УДК 614.7:616-007-053.1(470.313)
DOI: https://doi.org/10.17816/PAVLOVJ109333

Влияние загрязнений атмосферного воздуха на частоту врожденных пороков развития (на примере региона)

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АННОТАЦИЯ

Введение. Загрязнение атмосферного воздуха лежит в основе большого количества заболеваний человека как в промышленно развитых, так и в экономически развивающихся странах. Исследования показывают, что воздействие загрязнений атмосферного воздуха во время беременности может быть связано с повышенным риском врожденных пороков развития (ВПР).

Цель. Проанализировать влияние загрязняющих веществ атмосферного воздуха в г. Рязани на частоту встречаемости ВПР у новорожденных.

Материалы и методы. Приведены данные мониторинга ВПР Областного перинатального центра Рязанской области; сведения о загрязнении атмосферного воздуха Федеральной службы по гидрометеорологии и мониторингу окружающей среды, Рязанского центра по гидрометеорологии и мониторингу окружающей среды, Роспотребнадзора по Рязанской области. Статистический анализ проводился с использованием свободной программной среды вычислений R (ver. 4.1.2).

Результаты. За 2019 г. распространенность ВПР в г. Рязани составила 24,09 на 1000 новорожденных; за период 2010–2021 гг. абсолютное количество зарегистрированных ВПР увеличилось на 244,57%. Наиболее часто встречающимися врожденными аномалиями были Q21.0 Дефекты межжелудочковой перегородки (28,5%, 95% ДИ: 20,8–36,2%) и Q62.0 Врожденный гидронефроз (7,3%, 95% ДИ: 2,9–11,7%). Зарегистрирована корреляция с таким загрязнителем воздуха, как диоксид серы (SO_2) на втором месяце беременности (аОШ 1,39; 95%; ДИ 1,05–1,83, $p < 0,05$) и третьем месяце беременности (аОШ 1,59; 95% ДИ 1,17–2,16, $p < 0,05$). Не обнаружено статистически значимой связи между ВПР и оксидом углерода (CO), диоксидом азота NO_2 и озоном (O_3, $p > 0,05$).

Заключение. Исследование подтверждает связь между загрязнением атмосферного воздуха и частотой ВПР. В частности, SO_2 оказывает негативное влияние на втором и третьем месяцах беременности. В связи с этим важно указать на то, что органам власти региона, государственным надзорным органам необходимо направить усилия на снижение загрязнения окружающей среды, что должно способствовать снижению частоты ВПР у детей.

Ключевые слова: *загрязнение атмосферного воздуха; врожденные пороки развития; диоксид серы; загрязняющие вещества; динамика заболеваемости*

Для цитирования:
Кирюшин В.А., Боботина Н.А., Демченко М.А., Моталова Т.В. Влияние загрязнений атмосферного воздуха на частоту врожденных пороков развития (на примере региона) // Российский медико-биологический вестник имени академика И. П. Павлова. 2023. Т. 31, № 1. С. 29–36. DOI: https://doi.org/10.17816/PAVLOVJ109333

Рукопись получена: 14.07.2022 **Рукопись одобрена:** 22.09.2022 **Опубликована:** 31.03.2023

ЭКО•ВЕКТОР

DOI: https://doi.org/10.17816/PAVLOVJ109333

Influence of Atmospheric Air Pollution on Frequency of Congenital Anomalies (on an example of a region)

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ABSTRACT

INTRODUCTION: Atmospheric air pollution is the underlying factor of a great number of human diseases in both industrialized and developing countries. Studies show that exposure to atmospheric pollutions in pregnancy can be associated with an increased risk of congenital anomalies (CAs).

AIM: To analyze the impact of atmospheric air pollutants in Ryazan city on the incidence of CAs in newborns.

MATERIALS AND METHODS: The data of monitoring of CAs by Ryazan Regional Perinatal Center; information on atmospheric air pollution of the Federal Service for Hydrometeorology and Environmental Monitoring, of Ryazan Center for Hydrometeorology and Environmental Monitoring, of Rospotrebnadzor of the Ryazan region are presented. The statistical analysis was conducted using free R computing environment (ver. 4.1.2).

RESULTS: In 2019, the prevalence of CAs in Ryazan was 24.09 per 1,000 newborns; in the period 2010–2021, the absolute number of recorded CAs grew by 244.57%. The most common congenital anomalies were Q21.0 Ventricular septal defects (28.5%, 95% CI: 20.8–36.2%) and Q62.0 Congenital hydronephrosis (7.3%, 95% CI: 2.9–11.7%). Correlation was recorded with such air pollutant as sulfur dioxide (SO_2) in the second month of pregnancy (AOR 1.39; 95%; CI 1.05–1.83, $p < 0.05$) and the third month of pregnancy (AOR 1.59; 95% CI 1.17–2.16, $p < 0.05$). No statistically significant relationship was established between CAs and carbon monoxide (CO), nitrogen dioxide (NO_2) and ozone (O_3, $p > 0.05$).

CONCLUSION: The study confirms the association between atmospheric air pollution and frequency of CAs. In particular, SO_2 has a negative effect in the second and third months of pregnancy. In this context, it is important that the authority bodies of the region and governmental regulatory agencies direct their efforts to reduction of the pollution of the environment which should help reduce the frequency of CAs in children.

Keywords: *atmospheric air pollution; congenital anomalies; sulfur dioxide; pollutants; morbidity dynamics*

For citation:
Kiryushin VA, Bobotina NA, Demchenko MA, Motalova TV. Influence of Atmospheric Air Pollution on Frequency of Congenital Anomalies (on an example of a region). *I. P. Pavlov Russian Medical Biological Herald.* 2023;31(1):29–36. DOI: https://doi.org/10.17816/PAVLOVJ109333

Received: 14.07.2022 **Accepted:** 22.09.2022 **Published:** 31.03.2023

ECO•VECTOR

LIST OF ABBREVIATIONS

AAP — atmospheric air pollution
aOR — adjusted odds ratio
CA — congenital anomalies
CI — confidence interval
CNS — central nervous system
CO — carbon monoxide
MPC — maximal permissible concentration
MSA — musculoskeletal apparatus
NO_2 — nitrogen dioxide
NO_x — nitrogen oxides and dioxides
OR — odds ratio
O_3 — ozone
PM — particulate matter
RR — Ryazan region
SO_2 — sulfur dioxide

INTRODUCTION

The adverse effect of atmospheric air pollution on human health attracts the attention of the whole world. It underlies a great number of diseases both in industrialized and developing countries, especially in the 'vulnerable' groups of the population. The results of previous studies demonstrated a negative influence of AAP on most systems of an organism: nervous, respiratory, circulatory, reproductive, as well as on different groups of the population: elderly people, pregnant females and children. Climate is an important factor that determines the quality of the atmospheric air [1]. Thus, Y. Fang, et al. showed that from the preindustrial period (1860) to 2000, due to change of climate, the concentration of particulate matter (PM) up to 2.5 μm in diameter increased by 5%, and concentration of surface ozone (O_3) — by 2% [2]. According to the work of R. A. Silva, et al, transition from the pre-industrial period led to 111,000 and 21,000 additional emissions of fine particle matter and ozone, respectively. Over the past two decades, approximately every degree of warming (°F) has been associated with an increase in the concentration of O_3 by 1.2 μg/kg [4].

There is more and more information about the influence of various air pollutants on the formation of congenital anomalies (CAs). In particular, E. K. Chen, et al. (2014) established a relationship between the concentration of nitrogen dioxide (NO_2) and the frequency of coarctation of the aorta [5]. In a recent study by H. Zhang, et al., it was found that exposure to carbon monoxide (CO) in the first and second trimesters of pregnancy increases the risk of CAs: the adjusted odds ratio (aOR) and 95% confidence interval (CI) were 1.066 (1.010–1.125) and 1.065 (1.012–1.122), respectively. Exposure to NO_2 and CO in the first trimester, to PM up to 2.5 μm in size (PM2.5) and up to 10 μm (PM10) in the second trimester were associated with the risk of atrial septal defect. The authors did not report any positive relationship between AAP and the formation of Fallot's tetrology. Systemic CAs positively correlated with air pollution with PM10 (aOR 1.14, 95% CI 1.12–2.43; aOR 1.51, 95% CI 1.13–2.03 for every additional 10 mg/m^3) and CO (aOR 1.36, 95% CI 1.14–2.48; aOR 1.75, 95% CI 1.02–3.61 for every additional 1 mg/m^3) in the second and third months of pregnancy. Besides, CAs were also associated with exposure to sulfur dioxide (SO_2) two months before pregnancy (aOR 1.31; 95% CI 1.20–3.22) and in the third month of pregnancy (aOR 1.75; 95% CI 1.02–3.61). Congenital heart defects, polydactyly, cleft lip and/or cleft palate have also been associated with exposure to PM10, SO_2 and CO. With this, the authors did not find any significant relationship between congenital anomalies and exposure to O_3, PM2.5 and NO_2 ($p > 0.05$) [6].

A study by X. Huang, et al. (China) showed that the congenital heart disease, polydactyly, cleft lip and/or cleft palate were significantly associated with PM2.5. In a study of G. Al Noaimi, et al., the influence of exposure to PM2.5 during the first trimester on the general risk of CAs (OR 1.05, 95% CI 1.01–1.09), as well as on the risk of defects of urogenital system (OR 1.06, 95% CI 1.01–1.11) and defects of neural tube (OR 1.10, 95% CI 1.03–1.17); and the influence of SO_2 on the risk of defects of urogenital system (OR 1.17, 95% CI 1.08–1.26) were recorded [8]. Of importance is also a fact that in stillborn infants the incidence of congenital anomalies of the circulatory system exceeds 30%, which determines the importance of identification of risk factors for CAs and introduction of effective preventive measures [9]. Y. Yang, et al. have demonstrated the impact of different air pollutants (O_3 and NO_2) in the period of the formation of cardiovascular system in embryo on increase in the frequency of CAs of the circulatory system [10].

Maternal obesity is an independent risk factor for CAs [12, 13].

The **aim** of this study to analyze the impact of atmospheric air pollutants in Ryazan on the incidence of congenital anomalies in newborns.

MATERIALS AND METHODS

The materials of Ryazan Regional Perinatal Center; of the Federal Service for Hydrometeorology and Environmental Monitoring, of Ryazan Center for Hydrometeorology and Environmental Monitoring, of Directorate of the Federal Service for Supervision in the Sphere of Protection of Consumers' Rights and Human Well-Being of the Ryazan region were analyzed.

Monitoring of CAs on the base of the Regional Perinatal Center has been conducted since 2013 and included information on deliveries in the territory of the RR, including both live born and stillborn cases. The incidence of CAs among children born in Ryazan in 2019–2021 was analyzed. For this analysis, 683 deliveries were selected, in 122 of which infants with CAs were born (which corresponds to 24.09 per 1,000 infants; the data of 2019). The control group were healthy newborns (n = 141).

Criteria of exclusion from the group of CAs:

- existence of chromosomal mutations;
- region of residence (Ryazan region);
- insufficient data of deliveries;
- stillbirth;
- induced abortions.

Criteria of exclusion from the control group:

- region of residence (Ryazan region);
- year of birth (2018).

The analyzed data on mothers included age, date of the last menstruation, place of residence, parity; data on infants included the date of birth, gender, gestational age, weight. The summary characteristics of the studied sample are presented in Table 1. There were statistically significant differences between infants with and without CAs in the age (aOR 1.190; 95% CI 1.11–1.27) and parity of the mother (aOR 0.380; 95% CI 0.26–0.55, p < 0.001).

Table 1. Summary Characteristics of Newborns in Analyzed Groups

Parameters	With Congenital Anomaly		Without Congenital Anomaly		p
	n	%	n	%	
Mother's age					
< 20 year	0	0	4	2.8	< 0.005
20–24 years	15	12.3	21	14.9	
25–29 years	36	29.5	56	39.7	
30–34 years	38	31.1	45	31.9	
> 35 years	33	27.0	15	10.6	
Weight at birth					
< 1500 g	3	2.5	0	0.0	< 0.005
1500–2499 g	11	9.0	1	0.7	
2500–3499 g	74	60.7	105	74.5	
> 3500 g	34	27.9	35	24.8	
Child's gender					
male	69	56.6	71	50.4	0.38
female	53	43.4	70	49.6	
Parity					
1	57	46.7	36	25.5	< 0.005
2	39	32.0	59	41.8	
≥ 3	26	21.3	46	32.6	
Район проживания в г. Рязани					
Dashki-Pesochnye	45	36.9	32	22.7	0.035
Kanishchevo	49	40.2	74	52.5	
Kremin	28	23.0	35	24.8	
In total	***122***	***100***	***141***	***100***	–

Analyzed spectrum of CAs:

- Q21.0 Ventricular septal defect;
- Q62.0 Congenital hydronephrosis;
- Q60.0 Unilateral renal agenesis;
- Q37.1 Unilateral chryptorchism;
- Q69.1 Extra thumb (fingers) of the hand;
- Q50.1 Cystic ovarian malformation;
- Q54.0 Hypospadias of the glans penis;
- Q61.3 Polycystic kidney disease, unspecified;
- Q63.2 Ectopic kidney;
- Q66.9 Congenital deformity of the foot, unspecified.

Congenital anomalies not included in these 11 categories, were referred to 'Others' category.

The data of AAP were taken from the materials of the Federal Service for Hydrometeorology and Environmental Monitoring, and of Ryazan Center for Hydrometeorology and Environmental Monitoring for the period from December 2019 to December 2021 including the information of three governmental stations of automatic air control in Ryazan was used:

- Kanishchevo region (the territory of the Regional Clinical Hospital, Internatsionalnaya str.),

• Dashki-Pesochnye region (the territory of the Municipal Clinical Hospital No.11, Novosyolov str.),

• Kremlin region (Kremlin str.).

The controllable pollutants included CO, nitrogen oxides, dioxides (NOx), SO2, O3, hydrocarbons, PM.

Air sampling included taking concentrations of substances every 20 minutes throughout a day. Minimal and maximal values of one-time concentrations of pollutants in the atmospheric air and the average daily concentrations of substances in the atmospheric air were determined at the posts. In the work, data of average daily concentrations measured in three districts of the city, were used.

The *statistical analysis of the results* was performed using the free computing software environment R (ver. 4.1.2). The data were checked for the normal distribution using Kolmogorov criterion. The values with distribution differing from normal are represented as the median (Me), the 25th and 75th percentiles (Q25%–Q75%). The distribution of concentrations of pollutants in the atmospheric air is represented by Me, quartile ranges, maximum (max) and minimum (min) values. To assess the differences between the groups, $\chi 2$ test or Fisher exact test was used for the following categories: mother's age (< 20 years, 20–24 years, 25–29 years, 30–34 years, ≥ 35 years), number of pregnancies (1, 2, and ≥ 3), birth weight (< 1500 g, 1500–2499 g, 2500–3499 g, ≥ 3500 g), gender of infants. Smoking and alcohol consumption of the mother during pregnancy were not controlled.

To assess the effects of air pollution on the occurrence of CAs, logistic regression was used. The presence or absence of CAs was a dependent variable, and the individual exposure concentration of air pollutants during the first trimester of pregnancy, the age of the mother, the parity and the weight of the child were independent variables (predictors). The corresponding rough and adjusted OR and 95% CI were calculated for exposure to air pollutants at different stages of pregnancy, as well as for the age of the mother, parity and weight of the child. The significance level of the statistical test is 0.05.

RESULTS

Despite the gradual decrease in the index of atmospheric air pollution in Ryazan, it still remains at a high level. The average annual concentration of CO is 0.251 mg/m^3 (maximum permissible concentration, MPC, is 5,0000 mg/m^3), of NO_2 — 0.023 mg/m^3 (MPC 0.2000 mg/m^3), SO_2 — 0.008 mg/m^3 (MPC 0.5000 mg/m^3), O_3 — 0.027 mg/m^3 (MPC 0.1600 mg/m^3).

Figure 1 shows the dynamics of the detection of CAs in newborns in Ryazan for the period of 2010–2021 (Δ = 244.57%). There were no statistically significant differences between the analyzed groups of newborns with and without CAs living in three districts of Ryazan having governmental automatic air control posts (p > 0.05).

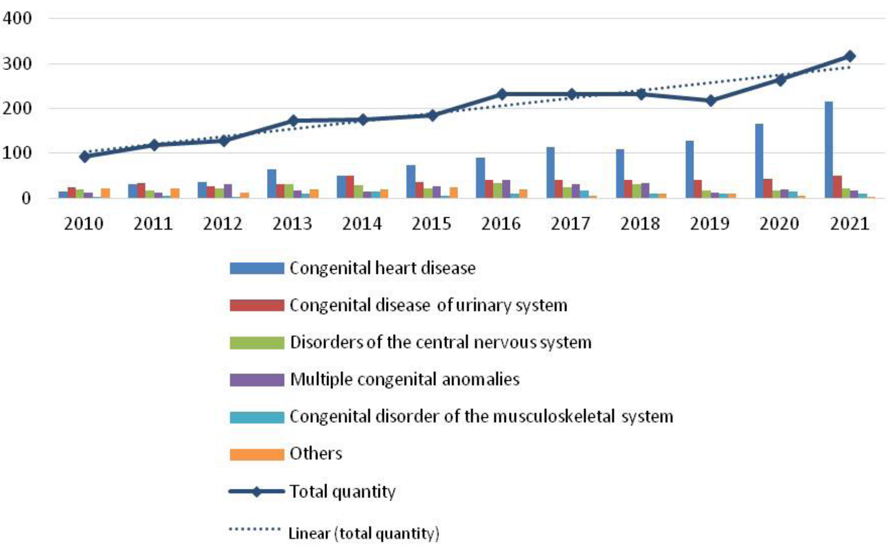

Fig. 1. The dynamics of identification of CAs (n) in newborns of Ryazan in 2010–2021.

Five most common CAs included Q21.0 Ventricular septal defect; Q62.0 Congenital hydronephrosis; Q60.0 Unilateral renal agenesis; Q37.1 Unilateral hard palate and lip cleft; Q53.1 Unilateral chryptorchism. Most commonly occurring congenital anomalies were Q21.0 Ventricular septal defect (28.5%, 95% CI: 20.8–36.2%) and Q62.0 Congenital hydronephrosis (7.3%, 95% CI: 2.9–11.7%).

The levels of exposure to atmospheric air pollution in the first trimester of pregnancy of women whose children were involved in the study groups, are shown in Table 2. The most adverse effect in the first trimester of pregnancy was demonstrated by CO at a concentration of 0.251 mg/m^3, a lesser effect was noted for NO_2 at a concentration of 0.023 mg/m^3 and for SO_2 — at 0.008 mg/m^3.

The highest level of individual impact of CO in the first three months of pregnancy was 0.251 mg/m^3. Practically the same impact was produced by NO_2 at the average concentration of 0.023 mg/m^3 and by O_3 at 0.027 mg/m^3.

Table 3 shows the influence of the analyzed air pollutants on formation of CAs in the first trimester of pregnancy.

Table 2. Concentration (mg/m^3) of Analyzed Pollutants in Different Period of Pregnancy of Women Whose Children Were Included in Study Groups

Pollutants	Me	Min	Max	Q25%	Q75%
1 month					
Carbon monoxide, CO	0.245	0.029	2.598	0.139	0.293
Nitrogen dioxide, NO_2	0.248	0.001	0.997148	0.013	0.023
Sulfur dioxide, SO_2	0.017	0.000	0.049	0.001	0.013
Ozone, O_3	0.002	0.000	0.082	0.008	0.045
2 month					
Carbon monoxide, CO	0.018	0.029	3.008	0.147	0.300
Nitrogen dioxide, NO_2	0.259	0.001	0.996	0.012	0.022
Sulfur dioxide, SO_2	0.016	0.000	0.046	0.000	0.013
Ozone, O_3	0.003	0.000	0.121	0.009	0.045
3 month					
Carbon monoxide, CO	0.018	0.030	1.386	0.139	0.295
Nitrogen dioxide, NO_2	0.261	0.001	1.018	0.012	0.021
Sulfur dioxide, SO_2	0.015	0.000	0.045	0.001	0.015
Ozone, O_3	0.003	0.000	0.170	0.007	0.043

Notes: Me — median; Q25% and Q75% — 25th and 75th percentiles; min — minimum value, max — maximum value

Table 3. Influence on Exposure to Analyzed Air Pollutants on Formation of CAs in First Trimester of Pregnancy

Period of Pregnancy	OR (95% CI)	aOR (95% CI)	p
Carbon oxide, CO			
1 month	0.97 (0.76–1.25)	0.920 (0.69–1.24)	0.596
2 month	0.97 (0.75–1.24)	0.93 (0.69–1.26)	0.631
3 month	0.92 (0.72–1.18)	0.890 (0.68–1.18)	0.435
Nitrogen dioxide, NO_2			
1 month	0.46 (0.03–6.67)	0.61 (0.2–1.88)	0.051
2 month	1.16 (0.78–1.74)	1.25 (0.64–2.42)	0.262
3 month	0.41 (0.06–2.91)	0.43 (0.04–4.36)	0.346
Sulfur dioxide, SO_2			
1 month	1.32 (1.03–1.7)	1.28 (0.97–1.68)	0.076
2 month	1.39 1.08–1.78	**1.39 (1.05–1.83)**	***0.018***
3 month	1.5 1.16–1.95	**1.59 (1.17–2.16)**	***0.02***
Ozone, O_3			
1 month	1.1 (0.86–1.4)	1.18 (0.89–1.57)	0.241
2 month	0.99 (0.78–1.27)	1.01 (0.77–1.34)	0.926
3 month	0.8 (0.62–1.04)	0.89 (0.67–1.18)	0.407

Notes: aOR — adjusted odds ratio, OR — odds ratio, CI — confidence interval

As for air pollutants in the studied period of pregnancy (the first trimester), a significant relationship was observed between CAs and SO_2, especially in the second (aOR 1.39; 95% CI 1.05–1.83, $p < 0.05$) and third months of pregnancy (aOR 1.59; 95% CI 1,17–2.16, $p < 0.05$); with this, no statistically significant relationship was found between CAs and CO, NO_2, O_3 ($p > 0.05$).

DOI: https://doi.org/10.17816/PAVLOVJ109333

DISCUSSION

The presented data, first of all, demonstrate increase in the quantity of recorded cases of CAs in newborns of Ryazan in the period of 2010–2021. One of reasons for this may be the development and introduction of diagnostic technologies in clinical practice in Ryazan (which permitted to improve prenatal diagnostics and screening methods for CAs), and of Astraia data base for ACs monitoring (since 2016).

Multivariate logistic regression analysis demonstrated that exposure to SO_2 in the second and third months of pregnancy is associated with the risk of the formation of CAs. It is worth noting that we have chosen the first trimester of pregnancy, because the period *from the third to the eighth week of embryonic development* is most sensitive to the environmental factors. In this period, embryonic cells are highly differentiated and sensitive to many teratogenic factors. Our conclusions are confirmed by previously published results showing the relationship between CAs and exposure to SO2 [5, 14–16].

Practical recommendations based on the results obtained:

1. To introduce *regional reporting form* for effective monitoring of the health of newborns.
2. To improve the system of social and hygienic monitoring in part of acquisition, evaluation and prediction of the state of habitat (increase in the number of observation stations and monitoring posts for dynamic observation of AAP with expansion of the list of controlled substances) and the frequency of occurrences of CAs to form the *regional register of CAs*.
3. To use the results of the study for elaboration of preventive programs at the regional level to improve ecologic and hygienic situation in the RR and reduce the risk of the formation of CAs, taking into account cause-and-effect relationships and dependences.

CONCLUSION

The number of congenital anomalies in Ryazan is growing with each year. Our study confirms the data of foreign authors about the relationship between atmospheric air pollution and formation of congenital anomalies. In particular, exposure to SO_2 in the second and third months of pregnancy enhances the risk of a congenital anomaly in a newborn.

In this regard, it is important to emphasize that the regional authorities and state supervision agencies should direct their efforts to reduction of the environmental pollution, which should help reduce the frequency of CAs in children.

ADDITIONALLY

Funding. The authors declare that there is no funding for the study.
Conflict of interests. The authors declare no conflicts of interests.
Contribution of the authors: *N. A. Bobotina* — research concept and design, data collection and statistical processing, text writing, text editing; *M. A. Demchenko* — concept and design of the study, collection and statistical processing of data; *V. A. Kiryushin* — the concept and plan of the study, editing the text; *T. V. Motalova* — the concept and plan of the study, editing the text. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

Финансирование. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.
Конфликт интересов. Авторы заявляют об отсутствии конфликта интересов.
Вклад авторов: *Боботина Н. А.* — концепция и дизайн исследования, сбор и статистическая обработка данных, написание текста, редактирование текста; *Демченко М. А.* — концепция и дизайн исследования, сбор и статистическая обработка данных; *Кирюшин В. А.* — концепция и план исследования, редактирование текста; *Моталова Т. В.* — концепция и план исследования, редактирование текста. Авторы подтверждают соответствие своего авторства международным критериям ICMJE (все авторы внесли существенный вклад в разработку концепции и подготовку статьи, прочли и одобрили финальную версию перед публикацией).

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