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IMPACT OF THE COVID-19 PANDEMIC ON ALL-CAUSE MORTALITY IN THE OZERSK URBAN DISTRICT

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Introduction. In the context of the COVID-19 pandemic, which has impacted all-cause excess mortality, it appears relevant to evaluate the synergistic effects of occupational radiation exposure and the SARS-CoV-2 infectious agent on the overall mortality in the population of a nuclear industry city. This is especially important for increasing the effectiveness of health protection and prevention measures among population and professionals.
Objective. A retrospective analysis of all-cause mortality rates in the population of the Ozersk urban district (OUD) during the COVID-19 pandemic, adjusted for the influence of radiation and non-radiation risk factors.
Materials and methods. A retrospective cohort study among residents of the Ozersk urban district who died from various causes in 2020–2023 was conducted. Annual reports from Rosstat and the Municipal Statistics department were analyzed. Data on COVID-19 morbidity and mortality were provided by the Center for Hygiene and Epidemiology No. 71 in Ozersk. The survival function was assessed depending on COVID-19 status, with adjustment for age and external occupational radiation dose among workers of the Mayak Production Association, using the Kaplan–Meier method. The impact of COVID-19, considering occupational radiation dose, on all-cause mortality rates was analyzed using the Cox proportional hazards model.
Results. The analysis of mortality rate dynamics revealed the period associated with the peak of pandemic all-cause mortality in the OUD population. A significant influence of COVID-19 ($p < 0.05$) on all-cause mortality during the pandemic period, dependent on attained age and occupational radiation dose, was revealed. It was demonstrated that the pronounced effect of COVID-19 on all-cause mortality was a consequence of the multiplicative influence of several risk factors, among which attained age and external radiation dose had a significant impact.
Conclusions. The excess all-cause mortality rate in the OUD population during the pandemic period compared to the corresponding rate for the population of Russian Federation is a consequence of the impact of risk factors specific to population residing in the vicinity of nuclear industrial facilities. The results obtained are of interest for forecasting the potential detriment associated with the emergence of possible future pandemic situations.

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

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ВЛИЯНИЕ ПАНДЕМИИ COVID-19 НА ОБЩУЮ СМЕРТНОСТЬ СРЕДИ НАСЕЛЕНИЯ ОЗЕРСКОГО ГОРОДСКОГО ОКРУГА

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Введение. В условиях пандемии COVID-19, оказавшей влияние на избыточную смертность от всех причин, представляется актуальной оценка комплексного воздействия факторов производственного облучения и инфекционного агента SARS-CoV-2 на смертность среди населения города атомной промышленности в целях разработки эффективных мер профилактики и охраны здоровья населения и персонала.
Цель. Ретроспективный анализ интенсивности общей смертности населения Озерского городского округа (ОГО) в период пандемии COVID-19 в зависимости от влияния факторов риска радиационной и нерадиационной природы.
Материалы и методы. Проведено ретроспективное когортное исследование жителей Озерского городского округа, умерших от различных причин в период 2020–2023 гг. Анализировали ежегодные отчеты Росстата и муниципального отдела статистики. Данные о заболеваемости и смертности от COVID-19 предоставлены Центром гигиены и эпидемиологии № 71 г. Озерска. Оценка функции выживаемости в зависимости от наличия заболевания COVID-19 с учетом 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 выполнен методом пропорциональных рисков Кокса.

Результаты. На основании анализа динамики показателей смертности определен период, связанный с пиком пандемической смертности от всех причин среди населения ОГО. Выявлено значимое 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. Показано, что выраженный эффект наличия заболевания COVID-19 на общую смертность являлся следствием мультипликативного влияния нескольких факторов риска, из которых значимое влияние оказывали достигнутый возраст и доза внешнего облучения.
Выводы. Превышение показателя общей смертности среди населения Озерского городского округа в пандемический период по сравнению с аналогичным показателем по России является следствием влияния факторов риска, специфичных для населения, проживающего вблизи объектов ядерно-промышленного комплекса. Полученные результаты представляют интерес для прогноза возможного ущерба, связанного с возникновением возможных пандемических ситуаций.

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

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Соответствие принципам этики: не требовалось одобрение биоэтического комитета, поскольку исследование выполнено на основе обезличенных данных медицинских карт (архивные материалы).

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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 this study is a retrospective analysis of all-cause mortality rates in the population of the Ozersk urban district (OUD) during the COVID-19 pandemic, based on the influence of radiation and non-radiation 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 ≤ 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

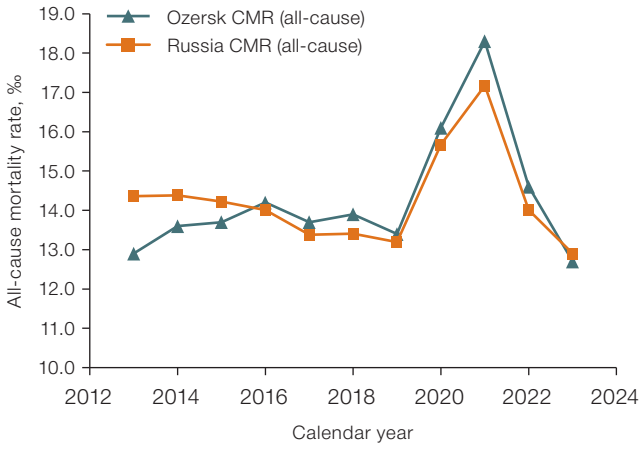

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Fig. 1. All-cause mortality rates (CMR) in Russia and the Ozersk urban district for the 2013–2023 period

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 was 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 significant increase in all-cause mortality in the population under 40 years of age, 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

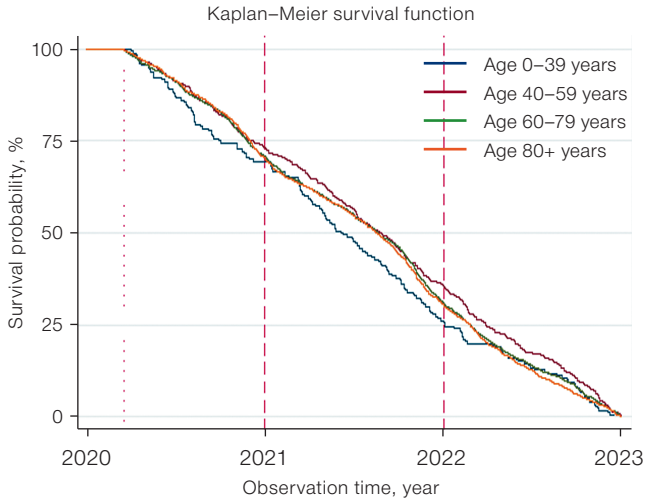

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Fig. 2. Survival function for different age subgroups in the OUD population who died during the pandemic period: the date (11.03.2020) is indicated by points

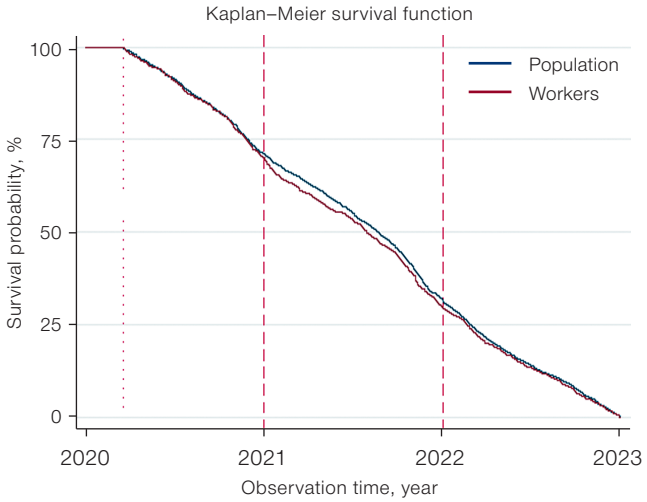

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Fig. 3. Survival function for deceased individuals in the OUD during the pandemic period, stratified by the presence of exposure to external occupational radiation

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 an increase in all-cause mortality among the Mayak PA occupational cohort compared to the general population, with the greatest deviation observed during the peak of the coronavirus infection spread in 2021. A comparison of survival functions within the occupationally exposed subgroup for marginal categories of cumulative external radiation dose (measured dose of 0 mSv and individuals with accumulated doses greater than 100 mSv) using the log-rank test showed a borderline statistically significant difference in all-cause mortality during the pandemic period ($p = 0.053$).

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 influence of the direct effect of cumulative external gamma radiation dose, included in the model as a linear predictor, showed a statistically significant increase ($p = 0.033$) in all-cause mortality hazard ratio of 0.1% per 1 mSv compared to the non-exposed subgroup.

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	*p*	[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

The exclusion from the analysis individuals for whom the underlying cause of death was COVID-19 (U07.X) led to an increase in the statistical significance of the radiation dose effect (p = 0.01) and an increase in all-cause mortality hazard ratio to 0.11% for each 1 mSv of external gamma radiation dose. This result indicates that chronic exposure to ionizing radiation among Mayak PA employees was a risk factor that, during the pandemic period, was more specific for deaths other than 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 employees 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.

The Cox regression model (Fig. 4) shows differences in the predicted all-cause mortality hazard during the pandemic period among personnel with different cumulative external gamma radiation doses — 10 mSv and 1 Sv. On this basis, accumulation of an external gamma radiation dose of 1 Sv, considering the mean attained age of 70 years, would have led to the death of 95% of Mayak PA workers within the first two years of the pandemic period.

The influence of a diagnosed COVID-19 disease in patients in 2020–2022 is presented in Figure 5.

The obtained results indicate that COVID-19 is a significant predictor, increasing the all-cause mortality hazard in the OUD population, after accounting for the influence of occupational external radiation dose and attained age. The assessment of the direct effect of COVID-19 indicates a 4.9-fold increase in the all-cause mortality hazard in the cohort for patients who sought medical care for at least one episode of the COVID-19 disease.

Including the interaction between COVID-19 status and attained age in the model showed that the direct effect of COVID-19 is disguised by the influence of the patient age. For every 20-year increase in age, the effect of having had COVID-19 increases the all-cause mortality hazard by 49%, while the influence of the direct effect remains statistically significant but decreases to a hazard ratio of 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 increased all-cause mortality rate in the OUD population during the COVID-19 pandemic compared to the Russian Federation data indicates the influence of risk factors specific to populations residing in nuclear industry cities [4]. In addition to the direct health impact caused by SARS-CoV-2, a significant risk factor is the aging population in Ozersk [12]. Another factor affecting the crude all-cause mortality rate is chronic radiation exposure of personnel of the nuclear industrial facility. The influence of occupational radiation exposure on the risk of death from various diseases, beyond cancer, has

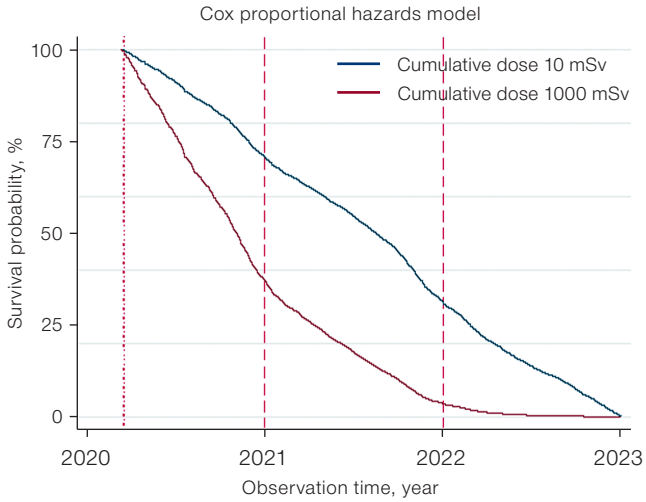

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Fig. 4. Predictive estimates of cause-specific mortality hazard during the pandemic period 2020–2023 for Mayak PA personnel, by cumulative external gamma radiation dose

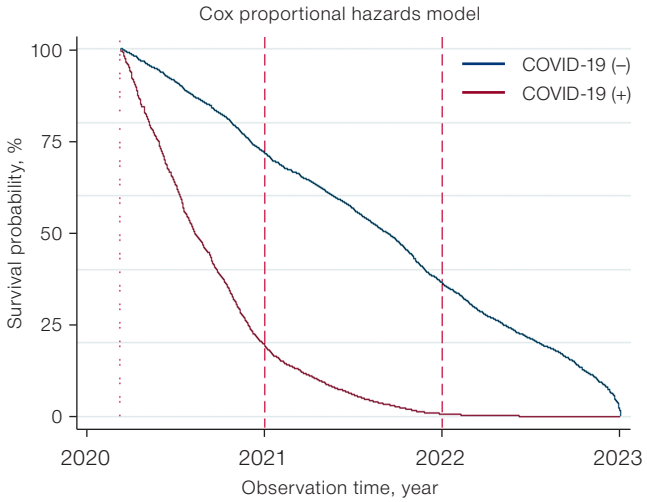

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Fig. 5. Predictive estimates of cause-specific mortality hazard during the pandemic period 2020–2023, stratified by the presence or absence of a confirmed COVID-19 disease

been widely studied recently [7, 13]. The results of this study indirectly suggest a substantial role of ionizing radiation as a risk factor for mortality from both malignant neoplasms and non-cancer diseases.

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 COVID-19-associated deaths 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. Although the pandemic officially lost its status as a public health emergency of international concern in 2022, the persistent presence of the highly mutagenic SARS-CoV-2 infectious agent in the population [14] continues to pose a threat of potential adverse health outcomes, especially for nuclear industry personnel. This fact could be highly significant for the manifestation of potential long-term consequences of COVID-19, the impact of which on mortality risk remains insufficiently studied. For a more comprehensive analysis of this issue, it would be advisable to incorporate the data on the dynamics of novel coronavirus infection spread (pandemic waves), as well as differences in viral strains, and the number of infected individuals who experienced mild symptoms and did not seek medical care.

For a deeper understanding of the mechanisms of pandemic impact within the context of public and occupational health in nuclear industrial facilities, a detailed examination of the relationship between radiation risk factors and specific causes of death is necessary. Furthermore, investigating the patterns of COVID-19 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

The conducted retrospective analysis of all-cause mortality in the population of the Ozersk urban district during the COVID-19 pandemic revealed an association with the influence of specific risk factors of both radiation and non-radiation origin. In the population of the nuclear industry city of Ozersk, the pandemic period was associated with an increased all-cause mortality. The most vulnerable categories with the highest mortality intensity during the pandemic period were young and elderly individuals, as well as occupationally exposed persons. The influence of COVID-19 on the all-cause mortality acts through both direct and indirect mechanisms. The most significant modifier of all-cause mortality risk in individuals with COVID-19 is the attained age.

The observed excess in all-cause mortality among the Ozersk population during the pandemic period, compared to the corresponding rate for the Russian Federation, is a consequence of the impact of risk factors specific to populations residing near to nuclear industrial facilities. A significant impact on the all-cause mortality is anticipated among personnel with accumulated high external radiation doses on the order of 1 Sv, whereas accumulated low doses up to 10 mSv have a negligible effect on the change in all-cause mortality during the pandemic.

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