurrence of health risks caused by such exposure need to be investigated. Among such materials, we should not fail to consider nanoparticles and nanomaterials.

Nanoparticles and nanomaterials have specific physical and chemical properties and are able to produce biological effects that often differ drastically from properties or effects of the same chemicals in a form of solid phases or macroscopic dispersions. Nanosized structures have several specific physical and chemical traits such as an elevated chemical potential on the interphase boundary with a high curvature (nanoparticles usually have high surface curvatures and atomic bonds on their surfaces have specific topology; this leads to changes in their chemical potentials and, as a result, substantial changes in solvability, as well as reactivity and catalytic capabilities of nanoparticles and their components); nanomaterials usually have large specific surface area and this increases their absorption capacity, chemical reactivity and catalytic properties and results in greater production of free radicals and reactive oxygen species and lesions of biological structures; nanoparticles tend to have smaller sizes and are very variable in their shapes (due to their small sizes, nanoparticles can get bonded to nucleic acids and proteins, penetrate membranes and cell organelles thereby changing functions of biological structures); high adsorption activity (given their high developed surfaces, nanoparticles are effective adsorbents and are able to absorb much greater volumes of adsorbates per a unit of their mass than macroscopic dispersions); great capability to accumulate.

All the aforementioned indicates that nanomaterials, which have physical and chemical properties different from those of their traditional analogues and are able to produce different biological effects as well, should be considered a new type of materials and articles. It is mandatory to create profiles of their potential risks for human health and life.

Conceptual postulates of the health risk assessment methodology, methods for identification and quantification of nanomaterials are being developed at the moment within assessing health risks caused by new sources and other hazard factors. The Concept of Toxicological Studies, Risk Assessment Methodology, Methods for Identification and Quantification of Nanomaterials was approved in 2007[2].

To develop the approved Concept, several methodical documents have been created. They stipulate how to identify nanomaterials that are potentially hazardous for human health, how to assess them and organize con-

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[2] Ob utverzhdenii Kontseptsii toksikologicheskikh issledovanii, metodologii otsenki riska, metodov identifikatsii i kolichestvennogo opredeleniya nanomaterialov: Postanovlenie Glavnogo gosudarstvennogo sanitarnogo vracha RF ot 31.10.2007 № 79 [On Approval of the Concept of Toxicological Studies, Risk Assessment Methodology, Methods for Identification and Quantification of Nanomaterials: the Order by the RF Chief Sanitary Inspector issued on October 31, 2007 No. 79]. *GARANT: information and legal support*. Available at: https://base.garant.ru/12157240/ (September 18, 2023) (in Russian).

trol over them[3]. These documents point out that any report issued after a control procedure that covered nanoparticles / nanomaterials should contain assessment of human health risks associated with exposure to them as well as suggestions on necessary activities and their scope to mitigate human health risks caused by nanomaterials. An algorithm was suggested with its aim to identify nanomaterials that could be potentially hazardous for human health. It should ensure, with the highest authenticity which is possible given the available scientific knowledge, that an estimated nanomaterial is ranked as having one out of at least three levels of potential hazards, namely:

– low potential hazards. Toxicological assessment of a nanomaterial relies on using indicators recommended for its components in a traditional form (macro-dispersed or solid phase). Any studies on specific biological effects produced by nano-sized components can be conducted on a selective basis;

– medium potential hazards. General toxicity of a material in its nano-form is assessed; if necessary, some specific examinations may also be conducted;

– high potential hazards. A whole set of necessary studies is conducted to investigate how a nanomaterial penetrates through biological membranes and body barriers; how it is distributed and accumulated in organs and tissues and then excreted from the body; its general toxicity is estimated (acute, sub-acute, and chronic); a complex of specific studies is accomplished including tests to establish genotoxicity, mutagenicity, embryotoxicity, gonadotoxicity, teratogenicity, effects of a nanomaterial on genomic (gene expression), proteomic and metabolomic profiles, immunotoxicity, toxicity for specific organs, ability to penetrate through the GIT barriers, and allergenic potential.

Mathematical modeling is an eligible methodical approach to implementations of the aforementioned algorithms. It allows identifying nanomaterials that are hazardous for human health with the highest authenticity. The method was described as regards technical, biological, and ecological objects in works by V.G. Gmoshinskiy[4]. Some nanomaterials in food products have been examined in research works by the Federal Research Center of Nutrition and Biotechnology [23, 24] and the federal Scientific Center for Medical and Preventive Health Risk Management Technologies [25–27].

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[3] MU 1.2.2520-09. Toksikologo-gigienicheskaya otsenka bezopasnosti nanomaterialov: Metodicheskie ukazaniya, utv. Rukovoditelem Federal'noi sluzhby po nadzoru v sfere zashchity prav potrebitelei i blagopoluchiya cheloveka, Glavnym gosudarstvennym sanitarnym vrachom RF G.G. Onishchenko 05.06.2009 [Toxicological-hygienic assessment of nanomaterials safety: Methodical Guidelines, approved by G.G. Onishchenko, the Head of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing, the RF Chief Sanitary Inspector on June 05, 2009. *KODEKS: electronic fund for legal and reference documentation.* Available at: https://docs.cntd.ru/document/1200074057 (September 18, 2023) (in Russian); MR 1.2.2522-09. Metodicheskie rekomendatsii po vyyavleniyu nanomaterialov, predstavlyayushchikh potentsial'nuyu opasnost' dlya zdorov'ya cheloveka: Metodicheskie rekomendatsii, utv. Glavnym gosudarstvennym sanitarnym vrachom RF 01.07.2009 [Methodical Guidelines on identification of nanomaterials that pose potential hazards for human health: Methodical Guidelines, approved by RF Chief Sanitary Inspector on July 01, 2009]. *GARANT: information and legal support.* Available at: https://www.garant.ru/products/ipo/prime/doc/4088803/ (September 18, 2023) (in Russian); MR 1.2.0054-11. Poryadok i metody otsenki vozdeistviya iskusstvennykh nanochastits i nanomaterialov na toksicheskoe deistvie khimicheskikh veshchestv: Metodicheskie rekomendatsii, utv. Federal'noi sluzhboi po nadzoru v sfere zashchity prav potrebitelei i blagopoluchiya cheloveka, Glavnym gosudarstvennym sanitarnym vrachom RF 29 dekabrya 2011 g. [The procedure and methods for assessing influence of artificial nanoparticles and nanomaterials on toxic effects of chemicals: Methodical Guidelines, approved by the Head of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing, the RF Chief Sanitary Inspector on December 29, 2011]. *GARANT: information and legal support.* Available at: https://www.garant.ru/products/ipo/prime/doc/70041074/ (September 18, 2023) (in Russian); MU 1.2.2966-11. Poryadok i organizatsiya kontrolya za nanomaterialami: Metodicheskie ukazaniya, utv. Federal'noi sluzhboi po nadzoru v sfere zashchity prav potrebitelei i blagopoluchiya cheloveka, Glavnym gosudarstvennym sanitarnym vrachom RF 17.10.2011 [The procedure and organization of control over nanomaterials: Methodical Guidelines, approved by the Head of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing, the RF Chief Sanitary Inspector on October 17, 2011]. *GARANT: information and legal support.* Available at: https://base.garant.ru/70141078/#friends (September 18, 2023) (in Russian).

[4] Gmoshinskii V.G. Inzhenernaya ekologiya [Engineering ecology]. Moscow, Znanie Publ., 1977, 64 p. (in Russian); Gmoshinskii V.G. Praktika prognozirovaniya [Prediciton practices]. Moscow, Znanie Publ., 1972, 63 p. (in Russian).

Workers' health is a most important indicator of a healthy society. It determines quality of human resources and a demographic situation in a country, labor productivity, and a volume of a gross domestic product [28, 29]. Unfavorable working conditions pose permanent threats for workers' health [30, 31].

Some enterprises have been updating technological processes introducing more operator work and thereby reducing a share of manual work and have also introduced continuous technological processes with minimal involvement of human resources. Nevertheless, some operations still require direct control and involvement of personnel. Workers are exposed to a whole range of various occupational factors, which, if taken separately, might be within the established hygienic standards but their combinations can produce adverse effects. Harmful occupational factors can not only cause occupational diseases but also act as pathogenetic mechanisms of occurrence and progression of common non-communicable diseases that cannot be considered occupational [32]. Variety of occupational exposures and their combined effects on workers call for a complex approach when developing activities aimed at improving working conditions, preventing occupational and work-related diseases in workers and mitigating occupational health risks.

Health risks for workers are mostly determined by a level of occupational exposures; however, a worker's natural resistance to effects of various occupational factors also has a significant role in occurrence of occupational health risks. Consequently, likelihood of adverse health outcomes due to various exposures, occupational ones included, can be largely modified by an individual susceptibility of the body [33]. Given that, occupational risk personalization is a relevant trend in the development of the health risk assessment methodology. An issue related to assessing current individual's health and control of any changes in it is becoming more and more important for workers under exposure to harmful occupational factors. Some studies report that development of negative effects caused by environmental exposures is likely to depend on individual susceptibility of the body [34]. Some peculiarities may occur against developing non-specific reactions due to an essence of an affecting factor, direction and localization of functional disorders in the body systems.

Methodical approaches to assessing occupational risk (OR) caused by work intensity (WI) are being developed at present. They make it possible to perform personalized health risk assessment using workers with predominantly mental work as an example [35]. Some approaches have been suggested to assess levels of personalized occupational risks caused by different diseases in workers that are associated with work environment and working conditions [36]. Personalized risk assessments are considered a promising trend as regards investigations of impacts exerted by environmental factors [37].

As new global challenges emerge, such as infectious pandemics, it becomes more and more relevant to investigate combined effects of factors that induce communicable and non-communicable diseases. The necessity to establish peculiarities and regularities in COVID-19 spread requires further research with its focus on formalization and spatiotemporal modeling of the infection spread considering non-infection risk factors that influence it. Modeling established priority risk factors that authentically ($p < 0.05$) modify COVID-19 spread and explain regional differences in intensity of infection, recovery, and fatality. Among anti-epidemic measures, the authentic most positive effects on reduction of the basic reproduction number (R0) were established to be produced by a share of vaccinated people, especially those aged 31–40 years ($r = -0.37$). A growth in average monthly day temperatures in autumn and winter and a year as a whole facilitates transition from susceptible to infected category ($r = 0.21$–0.22). Greater solar insolation during a year and especially in summer slows down this transition from susceptible to infected category; from $r = -0.02$ to $r = -0.23$. Infection rates grow due to influence of such sanitary-epidemiological indicators as working conditions not conforming to hygienic standards (physical factors), ambient air quality in settlements as per chemical pollution and noise (r = 0.29–0.24). Recovery takes authentically longer in regions with comparatively higher levels of alcohol consumption (r = -0.32). The observed regional differentiation in development of specific stages in the epidemic process associated with the COVID-19 delta-strain occurs due to complex interactions and influence of modifying factors. They create a certain multi-level and multi-component system, which is able to transform the epidemic process, either potentiating it or slowing it down [38].

The health risk assessment methodology has been developed in Russia over a rather short period as opposed to developed countries. Still, scientific knowledge has been accumulated over this time and this allows using this methodology in routine practices. Development of Russian scientific approaches to hygienic health risk assessment made it possible to use its results to provide more effective risk management.

At present, health risk analysis is developed in Russia to an extent that allows the country to carry its point in international debate. This concerns hygienic standards that stipulate levels of veterinary drugs in food products and are substantiated as per health risk criteria. Meeting requirements to substantiation of maximum permissible levels in foods as per health risk criteria as regards residual quantities of antibiotics [39, 40], biological agents [41] and muscle growth stimulators [42] allowed including new hygienic standards that do not permit these pollutants in food products into technical regulations.

New methodical approaches have been developed to substantiate maximum permissible levels (MPLs) of chemical pollutants in ambient air as per permissible health risks [43]. Owing to it, a complex system of hygienic standards for levels of adverse chemicals in ambient air has been created in the Russian Federation. The system is unique and includes single maximum levels as well as average daily and average annual ones; the latter ensure that both carcinogenic and non-carcinogenic health risks are acceptable (permissible). By now, average annual MPLs have been substantiated and approved as per health risk criteria for 27 priority chemicals and compounds[5]. However, it is not always possible to make quality of the environment conform to hygienic standards in a short time; therefore, it is still relevant to mitigate health risks for population while technological and sanitary-technical activities aimed at reducing pollution are being accomplished.

In this respect, a promising trend is to develop medical and preventive technologies for risk mitigation.

Technologies aimed at preventing diseases associated with exposure to hazardous factors are based on the following:

– recovery of membrane-cellular mechanisms that provide biotransformation of technogenic chemicals;

– stimulation of natural mechanisms responsible for excreting technogenic chemicals and their metabolites;

– recovery of redox balance at the system level by stimulating functional activity at the cellular and sub-cellular levels;

– stimulation of immune protection and non-specific reactivity;

– recovery of adaptation reserves and vegetative reactivity of the body;

– correction of pathophysiological and pathomorphological disorders in target organs [44].

Medical and preventive health risk management technologies help find solution to the following problems:

[5] Ob utverzhdenii sanitarnykh pravil i norm SanPiN 1.2.3685-21 «Gigienicheskie normativy i trebovaniya k obespecheniyu bezopasnosti i (ili) bezvrednosti dlya cheloveka faktorov sredy obitaniya»: Postanovlenie Glavnogo gosudarstvennogo sanitarnogo vracha Rossiiskoi Federatsii № 2 ot 28 yanvarya 2021 g. [On Approval of the sanitary norms and rules SanPiN 1.2.3685-21 "Hygienic standards and requirements to providing safety and (or) harmlessness of environmental factors for people": the Order by the RF Chief Sanitary Inspector No. 2 dated January 28, 2021]. *The Official Internet-portal of legal information*. Available at: http://publication.pravo.gov.ru/Document/View/0001202102030022 (August 11, 2023) (in Russian).

– identification of target risk groups for providing them with specialized targeted prevention;

– early detection (at the stage when functional disorders occur) of a somatic pathology associated with exposure to hazardous factors;

– optimization of organizational and functional model of prevention under exposure to factors together with implementation of prevention technologies provided with solid etiopathogenetic basis;

– planning of future prevention activities based on assessment of technology effectiveness;

– revision and enrichment of regulatory documents that stipulate provision of preventive care for people suffering from diseases associated with exposure to technogenic chemicals in the environment (standards, protocols, consensuses etc.). Implementation of such programs involves preliminary risk-based clinical and laboratory examinations of risk groups, chemical analyses, functional and laboratory tests aimed at identifying markers of response adequate to risk factors. Therefore, all this ensures targeted implementation of specialized medical and preventive technologies and programs; as a result, their effectiveness is estimated as quite high.

When substantiating and selecting any available risk management techniques, one should bear in mind a considerable role that belongs to the economic component in the process, which considers expenses on implementation of activities and an expected effect, or, in our case, prevented health risks. Consequently, economic health risk assessment is a necessary tool for providing hygienic safety of the population and, as a result, for managing human resources as an extremely important production factor. The suggested methodical approaches to economic health risk assessment include the following:

– assessment of disability period caused by risk realization (fractions of a year);

– assessment of products that have not been manufactured and a value of its lost contribution to an economy of a given terror;

– assessment of changes in cash flows between different RF budgets;

– assessment of changes in cash flows between off-budget funds such as the Social Fund of Russia, Federal Compulsory Medical Insurance Fund, Territorial Compulsory Medical Insurance Funds, etc.

Estimation of losses borne by economic entities due to disability periods caused by risk realization, including budget losses at different levels in the budget system, makes it possible to obtain detailed assessment for management goals [45]. Issues related to economic assessment of health risks for workers [46] and for unemployed population [47] have been given methodical consideration.

When managing risks, we should consider challenges that arise from the current political situation as well as regularities and trends of the state socioeconomic policy within the context of health risk management as a part of the economic safety of a given region or the country as a whole.

At present, Russia is facing strict international sanctions as a specific policy aimed at reducing the GDP growth. Given that, finding solutions to the task of ‘providing economic safety of the RF regions by accomplishing relevant Rospotrebnadzor activities aimed at mitigating population health risks caused by the current sanitary-epidemiological situation’ calls for identifying a system of additional management impacts [48] aimed at improving quality of the environment. It is necessary to assess success and effectiveness of state strategies aimed at health promotion and socioeconomic development with simultaneous provision of economic safety of a given region or the country as a whole due to additional management impacts by Rospotrebnadzor under international sanctions. This assessment can be accomplished considering the following indicators (Figure 3) [49].

The existing safety challenges for population health in the Russian Federation include the necessity to protect population health in order to extend a period of economic activity of the population and to develop labor and economic potential of the country; high levels of adverse impacts on the public health exerted by chemical, physical, and biological environmental factors; insufficient ‘digital maturity’ of methods employed to predict threats and provide sanitary-epidemiological wellbeing of the population. Given all the aforementioned, it is advisable to outline the

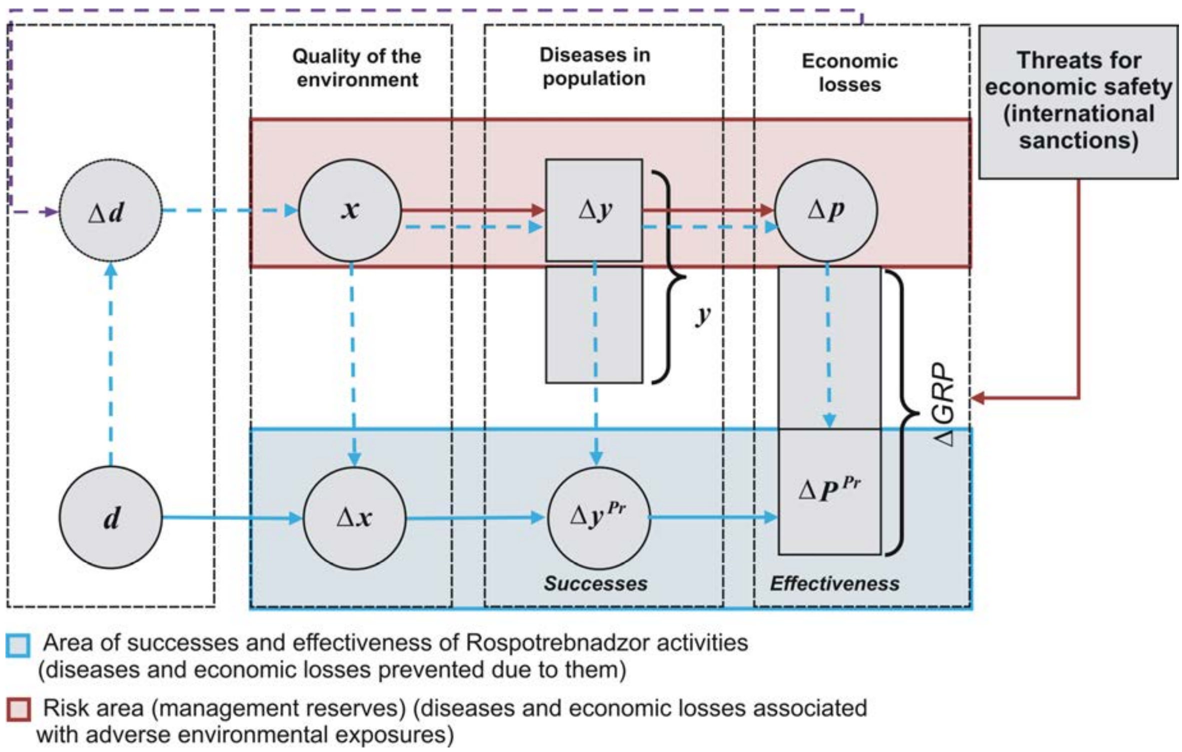

Figure 3. Provision of the state strategies aimed at health promotion and socioeconomic development with simultaneous provision of economic safety of a given region or the country as a whole due to Rospotrebnadzor activities under international sanctions:

y is adverse health outcomes (population incidence or mortality, cases/100,000);

x is an indicator that describes quality of the environment;

Δ*x* is a change in quality of environmental objects due to activities of Rospotrebnadzor;

Δ*y* shows adverse health outcomes (mortality, incidence) associated with poor quality of environmental objects, cases/100,000;

Δy^{Pr} shows adverse health outcomes (mortality, incidence) prevented by activities of Rospotrebnadzor institutions and organizations, cases/100,000;

d is an indicator describing activities of Rospotrebnadzor;

Δd shows additional managing effects produced by Rospoterbnadzor activities;

Δ*P* is probable economic losses associated with adverse health outcomes (diseases and deaths) caused by poor quality of environmental objects, rubles;

ΔP^{Pr} is economic losses prevented by activities of Rosporebnadzor institutions and organizations associated with a decrease in adverse health outcomes (diseases and deaths) caused by environmental exposures, rubles;

ΔGRP is a growth in gross regional product associated with absence of diseases or deaths prevented by activities of Rospotrebnadzor institutions and organizations, rubles.

following basic promising trends in the development of the risk assessment methodology:

– developing the fundamentals the methodology is based on;

– enlarging practical use of health risk assessment results in everyday activities of the Rospotrebnadzor;

– creating an information platform and digitalizing health risk analysis;

– developing a methodology for substantiating effective preventive programs aimed at health risk management.

Issues related to using the risk analysis methodology within providing sanitary-epidemiological safety of the population have been discussed most comprehensively in the reviewed and supplemented edition of the monograph Health Risk Analysis in the Strategy of State Social and Economic Development.

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