COMPARATIVE ASSESSMENT OF THE INCIDENCE OF MALIGNANT NEOPLASMS OF THE OVARIES IN WOMEN LIVING IN THE ENVIRONMENTALLY DISADVANTAGED AREAS (2000–2019)

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Radioactive and chemical contamination can affect carcinogenesis, including the development of malignant neoplasms of the ovaries (MNOs) in women. The study aimed to perform comparative assessment of environmental situation in the towns and districts of the Bryansk Region based on chemical, radioactive, and combined radioactive contamination, as well as primary incidence of MNOs in women in accordance with official statistics for the years 2000–2019. The data for the study were provided by the Bryansk Regional Oncology Dispensary, Bryanskstat, Rostekhnadzor, Rospotrebnadzor. Neither significant differences in primary incidence of MNOs, nor increased risk of MNO were revealed in female population aged 18–80 years, regardless of the environmental conditions of living in 2000–2019. We revealed a significantly elevated relative risk (RR) of primary incidence of low-grade MNOs in women aged 41–60 years living in the environmentally disadvantaged areas compared to women living in the control areas: RR 1.88 (95% CI: 1.43–2.48); $p < 0.0001$). The rate of low-grade MNOs in women aged 41–60 years in the areas of the combined exposure is 17.6 ± 1.96, which 1.5-fold exceeds the values reported for radioactively contaminated areas (11.7 ± 2.73) and 1.2-fold exceeds the values reported for chemically contaminated areas (15.2 ± 1.31). The combined effects of radioactive and chemical contamination results in the higher RR of low-grade MNOs compared to the areas with only one pollution factor, i.e. radioactive contamination (RR 1.51 (95% CI: 1.00–2.28)), chemical contamination (RR 1.17 (95% CI: 0.90–1.50)). The findings suggest synergistic effect of radiation and chemical factors on the incidence of low-grade MNOs.

Keywords: Chernobyl accident, malignant neoplasms of the ovaries, radioactive contamination, chemical pollution, combined contamination, regression analysis, relative risk, Bryansk region

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Compliance with ethical standards: the study involved the use of impersonal statistical information about the incidence of MNOs in women in the areas of the Bryansk Region for the years 2000–2019.

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СРАВНИТЕЛЬНАЯ ОЦЕНКА ЗАБОЛЕВАЕМОСТИ ЗЛОКАЧЕСТВЕННЫМИ НОВООБРАЗОВАНИЯМИ ЯИЧНИКОВ ЖЕНЩИН, ПРОЖИВАЮЩИХ НА ЭКОЛОГИЧЕСКИ НЕБЛАГОПОЛУЧНЫХ ТЕРРИТОРИЯХ (2000–2019 ГГ.)

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Радиоактивное и химическое загрязнение может влиять на процессы канцерогенеза, в том числе на формирование злокачественных новообразований яичников (ЗНОЯ) у женщин. Целью исследования было выполнить сравнительную оценку состояния окружающей среды в городах и районах Брянской области по химическому, радиоактивному и сочетанному радиационно-химическому загрязнению и уровня первичной заболеваемости женщин ЗНОЯ на основании данных официальной статистики за 2000–2019 гг. Данные для исследования предоставили Брянский областной онкологический диспансер, Брянскстат, Ростехнадзор, Роспотребнадзор. Не выявлено как значимых различий уровня первичной заболеваемости ЗНОЯ, так и повышенного риска заболеваемости ЗНОЯ у женского населения 18–80 лет, независимо от экологических условий проживания в 2000–2019 гг. Установлено значимое повышение относительного риска (ОР) первичной заболеваемости низкодифференцированными формами ЗНОЯ у женщин 41–60 лет, проживающих в экологически неблагополучных районах, по сравнению с проживающими на контрольных территориях — ОР 1,88 (95% ДИ: 1,43–2,48); $p < 0,0001$). Частота низкодифференцированных форм ЗНОЯ у женщин 41–60 лет на территориях сочетанного воздействия составляет 17,6 ± 1,96, что в 1,5 раза превышает значения территорий радиоактивного загрязнения (11,7 ± 2,73) и в 1,2 раза — значения территорий химического загрязнения (15,2 ± 1,31). Сочетанное воздействие радиационно-химического загрязнения привело к более высокому ОР заболеваемости низкодифференцированными формами ЗНОЯ по сравнению с территориями, где присутствует только один фактор загрязнения — радиоактивное загрязнение (ОР 1,51 (95% ДИ: 1,00–2,28)), химическое загрязнение (ОР 1,17 (95% ДИ: 0,90–1,50)). Полученные результаты позволяют предположить синергическое влияние радиационного и химического факторов на заболеваемость низкодифференцированными формами ЗНОЯ.

Ключевые слова: авария на ЧАЭС, ЗНОЯ, радиоактивное загрязнение, химическое загрязнение, сочетанное загрязнение, регрессионный анализ, относительный риск, Брянская область

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Соблюдение этических стандартов: для исследования использовали обезличенную статистическую информацию о заболеваемости женщин ЗНОЯ на территориях Брянской области в период с 2000 по 2019 г.

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Acording to recent WHO GLOBOCAN 2020 estimates [1], the increase in the global rate of malignant neoplasms (MNs) to 19.3 million incident cases and 10.0 deaths is reported. Malignant neoplasms of the ovaries (MNOs) occupy the seventh place among all cancer types being generally one of fatal diseases affecting female reproductive system [2]. According to the data provided by the Blokhin National Medical Research Center of Oncology, MNOs are second only to endometrial cancer and cervical cancer based on the incidence rate in Russia [3].

The papers [4–12] report a significant correlation between the risk of MNOs and the increase in environmental ill-being.

Radioecological monitoring of the South-Western areas of the Bryansk Region suggests that the cesium-137 (^{137}Cs) contamination density exceeds the established radiological standards 37 years after the Chernobyl accident, and the average annual effective doses reach hundreds mSv [13–18]. Furthermore, an increase in the emission of pollutants into the atmosphere is reported for the Bryansk Region in recent years [19].

In certain areas of the Bryansk Region, the population is exposed to combined effects of radioactive and chemical contamination [20–22].

Table 1. Ranking of the Bryansk Region territories based on the levels of radioactive, chemical, and combined environmental pollution, and primary incidence of MNOs (2000–2019)

Territories	Major gaseous pollutants in atmospheric air					Radioactive contamination density, kBq/m^2		Primary incidence of MNOs, M ± *m*
	Total	Из них:						
		VOCs	NO_x	SO_2	CO	^{137}Cs	^{90}Sr	
	Gross emissions per area of the district, g/m^2							
Rognedinsky District	11.5	0	6	0	7	21.7	0.8	25.8 ± 6.5
Suzemsky District	27	5	9	1	13	18.6	2.5	26.3 ± 4.5
Mglinsky District	31	6	6	2	17	6.6	0.6	17.5 ± 3.1
Kletnyansky District	47	27	5	5	10	5.4	0.5	21.6 ± 3.5
Navlinsky District	53	12	13	4	25	18.9	0.8	18.7 ± 3.6
Dubrovsky District	56	13	17	0.4	26	7.2	0.4	19.4 ± 5.0
Brasovsky District	64	10	19	6	29	25.2	0.4	20.0 ± 3.2
Sevsky District	68	20	10	24	14	18.9	1.4	19.4 ± 4.5
Komarichsky District	98.7	24.9	18.9	9.2	46.1	27	1	15 ± 2.9
Karachevsky District	114.8	28.8	35.1	1.1	50.8	14	0.9	25.7 ± 2.7
Surazhsky District	128.2	35.1	34.8	5.8	51.9	8	0.3	18 ± 3.2
Average value	**63.5**	**16.1**	**15.7**	**5.3**	**26.4**	**15.6**	**0.9**	**20.5 ± 1.3 (–8.8%*)**
Pogarsky District	123	65	22	4	32	29.9	1.1	29.3 ± 3.9
Zhiryatinsky District	154.8	103	17	0.9	34.9	5	0.84	18 ± 4.5
Zhukovsky District	195.9	23	52	40.5	80.7	6.68	0.85	20 ± 1.7
Trubchevsky District	276	87	28	2.1	157.7	23.67	0.88	16.3 ± 2.5
Pochepsky District	363.8	224	33	2.9	105.9	5	0.54	19 ± 3.2
Unechsky District	559	292	58	32	177	7.2	0.8	24.1 ± 3.1
Vygonichsky District	857	749	37	2	70	9.5	0.4	12.7 ± 3.9
Bryansky District	959	813	47	13	86	5.7	0.4	23.8 ± 1.9
Town of Seltso	5207.6	772	2406	96.8	1935	4	0.86	23 ± 2.7
Dyatkovsky District	8044.8	340	3759	1140	2808	38	1	22.2 ± 1.8
City of Bryansk	32189	5218	10887	2617.7	13471	9	6	24 ± 1.5
Average value	**4450.8**	**792.2**	**1576.8**	**359.4**	**1723.4**	**13.7**	**1.39**	**22.8 ± 1.2 (+0.4%*)**
Krasnogorsky District	16	1	5	0	9	303.4	9.3	18.8 ± 4.2
Gordeyevsky District	29	2	11	0.2	15	328.6	5	11.0 ± 4.2
Zlynkovsky District	36.8	4.8	10.8	4.1	18.1	412	16	18 ± 3.7
Novozybkovky District	52	11	0.1	0.2	40.7	460	8.6	14.8 ± 5.7
Klimovsky District	71.9	15.9	8.1	14.5	32.9	139.8	6.3	21 ± 3.6
Klintsovsky District	169.3	16.8	69.8	2.1	81	194	4.8	20.2 ± 3.1
Average value	**62.2**	**8.4**	**17.6**	**3.6**	**32.6**	**305.8**	**8.3**	**18.2 ± 2.0 (–19.0%*)**
Starodubsky District	392	316	24	9	43	45.4	1.4	20.9 ± 2.4
Town of Klintsy	7264	2059	2616	139	2450	195.6	3	17.4 ± 1.1
Town of Novozybkov	7422	1778	2159	406	3079	456.5	9.7	24.0 ± 2.1
Average value	**5026**	**1384.3**	**1599.7**	**184.7**	**1857.3**	**232.5**	**4.7**	**20.1 ± 0.9 (–11.1%*)**

Note: * — difference (%) from the all-Russian level of primary incidence of MNOs (2000–2019). Differences in primary incidence of MNOs based on the Mann–Whitney *U* test: in environmentally safe territories and territories with chemical ($p = 0.67$), radioactive ($p = 0.22$), and combined ($p = 0.95$) contamination; chemical and radioactive ($p = 0.11$), chemical and combined ($p = 0.94$), radioactive and combined ($p = 0.30$) contamination.

Table 2. Relative risk (RR) of primary incidence of MNOs in women aged 18–80 years living in the territories with varying levels of radioactive, chemical, and combined environmental contamination for the years 2000–2019

Territory type	Population	Affected, abs.	Unaffected, abs.	RR (95% CI)
With chemical, radioactive, and combined contamination (total)	9599974	2096	9597878	1.07 (0.96–1.19)
Environmentally safe	2058551	420	2058131	
Chemically contaminated	7319942	1657	7318285	1.11 (1.00–1.23)
Environmentally safe	2058551	420	2058131	
Radioactively contaminated	906651	163	906488	0.88 (0.74–1.06)
Environmentally safe	2058551	420	2058131	
With combined contamination	1373381	276	1373105	0.98 (0.85–1.15)
Environmentally safe	2058551	420	2058131	
Chemically contaminated	7319942	1657	7318285	1.26 (1.07–1.48)
Radioactively contaminated	906651	163	906488	
With combined contamination	1373381	276	1373105	0.89 (0.78–1.00)
Chemically contaminated	7319942	1657	7318285	
With combined contamination	1373381	276	1373105	1.12 (0.92–1.36)
Radioactively contaminated	906651	163	906488	

Thus, environmental pollution results in the mutation rate increase, which creates a threat to the genetic security of all living things [23].

The study aimed to perform comparative assessment of environmental situation in the towns and districts of the Bryansk Region based on chemical, radioactive, and combined radioactive contamination, as well as primary incidence of MNOs in women in accordance with official statistics for the years 2000–2019.

METHODS

The analysis of density of the cesium-137 (^{137}Cs) and strontium-90 (^{90}Sr) contamination resulting from the Chernobyl accident was conducted based on the data [17], the average cumulative effective doses (CED_{90}) were assessed based on the data [24], the levels of the atmospheric air chemical pollution with CO, NO_x, SO_2, and volatile organic compounds (VOCs) were assessed based on the data [25] for the years 2010–2019.

The incidence of newly diagnosed MNOs in female population (aged 18–80 years) of the Bryansk Region was analyzed using the official data provided by the Bryansk Regional Oncology Dispensary [26]. A total of 2647 MNO cases were revealed in 2000–2019. The analysis of the MNO histological forms was performed in the reported 942 cases (age 41–60 years). Absolute values were recalculated per 100,000 population.

Linear regression and relative risk (RR) of primary MNO incidence were calculated depending on chemical and radioactive contamination levels for the period of 2000–2019. Statistical analysis was performed using the Shapiro–Wilk test, Mann–Whitney *U* test, Spearman's rank correlation, linear regression; 95% confidence intervals (95% CI) were calculated; the significance levels were as follows: $p < 0.05$, $p < 0.01$, $p < 0.001$. Statistical analysis of the data obtained was performed using the MyOffice software package (New Cloud Technologies; Russia).

RESULTS

Towns and districts of the Bryansk Region were divided into four groups based on chemical and radioactive contamination levels, as well as primary incidence of MNOs in 2000–2019 (Table 1). Analysis of the results provided in the table was earlier reported in the paper [27].

Analysis of the data provided in Table 2 showed that there was no increase in the RR of MNOs among women in the territories with chemical, radioactive, and combined contamination compared to the control (environmentally safe) territories: RR 1.07 (95% CI: 0.96–1.19). However, the risk of MNOs in women living in the chemically contaminated territories was slightly higher, than in women living in the control districts (RR 1.11 (95% CI: 1.00–1.23)), but the differences were non-significant ($p = 0.06$). It should be noted that we revealed a significantly ($p = 0.005$) increased risk of MNOs in the chemically contaminated territories relative to the radioactively contaminated areas: RR 1.26 (95% CI: 1.07–1.48). No such patterns were revealed in other territories (Table 2).

As shown in Fig. 1, a significant increase in the long-term trend of primary MNO incidence was revealed in the group of chemically contaminated territories only ($p < 0.05$).

Comparative assessment of primary incidence of high-grade, intermediate grade, and low-grade MNOs among women aged 41–60 years living in environmentally different territories of the Bryansk Region in 2000–2019 showed that the rate of high-grade MNOs in the environmentally safe territories was 7.1 ± 0.83, which exceeded the values of the territories with radioactive (1.4 ± 0.65), chemical (1.6 ± 0.35), and combined (3.2 ± 0.75) contamination 5.1-fold, 4.4-fold, and 2.2-fold, respectively ($p < 0.001$) (Table 3).

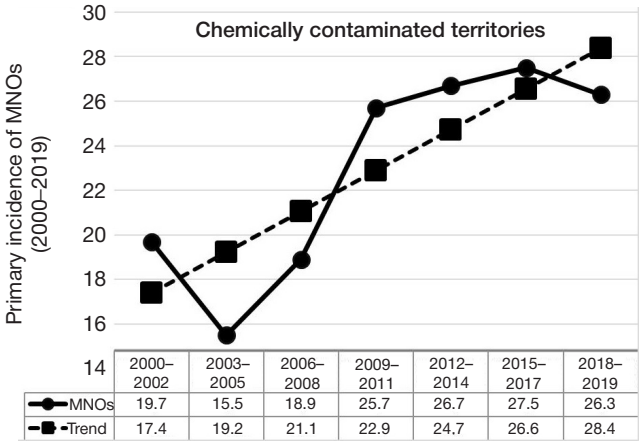
We revealed no significant differences in the rate of intermediate grade MNOs in the towns and districts of the Bryansk Region, regardless of the living conditions (the values vary between 7.0 and 8.8) (Table 3).

The rate of low-grade MNOs in the chemically contaminated territories is 15.2 ± 1.31, which 1.3-fold ($p < 0.05$) exceeded the values of the radioactively ccontaminated territories (11.7 ± 2.73), suggesting the leading role of chemical factor vs. radioactive in shaping the incidence of MNOs (Table 3).

The rate of low-grade MNOs in the areas with combined contamination reaches its maximum (17.6 ± 1.96), it 2.2-fold exceeds ($p < 0.001$) the values of the control areas (8.1 ± 1.20), 1.5-fold ($p < 0.05$) the values of the radioactively contaminated areas (11.7±2.73), and 1.17-fold ($p > 0.05$) the values of the chemically contaminated areas (15.2 ± 1.31). The results obtained suggest synergistic effect of radiation and chemical factors on the incidence of low-grade MNOs (Table 3).

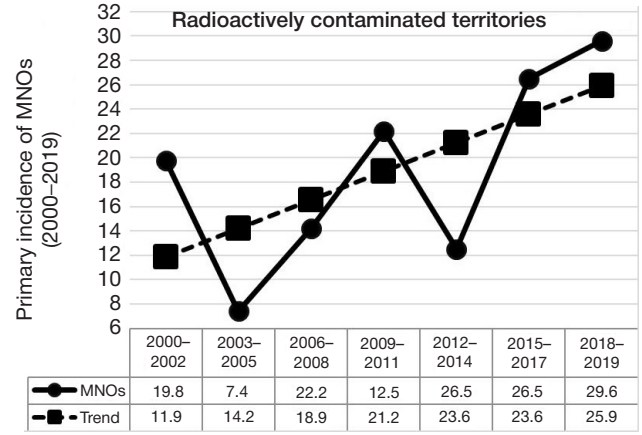
Analysis of the data provided in Table 4 revealed a significant increase in the RR of primary incidence of low-grade MNOs

Trend
$y = 1.833\ x + 15.6$
Fisher's exact test = 0.02
Standard error = 0.54
Spearman's rank correlation coefficient
$\rho = 0.79$, $p = 0.04$
Coefficient of determination = 0.70
95% CI of coefficient A (0,45; 3,22)



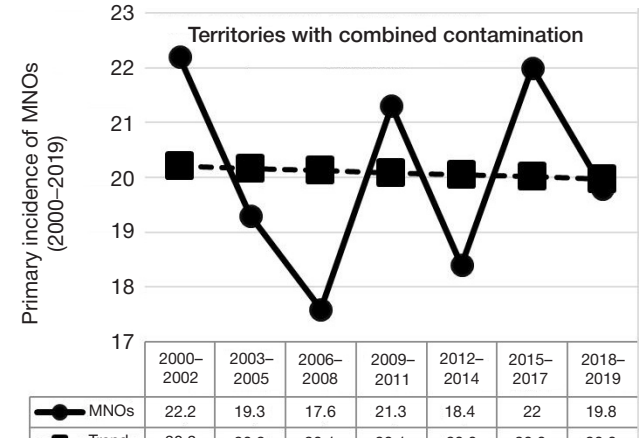
	2000–2002	2003–2005	2006–2008	2009–2011	2012–2014	2015–2017	2018–2019
MNOs	19.7	15.5	18.9	25.7	26.7	27.5	26.3
Trend	17.4	19.2	21.1	22.9	24.7	26.6	28.4

Trend
$y = 2.338\ x + 9.53$
Fisher's exact test = 0.12
Standard error = 1.27
Spearman's rank correlation coefficient
$\rho = 0.64$, $p = 0.12$
Coefficient of determination = 0.41
95% CI of coefficient A (–0.91; 5.59)



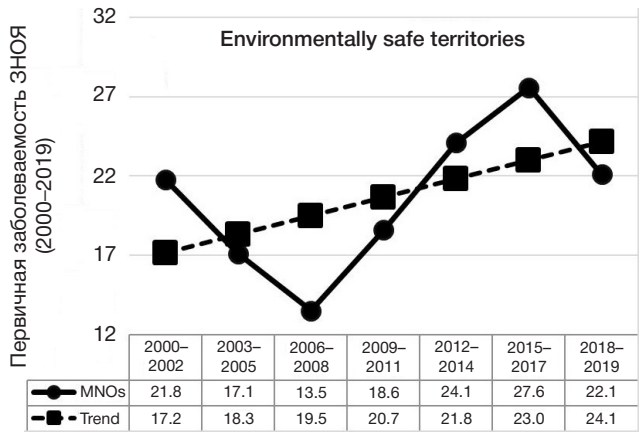
	2000–2002	2003–2005	2006–2008	2009–2011	2012–2014	2015–2017	2018–2019
MNOs	19.8	7.4	22.2	12.5	26.5	26.5	29.6
Trend	11.9	14.2	18.9	21.2	23.6	23.6	25.9

Trend
$y = -0.038\ x + 20.2$
Fisher's exact test = 0.92
Standard error = 0.37
Spearman's rank correlation coefficient
$\rho = -0.07$, $p = 0.88$
Coefficient of determination = 0.002
95% CI of coefficient A (–0.99; 0.92)



	2000–2002	2003–2005	2006–2008	2009–2011	2012–2014	2015–2017	2018–2019
MNOs	22.2	19.3	17.6	21.3	18.4	22	19.8
Trend	20.2	20.2	20.1	20.1	20.0	20.0	20.0

Trend
$y = 1.164\ x + 16.0$
Fisher's exact test = 0.21
Standard error = 0.82
Spearman's rank correlation coefficient
$\rho = 0.64$, $p = 0.12$
Coefficient of determination = 0.29
95% CI of coefficient A (–0.94; 3.27)



	2000–2002	2003–2005	2006–2008	2009–2011	2012–2014	2015–2017	2018–2019
MNOs	21.8	17.1	13.5	18.6	24.1	27.6	22.1
Trend	17.2	18.3	19.5	20.7	21.8	23.0	24.1

Fig. Dynamics of primary incidence of MNOs in women living in environmentally different territories of the Bryansk Region with the long-term trends by 3-year periods for the years 2000–2019 (recalculated per 100,000 population)

Table 3. Comparative assessment of primary incidence of high-grade, intermediate grade, and low-grade MNOs among women aged 41–60 years living in environmentally different territories of the Bryansk Region for the years 2000–2019 (recalculated per 100,000 population)

Studied territories MNO forms	Environmentally safe territories (control)	Chemically contaminated territories	Radioactively contaminated territories	Territories with combined contamination	Significantce of intergroup differences based on the Mann–Whitney *U* test: p_1 (I–II), p_2 (I–III), p_3 (I–IV), p_4 (II–III), p_5 (II–IV), p_6 (III–IV).
	I (n = 166)	II (n = 603)	III (n = 62)	IV (n = 111)	
All forms	23.9 ± 2.00	25.4 ± 2.55	22.0 ± 3.84	27.6 ± 2.5	p_1n/s; p_2n/s; p_3n/s; p_4n/s; p_5n/s; p_6n/s
of those:					
High-grade	7.1 ± 0.83	1.6 ± 0.35	1.4 ± 0.65	3.2 ± 0.75	p_1**; p_2**; p_3**; p_4*; p_5n/s; p_6n/s
Intermediate grade	8.7 ± 1.20	8.6 ± 1.11	8.8 ± 2.17	7.0 ± 1.32	p_1n/s; p_2n/s; p_3n/s; p_4n/s; p_5n/s; p_6n/s
Low-grade	8.1 ± 1.20	15.2 ± 1.31	11.7 ± 2.73	17.6 ± 1.96	p_1**; p_2n/s; p_3**; p_4*; p_5n/s; p_6*

Note: * — the differences are significant at $p < 0.05$; ** — the differences are significant at $p < 0.001$; n/s — the differences are non-significant at $p > 0.05$.

in women aged 41–60 years living in the environmentally disadvantaged areas (territories with chemical, radioactive, and combined contamination in total) relative to the environmentally safe (control) territories (RR 1.88 (95% CI: 1.43–2.48); $p < 0.0001$). Furthermore, RR was significantly increased in the territories with radioactive (RR 1.45 (95% CI: 0.95–2.23)), chemical (RR 1.88 (95% CI: 1.42–2.50)), and to the greater extent combined contamination (RR 2.20 (95% CI: 1.55–3.11)) of the environment compared to the control areas.

The combined effects of radioactive and chemical contamination resulted in the higher RR of low-grade MNOs compared to the territories with only one pollution factor, i.e. radioactive contamination (RR 1.51 (95% CI: 1.00–2.28)), chemical contamination (RR 1.17 (95% CI: 0.90–1.50)) (Table 4). The findings have been fully confirmed by analysis of the data provided in Table 3.

DISCUSSION

The papers [28, 29] report that the incidence of solid low-grade MNOs became higher compared to the incidence of high-grade MNOs with increasing levels of chemical [28] and radioactive [29] environmental contamination, which suggests worse outcomes characterized by low 5-year survival and early metastasis.

The findings confirm the research data [28, 29] and suggest the increase in the rate of low-grade MNOs in women aged 41–60 years living in the environmentally disadvantaged territories, with the most significant increase under combined exposure to radiation and chemical factors.

It should be noted that the fact that the analysis of MNO incidence in female population did not consider the distribution by disease stages and immunohistochemistry profiles was a limitation of the study.

CONCLUSIONS

1. The study revealed neither significant differences in primary incidence of malignant neoplasms of the ovaries (MNOs), nor increased risk of MNOs in the female population aged 18–80 years, regardless of environmental conditions of living in 2000–2019.

2. We determined a significant increase in the relative risk (RR) of primary incidence of low-grade MNOs in women aged 41–60 years living in the environmentally disadvantaged areas (territories with chemical, radioactive, and combined contamination in total) relative to the environmentally safe (control) territories (RR 1.88 (95% CI: 1.43–2.48); $p < 0.0001$).

3. It was shown that the rate of low-grade MNOs in women aged 41–60 years in the territories with the combined

Table 4. Relative risk (RR) of primary incidence of low-grade MNOs in women aged 41–60 years living in the territories with various levels of radioactive, chemical, and combined contamination of the environment for the years 2000–2019

Territory type	Population	Affected, abs.	Unaffected, abs.	RR (95% CI)
With chemical, radioactive, and combined contamination (total)	153394	465	152929	1.89 (1.43–2.49)
Environmentally safe	34823	56	34767	
Chemically contaminated	119153	361	118792	1.88 (1.42–2.50)
Environmentally safe	34823	56	34767	
Radioactively contaminated	14127	33	14094	1.45 (0.95–2.23)
Environmentally safe	34823	56	34767	
With combined contamination	20114	71	20043	2.20 (1.55–3.11)
Environmentally safe	34823	56	34767	
Chemically contaminated	119153	361	118792	1.30 (0.91–1.85)
Radioactively contaminated	14127	33	14094	
With combined contamination	20114	71	20043	1.17 (0.90–1.50)
Chemically contaminated	119153	361	118792	
With combined contamination	20114	71	20043	1.51 (1.00–2.28)
Radioactively contaminated	14127	33	14094	

exposure was 17.6 ± 1.96, which 1.5-fold exceeded the values of the radioactively contaminated territories (11.7 ± 2.73) and 1.2-fold exceeded the values of the chemically contaminated territories (15,2 ± 1,31).

4. The combined effects of radioactive and chemical contamination resulted in the higher RR of the incidence of low-grade MNOs compared to the territories with only one pollution factor, i.e. radioactive contamination (RR 1.51 (95% CI: 1.00–2.28)), chemical contamination (RR 1.17 (95% CI: 0.90–1.50)).

5. The findings suggest synergistic effect of radiation and chemical factors on the incidence of low-grade MNOs.

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