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Research article

SUBSTANTIATING METHODICAL APPROACHES TO QUANTIFYING REPRODUCTIVE HEALTH RISKS CAUSED BY HARMFUL OCCUPATIONAL AND WORK-RELATED FACTORS

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The article dwells on methodical approaches to quantifying occupational risk (OR) which give an opportunity to spot out priority trends in prevention of reproductive losses caused both by occupational diseases (ODs) and work-related diseases (WRDs).

OR quantitative assessment takes into account an additional probability of developing disorders and their severity. When assessing OR for reproductive health, it is advisable to take into account sex-related peculiarities, sensitive periods in the reproductive cycle, variable physiological states, as well as health disorders in offspring caused by parental occupational exposures. The assessment is based on epidemiological research. The algorithm also involves determining OR of reproductive disorders; determining an integral OR of reproductive disorders (as a combined account of both ODs and WRDs caused by exposure to different factors); determining OR categories and assessing their acceptability regarding reproductive health. It is suggested to determine severity of reproductive health outcomes (health effects) using conventional coefficients recommended by the WHO and "loss of fertility" level which is significant in assessing consequences for offspring. In case a risk is detected, both for exposed workers and their offspring, it is recommended to consider selecting the priority (maximum) risk level to be the ultimate assessment result.

The suggested methodical approaches were tested on a group of women employed at a petrochemical production and exposed to several harmful occupational factors (chemical factor and labor intensity) with working conditions at their workplaces belonging to the hazard category 3.1. The assessment revealed the integral risk for reproductive health to be equal to $1.6 \cdot 10^{-2}$ thus indicating that the risk was unacceptable. Besides, occupational factors influencing a mother create an unacceptable risk for development of healthy offspring (the detected risk is $3 \cdot 10^{-3}$). Such a reproductive disorder as infertility causes "insignificant" risks for women whereas they grow up to being "high" for their potential offspring. The ultimate assessment result is selecting the maximum risk levels, that is, the "high" risk for offspring's health.

Key words: *methodical approaches, quantitative assessment, risk assessment, reproductive health, occupational factors, work-related factors, petrochemical production.*

The Concept of the demographic policy in the Russian Federation up to 2025 (approved by the Order of the RF President issued on October 09, 2007 No. 1351)[1] and tasks set within the "Demography" National Project which is to be implemented by 2024 determine several significant strategic trends. One of them is a growth in the total fertility rate (up to 1.7 children per 1 woman)[2].

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[1] Ob utverzhdenii Kontseptsii demograficheskoi politiki Rossiiskoi Federatsii na period do 2025 goda: Ukaz Prezidenta RF ot 09.10.2007 № 1351 [On Approval of the Concept of the demographic policy in the Russian Federation up to 2025: The Order by the RF President issued on October 9, 2007 No. 1351]. *KonsultantPlus*. Available at: http://www.consultant.ru/document/cons_doc_LAW_71673/7a46cb13de731db3333fcd77a4f7887e468287e3/ (December 26, 2021) (in Russian).

[2] Pasport natsional'nogo proekta «Demografiya» (utv. Prezidentom Soveta pri Prezidente RF po strategicheskomu razvitiyu i natsional'nym proektam, protokol ot 24.12.2018 g. № 16) [The profile of the "Demography" National Project (approved by the RF Presidential Council on strategic development and national projects, the meeting minutes dated December 24, 2018 No. 16)]. *The RF Ministry of Labor*. Available at: https://mintrud.gov.ru/ministry/programms/demography/ (December 26, 2021) (in Russian).

In 2010 a positive trend appeared in dynamics of demographic rates in the country; but by now this trend has reversed. Today the demographic situation is characterized with the decreasing fertility rate and growing mortality. According to the official statistic data in 2020 the total fertility rate amounted to 1.5 against 1.77 in 2015 when it reached its maximum value over the previous 20 years. The overall birthrate went down to 9.8 ‰ (or by 26 % lower than in 2015) but the overall mortality grew up to 14.6 ‰ (or by 12 % higher than in 2015); as a result, there was a natural decrease equal to 4.8 ‰.

Harmful occupational and work-related factors can both cause occupational diseases (ODs) and induce pathogenetic mechanisms of developing and progressing work-related diseases (WRDs) [1]. There are good examples of exposure to certain harmful chemicals detected at workplaces and known for a long period of time; one of them is exposure to lead at workplaces of female potters which can cause miscarriage, still birth and infertility among them. It has been established recently that harmful working conditions cause up to 61 % of female infertility cases and up to 87 % of uterine fibroids. An etiological fracture of negative impacts on the reproductive system is greater at workplaces with working conditions being more hazardous (belonging to higher hazard categories). Moreover, when a pregnant woman is exposed to harmful working conditions at her workplace, a contribution made by this exposure is significantly greater for a newborn than for her [2].

Hygienic assessment of working conditions doesn't rely on health disorders, including reproductive ones, as estimation criteria, there is a rather limited number of research works which mention established relationships between developing reproductive disorders and occupational exposures and descriptions of such relationships lack any quantitative parameters. Given that, in most cases it is not reasonable to perform a priori assessment of reproductive risks. A posteriori semi-quantitative assessment is accomplished only in case of ODs. So, it seems vital to develop methodical approaches to occupational risk (OR) quantification since this gives an opportunity to spot out priority activities aimed at preventing reproductive losses caused by both ODs and WRDs.

Our research goal was to substantiate methodical approaches to quantifying reproductive health risks caused by exposure to occupational and work-related factors.

Materials and methods. Science-based approaches and an algorithm for quantitative risk assessment were developed based on analysis of literature sources and regulatory and methodical documents containing some fundamentals regarding OR assessment. We also analyzed some studies with data on peculiarities of developing reproductive disorders and negative health outcomes in future offspring caused by exposure to harmful environmental factors [3, 4].

The approaches and algorithm were to be tested using a previously published study where the authors established cause-effect relations between reproductive health and harmful working conditions. To select an appropriate study, we analyzed publications in the conventional citation databases (eLibrary, CyberLeninka, GoogleScholar, Web of Science, Scopus, RSCI, HAC, etc.). Approximately 800 publications issued from 2011 to 2021 (a 10-year period) were found as per such key words as "occupational risk" and "reproductive health". The most interesting ones were those which described cross-sectional analytical epidemiological studies with detected probabilities of a negative response from the female reproductive system and offspring development in test and control groups. Working conditions in a test group should include harmful occupational factors and belong to a hazard category not lower than 3.1 (hazardous, class 1).

We chose a study by M.K. Gainullina who examined frequency of gynecological morbidity, fertile functions, and pregnancy outcomes in female workers employed at a petrochemical production (chemical engineers, chemical analysts, samplers, etc.). The overall sampling was made of 512 people [5]. Approaches to OR quantitative assessment are based on key stages in any risk assessment: hazards identification, exposure assessment, assessment of "exposure – response" relationship, and risk characterization [6].

Research results. There are peculiarities in development of reproductive disorders which require certain adjustments to be made at some stages in risk assessment. When a hazard is identified, it is advisable to anticipate negative answers which are specific for a male or female body due to sex-related physiological differences between them. There can also be certain responses specific for couples, that is, responses where both sexes play an important role in case both partners are exposed. Besides, it is necessary to take into account probable negative responses (health outcomes) in future offspring since they correlate with working conditions of a mother with their etiological fraction reaching 78 % [7–9]. An important difference is that some sensitive periods in the reproductive development (cycle) and certain physiological conditions (pregnancy or breast-feeding a newborn) also determine different reproductive outcomes and don't exclude their occurrence in a long-term period after an exposure to a factor has ended [4]. For example, when it comes down to the chemical factor, it is known that specific toxicants are hazardous in different periods in the reproductive cycle as it will be clearly stated in a marking provided for a specific substance[3].

Based on literature data, all the responses (outcomes) can be conditionally divided into specific and non-specific damages. Specific damages are such responses (outcomes) which most probably occur due to a relative number and a list of harmful factors as well as intensity of their influence. Non-specific responses (outcomes) develop due to weakened immune resistance, deteriorated detoxification functions, vegetative disorders etc.[4] [8–12]. Table 1 provides systemically organized data on responses (outcomes) represented by reproductive disorders caused by exposure to occupational and work-related factors. The systematized responses allow for such criteria as specificity of an outcome, sex-related peculiarities, different stages in the reproductive cycle, and different physiological conditions.

But at the same time regulatory and methodical documents determine only two negative reproductive outcomes as occupational diseases; they are female genital prolapse (N81) caused by hard physical labor (lifting and moving heavy weights combined with a forced working posture) and malignant neoplasms of female genital organs and breast (C50–C58) caused by exposure to ionizing radiation of chemicals[5].

The stage when "exposure – response" relationship is assessed involves determining cause-effect relations between levels of exposure to a factor and a probability (frequency) of negative health responses (outcomes) in workers. This allows spotting out quantitative regularities in changeability. Epidemiological criteria ($RR \geq 1.5$)[6] are usually applied to establish cause-effect relations between exposure and negative changes.

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Table 1

The list of reproductive disorders caused by exposure to occupational and work-related factors [8–17]

Sex and a period in the reproductive cycle	Specific responses (outcomes) represented by reproductive disorders	Non-specific responses (outcomes) represented by reproductive disorders
A woman not pregnant	– weaker fertilization or loss of it – disorders of menstrual function (N91, N92, N94), female infertility (N97), untimely menopause (N95); – non-inflammatory disorders of female genital tract (N80–N98): endometriosis (N80); non-inflammatory disorders of ovary (N83); hyperplasia in uterus (N85); dysplasia and leukoplakia of cervix uteri (N87–N88); – neoplasms in female genital organs (D25–D28): uterine fibroid (D26); – benign mammary dysplasia (N60); – *female genital prolapse* (N81); – *malignant neoplasms of female genital organs and breast* (C50–C58); – disorders of population hormonal markers profile in urine during two cycles to estimate ovarian dysfunction (LH, FSH, HCG in 100 women) (E28);	– non-specific inflammatory disorders of female pelvic organs (N60–N73, N76, N77);
A pregnant woman	– unfavorable conception outcome – spontaneous abortion (O03), ectopic pregnancy (O00), hydatidiform mole (O01), other abnormal products of conception (O02), habitual aborter (N96), stillbirth (Z37); threat of miscarriage (O20.0);	– complications of an existing somatic pathology – anemia of pregnant (O99); – pregnancy complications – excessive vomiting in pregnancy (O21), gestosis in the second half of pregnancy (O10–O16); – premature delivery (O42, O60), abnormalities of forces of labor (O62);
Negative responses (outcomes) in offspring	– effects on a developing fetus – congenital malformations (Q00–Q89), lesions of a fetus including those due to an occupational injury, poisoning, or occupational disease (P00); – physical (R20) and mental retardation (F80–F89), behavioral disorders (F91–F92), malignant and benign neoplasms in the first and next generations (D10–D36, C00–C97);	– fetus development disorders – intrauterine hypoxia (P20), slow fetal growth and fetal malnutrition (P05), certain conditions originated in the perinatal period (P00–P96);
A breast-feeding woman after a recent childbirth	– lactation disorders (O92);	
A fertile man	– weaker fertilization abilities (gonadotropic, gonadotoxic effects действие) – male infertility (N46) due to decreased sperm concentration in ejaculate, 2 mln/ml and lower, lower sperm motility and other deteriorated parameters of functional activity (sperm quality); – endocrine disorders – changes in the population profile of male hormones concentrations in blood serum (follicle-stimulating hormone, luteinizing hormone, testosterone, prolactin in 3-time detection in 50–100 men); – malignant neoplasms of testis (C62).	– sexual dysfunction (F52).

A design of an epidemiological study which is aimed at assessing reproductive health risks can change depending on a type of an examined outcome and a period when it occurs. A cross-sectional study or a prevalence study is preferable to assess risks of developing diseases in women who are not pregnant or in men since it usually describes health of a workers' group at a given moment of time [18]. But if we want to assess risks of reproductive disorders which occur in a certain period of time after an exposure to an occupa-

tional factor has ended both in women and men and their offspring, we should use a case-control study or case-referent study [19].

Risk characterization usually involves calculating risk rates, assigning them into risk categories, and detecting priority occupational and work-related factors which cause OR.

The algorithm applied to quantify OR for reproductive health include the following fundamental sequence:

– calculating probability, including additional one, that reproductive disorders would develop in a test and a control group;

– calculating an OR of reproductive disorders;

– calculating an integral OR of reproductive disorders;

– determining categories of OR rates and assessing acceptability of OR for reproductive health.

A probability that *i*-th reproductive disorder would develop ($p_{rd}^{\ i}$) in a test group (or "case") and a control group ("control") is determined by calculating frequency of such a disorder as per the following formula 1:

$$p_{rd}^{\ i} = n_{rd}^{\ i} / N^i, \qquad (1)$$

where $n_{rd}^{\ i}$ is a number of people with *i*-th reproductive disorder in each group, N^i is a number of workers in each group.

An additional probability $p_{rd\ add}^{\ i}$ that *i*-th reproductive disorder would develop in workers is determined by calculating a difference between probabilities of such a disease in a test group $p_{rd}^{\ i}$ and in a control one $p_{rd\ ref}^{\ i}$ as per the formula 2:

$$p_{rd\ add}^{\ i} = p_{rd}^{\ i} - p_{rd\ ref}^{\ i} \qquad (2)$$

A group risk of *i*-th reproductive disorder ($R_{rd}^{\ i}$) is calculated in analyzed groups as per the formula 3:

$$R_{rd}^{\ i} = p_{rd\ add}^{\ i} \cdot G^i, \qquad (3)$$

where $p_{rd\ add}^{\ i}$ is an additional probability that *i*-th reproductive disorder would develop, G^i is severity of outcomes caused by a reproductive disorder.

An integral risk allows for probable negative outcomes under exposure to a set of harmful occupational and work-related factors. An integral risk caused by both occupational and work-related reproductive disorders developing under exposure to harmful factors is calculated as per the formula 4:

$$R_{rd}^{int} = 1 - \prod_{i=1}^{n} \cdot \left(1 - R_{rd}^{i}\right). \qquad (4)$$

Risks are assigned into different risk categories as per the criteria suggested in the work by N.V. Zaitseva [3]. Negligible and low occupational risks are considered to be acceptable.

Severity of outcomes caused by an exposure to a harmful factor is a risk-characterizing determinant. It is advisable to determine severity of outcomes caused by variable responses (effects) of reproductive health using coefficient values recommended by the WHO [20, 21]. However, bearing in mind that the same outcomes can potentially be significant not only for workers but also for their offspring (a possibility to have any offspring), we suggest using "fertility loss" as a basic indicator. Its value is determined based on data about duration of a fertility period and a period during which all the attempts to conceive a child have failed. Thus, in case a man or a woman has completely lost a possibility to conceive a child, "fertility loss" is recommended to be taken as equal to 1; if this loss is only partial, it is necessary to calculate its value. Necessary data can be provided by social surveys or taken from clinical case histories. We should note that the final assessment takes into account all detected risks, both for exposed workers and outcomes for their offspring together with selecting the priority (maximum) risk level.

Therefore, when assessing reproductive risks, it is necessary to take into account sex-specific peculiarities, sensitive periods in the reproductive cycle, different physiological states, as well as health disorders in offspring caused by parental occupational exposures. Risk quantification involves taking into account an additional probability of developing disorders and their severity. Results produced by epidemiological studies are suggested as grounds for such quantitative risk assessment. Epidemiological studies can have various de-

signs depending on a type of an examined outcome and a period of its occurrence. A certain peculiarity of assessment which concentrates on severity of outcomes is its focus being not only on health losses borne by potential parents but also on damage caused by declining birthrates and developing disorders and diseases, including congenital ones, in children.

The suggested algorithm was tested on the results produced by a study which focused on gynecological morbidity, fertile functions, and pregnancy outcomes in women employed at a petrochemical production (chemical engineers, chemical analysts, samplers, etc.) [5]. Working conditions at their workplaces corresponded to hazard category 3.1 (hazardous, class 1). These conditions occurred due to a combined exposure to chemical factors (saturated, unsaturated, aromatic hydrocarbons and their derivatives, vapors of fatty acids and spirits, phenol, non-organic toxic compounds of carbon, sulfur, nitrogen, etc.) and labor intensity (work was organized in three shifts).

Table 2 provide initial data on the frequency of negative responses (outcomes) from women's reproductive health taking into account the reproductive cycle as well as epidemiological criteria (relative risk, *RR*; etiological fraction, *EF*) which confirm intensity of a correlation between a pathology and harmful occupational factors.

We determined an additional probability of each response (Table 3) using data on frequencies of reproductive losses borne by female workers employed at a petrochemical production in the test and reference group.

Reproductive risks were calculated and assessed bearing in mind severity of established health outcomes; the results are given in Table 3.

We established that a risk of infertility amounted to $4 \cdot 10^{-4}$ for female workers employed at a petrochemical production during a period in the reproductive cycle when they were not pregnant. This risk was classified as "low" whereas a risk of menstrual function

Table 2

Frequencies of negative responses from reproductive health of women employed at a petrochemical production and epidemiological criteria

A period in the reproductive cycle	Disease (ICD-10 code)	Frequency of a response	*RR*	*EF*, %	Intensity of a correlation
A woman not pregnant	Menstrual function disorders (N91, N92, N94)	27.1 ± 1.9	4.3	79.6	Very high
	Benign neoplasms (D25–D28)	18.7 ± 1.7	2.5	60.0	High
	Female infertility (N97)	9.4 ± 1.3	2.2	54.5	High
A pregnant woman	Threat of miscarriage (O20.0)	41.9 ± 2.7	1.6	37.5	Average
	Gestosis in the 2nd half of pregnancy (O10–O16)	48.9 ± 2.7	1.9	47.4	Average
Offspring	Intrauterine hypoxia (P20)	39.1 ± 2.6	5.2	80.8	Very high

Table 3

Results produced by calculating reproductive risks for female workers employed at a petrochemical production

A period in the reproductive cycle	Disease (ICD-10 code)	$p_{rd\ add}^{i}$	G^i	R^i	Risk category
A woman not pregnant	Menstrual function disorders (N91, N92, N94)	0.208	0.011	$2 \cdot 10^{-3}$	Moderate
	Benign neoplasms (D25–D28)	0.112	0.011	$1 \cdot 10^{-3}$	Moderate
	Female infertility (N97)	0.051	0.008	$4 \cdot 10^{-4}$	Low
A pregnant woman	Threat of miscarriage (O20.0)	0.157	0.008	$1 \cdot 10^{-3}$	Moderate
	Gestosis in the 2nd half of pregnancy (O10–O16)	0.232	0.049	$1.1 \cdot 10^{-2}$	Average
Offspring	Intrauterine hypoxia (P20)	0.316	0.01	$3 \cdot 10^{-3}$	Moderate

N o t e : $p_{rd\ add}^{i}$ is an additional probability of *i*-th reproductive disorder; G^i is severity of an outcome caused by a reproductive disorder; R^i is a risk level of a developing *i*-th reproductive disorder.

disorders and developing benign neoplasms rose up to being "moderate" and amounted to $2 \cdot 10^{-3}$ and $1 \cdot 10^{-3}$ accordingly. We established that pregnant woman were exposed to a "moderate" risk of developing disorders which threatened normal course of a pregnancy ($1 \cdot 10^{-3}$) and an "average" risk of gestosis during the second half of a pregnancy ($1.1 \cdot 10^{-2}$). Since we didn't detect any ODs causing reproductive losses, we assumed that the integral risk for women's reproductive age was created only by WRDs and amounted to $1.6 \cdot 10^{-2}$ ("average" risk).

As we noted earlier, occupational factors which parents (mothers) are exposed to have a correlation with development of healthy offspring. In our example a direct response from offspring is intrauterine hypoxia with its risk being "moderate" ($3 \cdot 10^{3}$).

Besides, certain occupational gynecologic diseases of a mother can have some influence on offspring's health. Thus, bearing in mind "fertility loss" indicator which should be considered equal to 1 in case of infertility, severity of health outcomes for offspring is also taken as equal to 1. Consequently, a risk rate rises and a risk becomes "high" ($5 \cdot 10^{-2}$) whereas it was only "low" for a woman herself. The ultimate assessment should be based on selecting the priority risk rate, that is, the health risk is "high".

Therefore, the results produced by testing the suggested methodical approaches to assessing reproductive risks indicate that working conditions at workplaces of female workers employed at a petrochemical production create unacceptable health risks both for women themselves (menstrual function disorders, developing benign neoplasms, unfavorable course of a pregnancy) and their offspring.

Discussion. The methodology for assessing OR has several key points; they are top priority assigned to safety, exposure assessment based on using the most relevant measurement techniques, and sticking to the correct order of stages in assessment[6]. We substantiated the necessity to take into account sex-related differences, sensitive periods in the reproductive cycle, and different physiological conditions when assessing reproductive risks. It is also important to remember that certain health disorders in offspring can be caused by parental occupational exposures.

Unfortunately, specific assessment of working conditions (a priori assessment) doesn't involve assessing workers' health or severity of probable health outcomes; as for semi-quantitative assessment, it focuses solely on those ODs which are proven to be related to a specific occupation. Given that, we have suggested new approaches to quantifying health risks which allow for an additional probability of health disorders and their severity.

Quantitative risk assessment should be based on results produced by epidemiological studies which establish and prove cause-effect relations between a health outcome and an occupational factor. These studies may have different design depending on a type of an examined reproductive disorder and a period of time when it occurs. Assessment of outcome severity has a peculiarity which is its focus being not only on health losses born by potential parents but also damage caused by declining birthrates and developing disorders and diseases in offspring, including congenital ones. According to the Order by the RF Ministry for Public Healthcare and Social Development No. 160[7], such reproductive health disorders as "abortion" and "loss of reproductive functions and ability to procreate" are considered to be severe damage (severe health outcomes). However, the Order doesn't provide any quantification to assess them. Therefore, we recommend using the coefficients developed by

[7] Ob opredelenii stepeni tyazhesti povrezhdeniya zdorov'ya pri neschastnykh sluchayakh na proizvodstve: Prikaz Minzdrava i sotsial'nogo razvitiya RF ot 24.02.2005 № 160 [On determining severity of damage to health caused by an occupational injury: The Order by the RF Ministry for Public Health and Social Development issued on February 24, 2005 No. 160]. *KODEKS: electronic fund for legal and reference documentation*. Available at: https://docs.cntd.ru/document/901927104 (December 27, 2021) (in Russian).

the WHO to assess severity of outcomes for reproductive health [20, 21]. We suggest using "fertility loss" as an indicator which helps determine severity of outcomes for offspring (a possibility to procreate). The indicator is calculated based on a duration of a fertility period and a period during which all the attempts to conceive a child have failed. It should be noted, that a reduction in a fertility period can be a deliberate choice made by a woman (contraception) and this, in its turn, creates an uncertainty in assessing severity of outcomes for offspring.

The results produced by testing the suggested approaches give an opportunity to detect an unacceptable occupational risk caused by chemical factors and labor intensity for reproductive health of women employed at a petrochemical production. The highest health risk for female workers was associated with developing gestosis during the 2nd half of pregnancy (moderate occupational causation); moderate health risks were associated with developing disorders of the menstrual function (very high occupational causation), benign neoplasms (high occupational causation) as well as threat of miscarriage (average occupational causation). We detected a moderate risk for offspring's health associated with intrauterine hypoxia (very high occupational causation) and a high risk associated with infertility (high occupational causation). Occurrence of such negative outcomes is quite probable and is explained with data available in literature. For example, benign neoplasms are assumed to develop under exposure to harmful working conditions which don't correspond to adaptation capabilities of a female body. Changes in the hormonal status and subsequent disorders of the menstrual function as well as infertility can be caused by chronic occupational stress (or labor intensity) and inhalation exposure to chemicals [10]. Chemicals which are used in production operations include saturated aromatic hydrocarbons, toxic carbon compounds, and vapors of various spirits. They exert negative influence on development thus creating unacceptable risks for offspring[8]. Obviously, the situation requires immediate actions aimed at elimination these risk factors. To do that, we can recommend using an algorithm for managing occupational risks for the reproductive system developed by experts from N.F. Izmerov's Scientific Research Institute for Occupational Medicine.

Conclusions:

1. Quantitative assessment of occupational health risks involves taking into account an additional probability of developing disorders and their severity. When assessing occupational risks for reproductive health, it is advisable to pay attention to sex-related peculiarities, sensitive periods in the reproductive cycle, different physiological conditions, as well as occupational causation of health outcomes in offspring caused by parental exposures.

2. The suggested methodical approaches involve epidemiological research with its results giving grounds for assessing an additional probability of developing reproductive disorders (a difference between a probability of negative health outcomes in test and control groups); determining OR rates as regards reproductive disorders; determining an integral OR of reproductive disorders; assigning occupational risks into risk categories and assessing acceptability of reproductive OR rates.

3. It is suggested to determine severity of responses (outcomes) for reproductive health and an indicator which describes a risk and is necessary to quantify it by using coefficients recommended by the WHO, in particular, "fertility loss" indicator since it is significant for assessing severity of outcomes for offspring.

[8] R 2.1.10.1920-04. Rukovodstvo po otsenke riska dlya zdorov'ya naseleniya pri vozdeistvii khimicheskikh veshchestv, zagryaznyayushchikh okruzhayushchuyu sredu: utv. Pervym zamestitelem Ministra zdravookhraneniya RF, Glavnym gosudarstvennym sanitarnym vrachom RF G.G. Onishchenko 05.03.2004 [Guide R 2.1.10.1920-04. Human Health Risk Assessment from Environmental Chemicals: approved by G.G. Onishchenko, the RF Chief Sanitary Inspector, the First Deputy to the RF Public Healthcare Minister on March 5, 2004]. Moscow, Rospotrebnadzor's Federal Center for Hygiene and Epidemiology, 2004, 143 p. (in Russian).

4. An integral risk of reproductive losses caused by harmful occupational and work-related factors covers both occupational and work-related diseases. Moreover, in cases when detected risks concern not only exposed workers but their offspring as well, it is recommended to select the priority (maximum) risk rate as the ultimate assessment result.

5. We tested the methodical approaches on a group of women employed at a petrochemical production and exposed to such harmful occupational factors as chemicals and labor intensity which allowed ranking working conditions at their workplaces as belonging to hazard category 3.1. The testing results revealed that the integral risk for their reproductive health amounted to $1.6 \cdot 10^{-2}$ thus indicating that the group risk was unacceptable. We detected such probable negative health outcomes as disorders of the menstrual function, developing benign neoplasms, and unfavorable course of pregnancy. Besides, when a mother is exposed to the examined occupational factors, this creates an unacceptable health risk for offspring, in particular, a risk of intrauterine hypoxia ($3 \cdot 10^{-3}$). Such a reproductive disorder as infertility creates "low" risks for a woman whereas the risk rate grows up to "high" risk when it comes to potential offspring. The ultimate assessment result is selecting the maximum risk rate, that is, the 'high" risk for offspring's health.

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