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FEATURES OF THE OVERALL MORTALITY DYNAMICS IN THE POPULATION OF OZERSK URBAN DISTRICT DURING THE COVID-19 PANDEMIC

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Introduction. The pandemic spread of COVID-19, observed in 2020–2021, had an impact on overall mortality among the population. Of particular interest to researchers is the study of trends in overall mortality rates among nuclear industry workers exposed to occupational radiation, as well as among the population living near nuclear facilities.

Objective. Analysis of the overall mortality dynamics among the population of Ozersk — a nuclear industry city — during the COVID-19 pandemic, depending on the combined effect of radiation and non-radiation risk factors.

Materials and methods. A retrospective cohort study was conducted among residents of the Ozersk Urban District (OUD) who died from various causes during the period 2020–2023. Annual reports from Rosstat and the municipal statistics department were analyzed. Data on COVID-19 incidence were provided by the Center for Hygiene and Epidemiology No. 71 in Ozersk. The assessment of survival function depending on the presence of COVID-19, as well as the influence of age and occupational external radiation dose among PA «Mayak» workers, was performed using the Kaplan–Meier method. The analysis of the impact of COVID-19 incidence, adjusted for occupational radiation dose, on the all-cause mortality rate across different age groups was carried out using the Cox proportional hazards model.

Results. Based on the analysis of overall mortality trends for the period 2013–2023, a period associated with the peak of pandemic activity was identified. The impact of COVID-19 on all-cause mortality during the pandemic period was revealed, depending on attained age and occupational radiation dose ($p < 0.05$). The effect of COVID-19 incidence on overall mortality was modified by several risk factors, among which attained age ($p < 0.001$) and accumulated external radiation dose ($p = 0.03$) exerted a significant influence.

Conclusions. COVID-19 incidence during the pandemic period had both direct and indirect effects on overall mortality among the population of Ozersk. Alongside the direct impact of COVID-19, age, and external radiation dose among PA «Mayak» workers, the combination of these factors is also important when assessing the dynamics of overall mortality during the pandemic. The obtained results are of interest for predicting the consequences of potential future pandemic situations and for developing effective strategies to protect the health of populations in nuclear industry cities.

Keywords: pandemic; COVID-19; all-cause mortality; occupational exposure; risk

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ОСОБЕННОСТИ ДИНАМИКИ ОБЩЕЙ СМЕРТНОСТИ НАСЕЛЕНИЯ ОЗЕРСКОГО ГОРОДСКОГО ОКРУГА В ПЕРИОД ПАНДЕМИИ COVID-19

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Введение. Пандемическое распространение заболеваемости COVID-19, наблюдавшееся в период с 2020 по 2021 год, оказало влияние на общую смертность среди населения. Особый интерес для исследователей приобретает изучение динамики показателя общей смертности среди работников атомной отрасли, подвергающихся профессиональному радиационному воздействию, и населения, проживающего вблизи объектов атомной промышленности.

Цель. Анализ динамики общей смертности населения города атомной промышленности Озерск в период пандемии COVID-19 в зависимости от совокупного влияния факторов риска радиационной и нерадиационной природы.

Материалы и методы. Проведено ретроспективное когортное исследование жителей Озерского городского округа (ОГО), умерших от различных причин в период 2020–2023 гг. Анализировали ежегодные отчеты Росстата и муниципального отдела статистики. Данные о заболеваемости от COVID-19 предоставлены Центром гигиены и эпидемиологии № 71 г. Озерска. Оценка функции дожития в зависимости от наличия заболевания COVID-19, а также влияния возраста и дозы внешнего профессионального облучения работников ПО «Маяк» выполнена с использованием метода Каплана – Майера. Анализ влияния заболеваемости COVID-19 с учетом дозы профессионального облучения на интенсивность смертности от всех причин среди различных возрастных групп выполнен методом пропорциональных рисков Кокса.

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Результаты. На основании анализа динамики показателей общей смертности за 2013–2023 годы определен период, связанный с пиком пандемической активности. Выявлено влияние заболевания COVID-19 ($p < 0,05$) в зависимости от достигнутого возраста и дозы профессионального облучения на смертность от всех причин в течение пандемического периода. Влияние заболеваемости COVID-19 на общую смертность модифицировалось воздействием нескольких факторов риска, из которых значимое влияние оказывали достигнутый возраст ($p < 0,001$) и накопленная доза внешнего облучения ($p = 0,03$).

Выводы. Заболеваемость COVID-19 в пандемический период оказывала как прямое, так и опосредованное влияние на общую смертность среди населения Озерска. Наряду с прямым влиянием заболевания COVID-19, возраста и дозы внешнего облучения работников ПО «Маяк» большое значение при оценке динамики общей смертности в период пандемии имеет сочетание этих факторов. Полученные результаты представляют интерес для прогнозирования последствий, связанных с возникновением возможных пандемических ситуаций, и выработки эффективных стратегий по охране здоровья населения городов атомной промышленности.

Ключевые слова: пандемия; COVID-19; общая смертность; профессиональное облучение; риск

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INTRODUCTION

The global spread of the novel SARS-CoV-2 coronavirus infection led to the COVID-19 pandemic, which resulted in an increase in the all-cause mortality rate among the population both in Russia and globally compared to previous years [1, 2]. The main risk factors influencing all-cause mortality during the pandemic, aside from COVID-19 itself, are considered to be attained age, male sex, the presence of comorbid conditions, and racial/ethnic disparities [3].

A distinctive feature of all-cause mortality in the population of the nuclear industry city of Ozersk is chronic exposure to ionizing radiation among employees of the Mayak Production Association (Mayak PA) [4]. Numerous studies have established the influence of ionizing radiation on the risk of mortality from malignant neoplasms and other causes [5–7], which may be considered an additional risk factor affecting mortality rates during the pandemic.

A review of scientific publications in domestic and international journals indexed in the eLibrary and PubMed databases revealed no studies assessing the risk associated with the impact of COVID-19, while accounting for other risk factors including occupational radiation doses, on all-cause mortality rates during the pandemic.

The aim of the study is to analyze the dynamics of overall mortality among the Ozersk population, a nuclear industry city, during the COVID-19 pandemic, depending on the combined effect of radiation-related and non-radiation-related risk factors.

MATERIALS AND METHODS

A retrospective cohort study among residents of the Ozersk urban district (OUD) who died from various causes in 2020–2023 was conducted. The crude all-cause mortality rate was calculated using official statistical data for the period 2013–2023.^{1,2} The all-cause mortality rate (μ) per 1000 individuals (‰) was calculated according to the standard methodology described in [1]. The mortality risk intensity analysis was performed in the cohort of individuals who were alive at the date of the COVID-19 pandemic declaration (11.03.2020) and who died from different causes during the subsequent three-year period.

The source of information for this study was data on COVID-19 morbidity and mortality provided by the Center for Hygiene and Epidemiology No. 71 in Ozersk. Data on external occupational radiation dose for employees of the Mayak Production Association (Mayak PA) were obtained from the Mayak Worker Registry [5, 6]. The Kaplan–Meier survival function for individuals who died from all causes during the period 2020–2023 was estimated based on the attained age at the time of death [8]. To characterize the attained age at the onset of observation, a categorical variable was used, comprising the following age intervals: 0–19 years, 20–39 years, 40–59 years, 60–79 years, and 80 years and older. The use of broad age intervals was implemented to increase statistical power for groups with a small number of observations ($n < 30$).

Based on employment status at the main or auxiliary production units of Mayak PA in 1948–2016, the

¹ Socio-Economic Development Statistics for Ozersk Urban District <http://ozerskadm.ru/regulatory/passport/> (access data 22.02.2025).

² Federal State Statistics Service (Rosstat) <http://rosstat.gov.ru/> (access data 22.02.2025).

OUD population was categorized into two groups: “general population” and “occupationally exposed” population. Data on the cumulative effective dose of external gamma radiation for the occupationally exposed persons were obtained using the Mayak Worker Registry [10]. A comparative analysis of mortality risk intensity across different age groups within the population, considering occupational radiation dose, was conducted using the Cox proportional hazards model [11]. The all-cause mortality hazard (h) was defined by the following equation:

$$h_t = h_0(t) \times e^{\beta_i x_i}, \quad (1)$$

h_t — all-cause mortality hazard at time t ; $h_0(t)$ — baseline hazard at time t ; β_i — regression coefficient; x_i — the value of the covariate determining the risk factor.

The regression model was developed by sequentially adding predictors to the base model. The Likelihood Ratio Test (LRT) was used to compare the base and extended models. The proportional hazards assumption was verified using the Cox proportional hazards test, with a critical p -value of 0.05 for rejecting the null hypothesis that the proportional hazards assumption is violated. The statistical significance of the regression coefficients was assessed using the Wald Chi-square test. Multicollinearity among parameters was checked by calculating the Variance Inflation Factor (VIF) using formula (2):

$$VIF = \frac{1}{1 - R_j^2}, \quad (2)$$

where R^2 — coefficient of determination for the j -th variable regression.

The permissible multicollinearity threshold for the j -th variable in the model was set at $VIF \leq 5$. The statistical significance of differences between survival functions for different risk factors was assessed using the non-parametric log-rank test [9]. The conventional significance level of $\alpha = 0.05$, corresponding to a 95% confidence interval, was used to determine statistical significance. Results were considered statistically significant at $p < 0.05$.

RESULTS

In this study, crude all-cause mortality rates (Crude Mortality Rate, CMR) were calculated for the OUD and the Russian Federation for the period 2013–2023, based on population size and number of deaths from all causes. The dynamics of the crude all-cause mortality rate in the OUD compared to the Russian Federation data over the period 2013–2023 are presented in Figure 1.

It was established that the dynamics of the all-cause mortality rate in the OUD in 2020–2023 followed a pattern similar to that of the Russian Federation. However, the all-cause mortality rate in the OUD was consistently

higher than the corresponding rates for the Russian Federation since 2016 and throughout the pandemic period (the maximum discrepancy was observed in 2021: 17.2‰ for the Russian Federation and 18.3‰ for Ozersk) (Fig. 1). The higher all-cause mortality rate in Ozersk compared to the Russian Federation data, when comparing unstandardized rates, may be a consequence of differences in the age distribution of the populations.

A statistically significant excess in the all-cause mortality rate in the OUD relative to its pre-pandemic average (13.7‰) [2] was recorded over the three-year period of 2020–2022. A pronounced deviation of the OUD all-cause mortality rate from its expected value was observed in 2020 at 16.2‰, peaked in 2021 (18.3‰), followed by a sharp decline in 2022 to 14.6‰, returning to pre-pandemic levels (12.7‰) in 2023. These findings indicate the necessity for a more detailed examination of the 2020–2022 period, which corresponds to the peak pandemic activity.

For this purpose, a cohort of OUD residents who were alive at the pandemic declaration date and died from all causes during the period 11.03.2020–31.12.2022 was selected. The distribution of the study cohort by sex, age, presence of COVID-19 as the underlying cause of death, and cumulative external gamma radiation dose intervals among the personnel is presented in Table 1.

The presented data indicate an almost equal distribution of male and female subjects among those who died from all causes during the pandemic period. The largest proportion of all-cause deaths during the pandemic period (81.4%) corresponded to an attained age over 60 years. The mean attained age at the onset of observation was 70.9 ± 0.25 years: for male subjects — 65.9 ± 0.35 years, for female subjects — 75.8 ± 0.32 years. The mean age at death in the OUD population during the pandemic period was

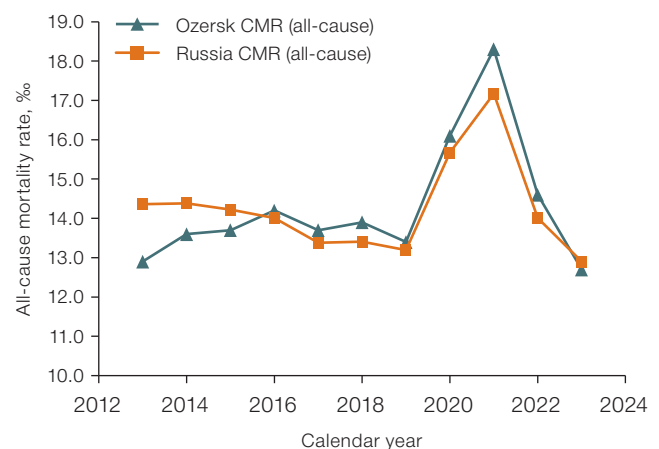


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Fig. 1. All-cause mortality rates (CMR) in Russia and the Ozersk urban district for the 2013–2023 period

Table 1. Characteristics of the cohort of OUD residents who died during the pandemic period, by attained age, sex, external occupational radiation dose, and COVID-19 status

Parameter	Absolute number	Proportion, %	COVID-19 (%)*
Gender			
Male	1961	49.4	459 (46.3)
Female	2008	50.6	532 (53.7)
Attained age, years			
0–19	21	0.5	3 (0.3)
20–39	188	4.7	30 (3.0)
40–59	638	16.1	135 (13.6)
60–79	1695	42.7	477 (48.1)
80+	1427	36.0	346 (34.9)
Cumulative dose, mSv			
0	117	2.9	23 (2.3)
0–9	389	9.8	100 (10.1)
10–99	339	8.5	78 (7.9)
100+	63	1.6	14 (1.4)
Not measured (general population)	3,061	77.1	776 (78.3)
Underlying cause of death			
U07.1, U07.2	425	10.7	370 (37.3)
Other causes	3421	89.3	621 (62.7)
Total	3969	100.0	991 (25.0)

Table prepared by the author

Note: * — the percentage is calculated from the total number of cases in each subgroup.

72.5 ± 0.32 years: for male subjects — 67.5 ± 0.35 years, for female subjects — 77.3 ± 0.32 years. The proportion of the deceased for whom the underlying cause of death was COVID-19 (including individuals without SARS-CoV-2 identification) was 10.7%.

In the study cohort, the proportion of COVID-19 cases accumulated during the pandemic period was 25%, being higher among the female subjects (53.7%). The distribution by attained age reached a maximum of 48.1% among individuals aged 60–80 years. The cumulative proportion of individuals who were diagnosed with COVID-19 during the pandemic period and were exposed to external gamma radiation was 21.7%. The proportion of individuals who sought medical care for COVID-19 during the pandemic period, for whom this disease became the underlying cause of death, was 37.2%.

The all-cause mortality in the OUD population, stratified by age, was assessed using the Kaplan–Meier survival function for the age intervals of 0–39 years,

40–59 years, 60–79 years, and 80 years and older. The dynamics of the all-cause mortality among the OUD population across age intervals are presented in Figure 2.

The survival function represents the empirically observed proportion (%) of individuals who survived to a specific observation time point, depending on their attained age. The data presented in Figure 2 indicate a change in the overall mortality rate among the population across different age groups, which was more pronounced during the first two years of the pandemic period (2020–2021). The working age (40–59 years) group exhibited the lowest all-cause mortality rates throughout the entire pandemic period. Pairwise comparison of survival functions using the log-rank test revealed statistically significant differences ($p = 0.012$) between the age subgroup 19–39 years (mean attained age 34 ± 0.33 years) and 40–59 years (mean attained age 51.7 ± 0.22 years).

The number of Mayak PA employees who died during the study period was 908 (22.9%). The mean

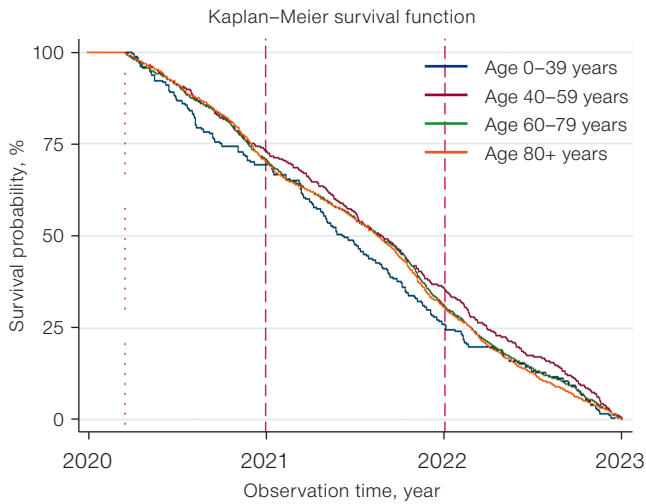


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Fig. 2. Survival function for different age subgroups in the OUD population who died during the pandemic period: the date (11.03.2020) is indicated by points

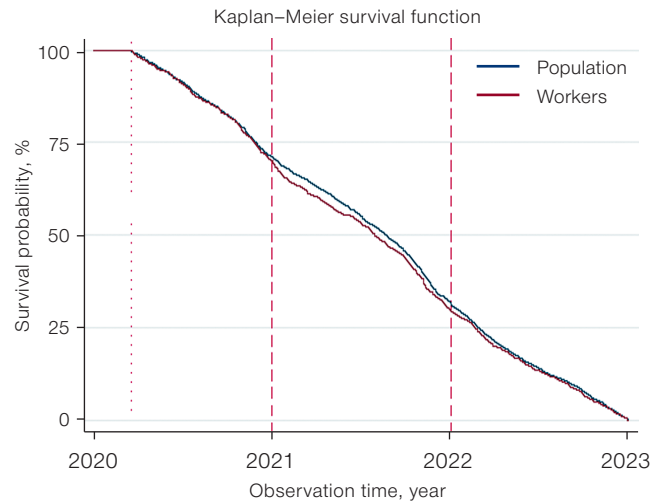


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Fig. 3. Survival function for deceased individuals in the OUD during the pandemic period, stratified by the presence of exposure to external occupational radiation

cumulative external gamma radiation dose for workers (including 117 individuals with zero measured doses) was 27.6 ± 1.97 mSv (median 7.11 mSv, maximum 547.05 mSv). The Kaplan–Meier survival function was constructed for the general population (“Population”) and occupationally exposed persons (“Workers”) categories. The dynamics of all-cause mortality in the OUD population, stratified by the population subgroups, are presented in Figure 3.

The data presented in Figure 3 indicate observed slight differences in overall mortality rates among the personnel of PA «Mayak» compared to the general population during the peak of the coronavirus infection spread in 2021. A comparison of survival functions among personnel for marginal categories of accumulated external radiation dose (measured dose value of 0 mSv and individuals who accumulated a dose exceeding 100 mSv)

using the log-rank test showed borderline statistical significance of differences in all-cause mortality rates during the pandemic ($p = 0,053$).

The results of the regression analysis of all-cause mortality hazard, considering age, sex, COVID-19 status, and cumulative external gamma radiation dose, performed using a multivariate Cox regression model, are presented in Table 2.

The model parameter estimates indicate that the influence of sex is not a linear predictor when comparing all-cause mortality during the pandemic period. The external gamma radiation dose, included in the model as a linear predictor, had a statistically significant effect on the outcome measure ($p = 0.033$), amounting to 0.1% per 1 mSv. Adjusting for the presence of COVID-19 (U07.X) increased the statistical significance of the resulting coefficient ($p = 0.01$) and changed the overall mortality rate

Table 2. Results of the all-cause mortality hazard modeling, adjusted for age, sex, and cumulative external radiation dose (95% confidence interval)

Parameter	Coefficient	Standard error	<i>p</i>	[95% CI]	
Gender (male)	1.064	0.034	0.062	0.997	1.137
Age (20-year categories)	1.093	0.022	<0.001	1.050	1.138
Cumulative dose, mSv	1.001	0.0005	0.033	1.0001	1.002
COVID-19	4.942	0.20	<0.001	4.560	5.357
Variable interaction					
COVID-19	1.424	0.228	0.027	1.041	1.948
Influence of age and COVID-19	1.494	0.074	<0.001	1.356	1.647
Influence of dose and COVID-19	1.002	0.001	0.050	0.999	1.004

Table compiled by the author

by 1%. This observation suggests that chronic exposure to ionizing radiation among employees of PA «Mayak» was a factor that, during the pandemic, was more specific to causes of death not related to COVID-19.

The all-cause mortality hazard increased by a factor of 1.001 with each 1 mSv increase in cumulative external radiation dose. Based on the predictive estimates obtained from the model, for Mayak PA workers exposed to a dose of 27.6 mSv (the mean value in the study cohort), the all-cause mortality hazard increased by 2.8% compared to the non-exposed subgroup. The predicted effect of the cumulative external gamma radiation dose on mortality intensity during the pandemic period among Mayak PA workers hired at main and auxiliary productions in 1948–2000 is presented in Figure 4.

Cox model risk estimates (Fig. 4) show that the actual accumulated levels of external radiation doses among workers hired for production in 1948–2010 and who survived until the date of the pandemic declaration (mean: $27,6 \pm 1,97$ mSv) led to a statistically significant, but quantitatively small change in the all-cause mortality hazard rate.

For risk prediction purposes, the impact of high external radiation doses of 1 Sv, typical for the initial operational period of PA «Mayak» (1948–1957), on the all-cause mortality hazard rate during the pandemic was modelled. The simulation results showed that if all members of the study cohort, as of the entry date into follow-up, had been able to accumulate an external occupational gamma radiation dose of 1 Sv (indicated by a dotted line in Figure 4), the effect of the external radiation dose on the overall mortality rate during the pandemic would have been comparable to the effect of having a COVID-19 diagnosis (Fig. 5).

The obtained results indicate that COVID-19 is a significant predictor increasing the all-cause mortality hazard rate among the population of the Ozersk Urban District (OUD), and is modified by the influence of occupational external radiation dose and attained age. The assessment of the direct effect of COVID-19 shows a 4.9-fold increase in the outcome measure within the cohort if a patient has had at least one episode of the disease requiring medical care.

Including an interaction term for COVID-19 status and attained age in the model revealed that the direct effect of the disease «masks» the influence of age (Table 2). For every 20 years of increased attained age, the effect of having COVID-19 increases the all-cause mortality hazard rate by 49 %, while the influence of the direct effect remains statistically significant but decreases to 1.42 ($p < 0,05$).

Including the interaction between occupational radiation dose and COVID-19 in the model revealed that, compared to the non-exposed general population, the all-cause mortality hazard among exposed individuals with a history of COVID-19 was higher by 0.2%. However, this coefficient had borderline statistical significance ($p = 0.05$), indicating a potential non-linearity of this interaction.

DISCUSSION

The study did not use data characterizing the spread dynamics of the novel coronavirus infection («pandemic waves»), differences in virus strains, as well as the number of infected individuals who had a mild form of the disease and did not seek medical care.

One of the confounding factors affecting the comparative assessment of the crude overall mortality rate

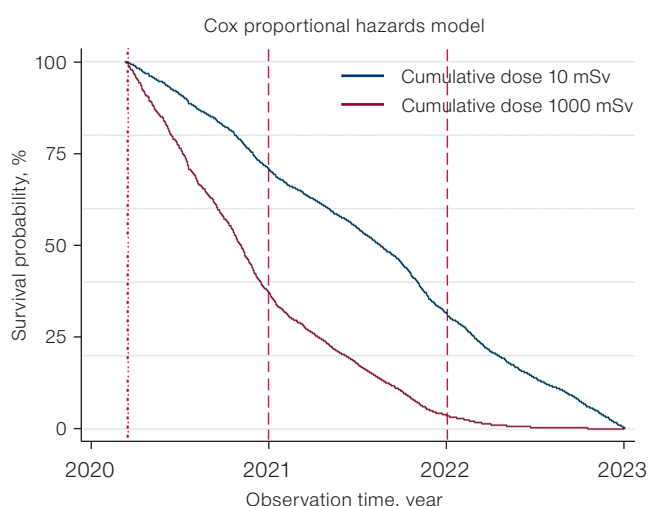


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Fig. 4. Predictive estimates of cause-specific mortality hazard during the pandemic period 2020–2023 for Mayak PA personnel, by cumulative external gamma radiation dose

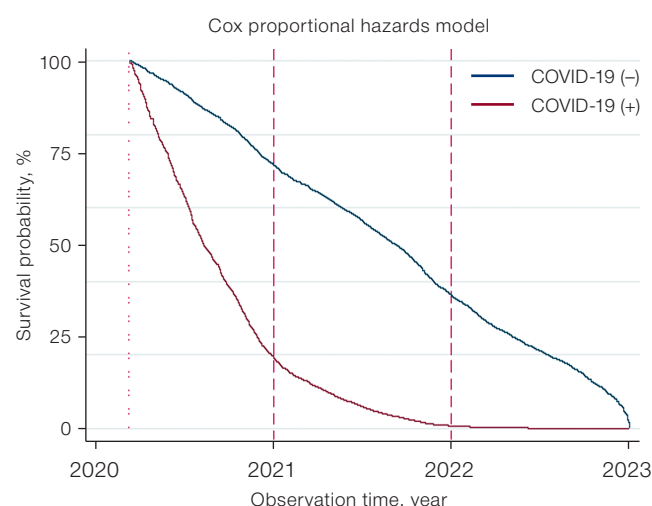


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Fig. 5. Predictive estimates of cause-specific mortality hazard during the pandemic period 2020–2023, stratified by the presence or absence of a confirmed COVID-19 disease

against national statistics is the difference in life expectancy between the population of the Ozersk Urban District and that of Russia [12].

A specific risk factor influencing the all-cause mortality rate is chronic radiation exposure experienced by personnel of nuclear industry facilities. The impact of occupational radiation exposure on the risk of death from diseases other than cancer has been widely studied recently [7, 13]. The results of the present study indirectly support the hypothesis of an association between ionizing radiation exposure and the risk of non-cancer mortality.

The structure of all-cause mortality during the pandemic period, beyond deaths directly from COVID-19 as the underlying cause (U07.1, U07.2), includes various clusters of diseases, such as malignant neoplasms (C00–C97). The influence of radiation, considered a potential cause of oncological diseases in the exposed occupational cohort [5], may explain the observed increase in all-cause mortality in the study cohort after excluding deaths from COVID-19 from the analysis.

Potential limitations of this study include the duration of the observation period, which encompasses only the first three years following the declaration of the COVID-19 pandemic. Despite the fact that the pandemic officially lost its status as a public health emergency in 2022, the presence of the SARS-CoV-2 infectious agent in the population [14] remains a relevant issue for monitoring, given the potential long-term consequences of COVID-19, whose impact on mortality risk has not yet been sufficiently studied.

For a deeper understanding of the pandemic's impact mechanisms within the context of public and occupational health in nuclear industrial complexes, a detailed examination of the relationship between radiation risk factors and specific causes of death is necessary. Furthermore, investigating the patterns of COVID-19's influence on the risk of death from malignant neoplasms is a relevant issue in international research [15]. Given the increased probability of developing lung malignant neoplasms among workers in plutonium production facilities

[16], a promising direction for future research is the study of the association between the dose from internal exposure to incorporated ^{239}Pu and lung cancer mortality during the pandemic period.

CONCLUSIONS

According to the World Health Organization's conclusion, the possibility of future pandemic spread of novel coronavirus infection cannot be ruled out. Based on this, analyzing the consequences of the past pandemic is relevant from the perspective of ensuring preparedness for similar situations in order to minimize potential harm to public health.

The results of the conducted study showed that during the pandemic period, the population of the Ozersk — a nuclear industry city — experienced a change in the all-cause mortality hazard rate, depending on the influence of various factors. The groups most affected by the pandemic were young and elderly individuals, as well as workers exposed to occupational external radiation.

The impact of COVID-19 on the all-cause mortality hazard rate occurred through both direct and indirect mechanisms. The most significant modifier of all-cause mortality risk among individuals with COVID-19 was attained age. Alongside the direct effects of COVID-19, age, and external radiation dose among workers at PA «Mayak», the combination of these risk factors is also important when assessing the dynamics of overall mortality during the pandemic.

The presence of a statistically significant modification in the combined effect of COVID-19 and radiation dose indicates the need for further, more detailed study of radiobiological patterns in the progression of pathological processes in individuals exposed to combined risk factors of both radiation and non-radiation nature.

The obtained results are also relevant for predicting the consequences of potential future pandemic situations and for developing effective health protection strategies for occupationally exposed workers.

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