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RESEARCH ARTICLE

Cancer Epidemiology



Mortality from cancer and non-cancer diseases in the Lithuanian cohort of Chernobyl cleanup workers (2001–2020)

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Abstract

We examined the mortality risk from cancer and non-cancer diseases from 2001 to 2020 among Lithuanian Chernobyl cleanup workers exposed to ionizing radiation while working in areas contaminated by the Chernobyl nuclear power plant (NPP) accident. The mortality risk was estimated by calculating the standardized mortality ratio (SMR) with a 95% confidence interval (CI). A total of 1922 deaths were registered among the 5562 traced men. The all-cause mortality was slightly elevated (SMR = 1.07, 95% CI, 1.03-1.12), as was the mortality from all malignant neoplasms (SMR 1.15, 95% CI, 1.06-1.26), with the highest risk observed for smoking-related cancers (SMR 2.70, 95% CI, 2.44-2.99). The SMR for all circulatory diseases was also a little higher compared with the general Lithuanian male population (SMR 1.09, 95% Cl, 1.02-1.18), particularly for cerebrovascular diseases (SMR 1.46, 95% Cl, 1.22-1.74). For diseases of the circulatory system and all malignant neoplasms, the mortality risks were similar in both groups of documented external radiation doses (<100 and ≥100 mSv). The only exception pertains to hypertensive disease, where the SMR was higher in the dose group exceeding 100 mSv, compared with the dose group of ≤100 mSv (SMR 1.68, 95% CI, 1.03-2.74 vs. 1.4, 95% CI, 0.84-2.32, respectively). Continuing follow-up of mortality patterns of cancer and non-cancer diseases within the cohorts of Chernobyl cleanup workers provides important information about the long-term impact of the Chernobyl accident on health.

KEYWORDS

cancer, Chernobyl, circulatory, ionizing radiation, mortality

Abbreviations: CI, confidence interval; ERR/Gy, excess relative risk per Gray; EXP, expected; Gy, Gray; ICD-10, International Statistical Classification of Diseases and Related Health Problems 10th Revision; mSv, millisievert; NPP, nuclear power plant; OBS, observed; PID, personal identification number; PTSD, post-traumatic stress disorder; RNMDR, Russian National Medical and Dosimetric Registry; SIR, standardized incidence rate; SMR, standardized mortality rate; Sv, Sievert.

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What's New?

Following the Chernobyl disaster, workers were recruited from formerly Soviet-occupied areas, including Lithuania, to participate in clean-up efforts. Radiation exposure incurred by workers during these efforts offers a unique opportunity for the study of long-term health effects. Here, the authors investigated cancer and non-cancer mortality among Lithuanian Chernobyl clean-up workers from 2001 to 2020. Compared with the general Lithuanian population, mortality from all causes and from malignant and circulatory system diseases was slightly elevated in workers. The highest excess mortality was observed for smoking-related cancers. The findings offer new insight into the effects of low and moderate radiation exposure.

1 | INTRODUCTION

The Chernobyl nuclear power plant (NPP) accident in 1986 remains the largest nuclear accident ever to occur in the history of nuclear power. In response to the large releases of radioactive materials and the necessity for extensive environmental cleanup, Soviet authorities recruited hundreds of thousands of cleanup workers from all over the country, including formerly occupied Lithuania, Latvia, and Estonia. During recovery operations, the predominant type of their exposure was external gamma irradiation. According to national registries of Belarus, the Russian Federation, Ukraine, Estonia, Latvia, and Lithuania, the average recorded external dose from gamma irradiation (the accuracy of which is difficult to assess) reached 150 mSv in 1986 and 100 mSv in 1987. The level of exposure received by cleanup workers offered a potential for studying health effects in the low and moderate dose range, which is most important for public health and radiation protection.

Several studies looked at cancer and non-cancer disease incidence and mortality, both in the individual cohorts as well as in the combined cohorts of cleanup workers.^{3–5} Some studies provided evidence of increases in the risk of thyroid cancer,^{6–9} leukemia, and other hematological malignancies, ^{10–14} and cataracts.¹⁵ Other studies suggested an increased risk of cardiovascular and cerebrovascular diseases.^{16–19} In addition to the somatic health effects, the impairment of mental health was shown to be one of the most profound consequences of the Chernobyl accident.^{20–24} However, the debate on the magnitude of the accident-related health effects continues to attract public interest, and further evaluation of the lifetime health risks of the Chernobyl accident is needed.²⁵

Due to the long-existing population-based cancer registry and the possibility to follow up on the basis of the unique personal identification numbers, the Lithuanian cohort of cleanup workers, similarly to the cohorts from other Baltic countries—Estonia and Latvia, provides high-quality data on cancer incidence and all-cause mortality. We have recently published results of cancer incidence follow-up until 2012. Here, for the first time, we report mortality risk from cancer and non-cancer diseases in the Lithuanian cohort of Chernobyl cleanup workers during 2001–2020. In our study, we also evaluated a possible association between the documented radiation doses and mortality from the selected diseases: cancer, cardiovascular, and cerebrovascular systems.

2 | MATERIALS AND METHODS

Multiple data sources were used to construct the Lithuanian cohort of Chernobyl cleanup workers: military lists and records from the former Soviet Army reservist offices (commissariats); the Lithuanian Chernobyl Radiation Registry; the Lithuanian Chernobyl Health Care Centre; the Ministry of Construction and the Ignalina NPP (a small group of plant personnel was sent to Chernobyl on mission). Officially documented doses from external exposure were extracted from the Chernobyl passport of a worker and from military lists. The procedures for assembling the cohort in Lithuania and obtaining documented external radiation doses are described in more detail elsewhere. ²⁶

Initially, the cohort in Lithuania comprised 6917 men who worked in the Chernobyl area (the 30 km zone around the Chernobyl NPP and the surrounding territories) during 1986–1990 and had an official record documenting their service. Information included personal identification number (PID), surname, given name(s), father's name (commonly used during Soviet time), date of birth, place of residence, dates of participation in the cleanup, and reported external radiation dose.

Information on vital status, emigration, and date of death was obtained by linkage with the Central Population Register. Causes of death were identified by linkage with the Lithuanian Causes of Death Registry (causes of death available from 2001) using PID. The cause of death was assigned using only the underlying cause of death.

Mortality follow-up started on 1 January 2001 and ended on 31 December 2020 or on the date of death, if it occurred first. Mortality risk in the cohort was assessed by calculating standardized mortality ratios (SMRs). SMRs were calculated as the ratios of observed to expected numbers of deaths in the cohort using national mortality rates for the general male population. The observed and expected numbers of deaths were stratified by 5-year age groups (≤19, 20–24, 25–29, ..., 80–84, ≥85) and calendar year. The expected number of deaths in the cohort was calculated by multiplying the accrued number of person-years by the national male mortality rates stratified by 5-year age groups and calendar year. Assuming that the cause-specific number of deaths followed a Poisson distribution, 95% confidence intervals (CIs) for SMRs were calculated.

The risk of death was assessed for all causes of diseases ranging from A00 to Y98, based on the ICD-10 classification. Special emphasis was placed on calculating the risk of death due to circulatory system

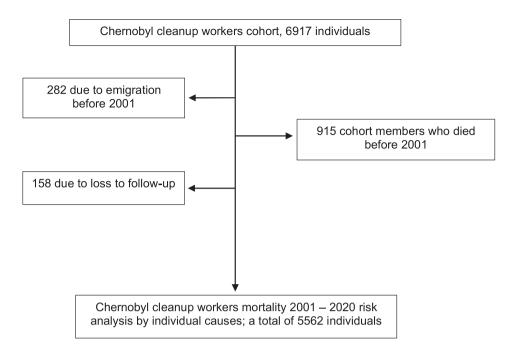
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FIGURE 1 Flowchart of Lithuanian cohort of cleanup workers composition for mortality analysis.



diseases (I00-I99) and all malignant neoplasms, which were analyzed by grouping the relevant ICD-10 codes from C00 to C97. To compare our results with the most recent reports from Estonia, we calculated SMR for three groups of cancers²⁷: radiation-related (C07-C08, C15, C16, C18, C33-C34, C40-C41, C44, C64-C68, C70-C73, C91-C95 [except C91.1]), alcohol-related (C01-C15, C18-C22, C32) and smoking-related cancers (C01-C16, C18-C22, C25, C30-C34, C64-C68, C92), as well as for alcohol-related diseases F10, G31.2, G62.1, 142.6, K70, K86.0, and X45.

Based on the officially documented external dose, the cohort members were divided into two groups—the low-dose (<100 mSv) group and the moderate-dose (≥100 mSv) group, using the common definition of low dose of radiation as values below 100 mSv.²⁸ For radiation-related and all cancer deaths, as well as for the deaths from all circulatory diseases combined, hypertensive disease, ischemic heart disease, myocardial infarction, and cerebrovascular diseases, we estimated the mortality risk in each dose group.

All statistical analyses were carried out using STATA, version 11; StataCorp., College Station, TX.

RESULTS 3

Out of the initial cohort of 6917 men, after excluding 915 cohort members who died, 282 who emigrated, and 158 who were lost to follow-up, we identified 5562 cleanup workers who lived in Lithuania on 1 January 2001 and contributed 93,545 person-years to the mortality analysis (Figure 1). The mean follow-up time was 16.8 years, and the median follow-up time was 20 years.

The mean age at the end of follow-up was 63.9 years (range from 50 to 88), with 65.4% of the cohort members being alive (Table 1). One-third of the cohort (34.7%) participated in the cleanup in 1986 when the radiation doses were the highest; 36.3% had a record of

TABLE 1 Characteristics of Lithuanian cohort of Chernobyl cleanup workers.

Characteristics	No.	%
Total	5562	100.0
Vital status (31 December 2020)		
Alive	3640	65.4
Dead	1922	34.6
Age at arrival in the Chernobyl area (years)		
<20	118	2.1
20-29	2076	37.3
30-39	2565	46.1
40-49	699	12.6
≥50	45	8.0
Unknown	59	1.1
Time of arrival in the Chernobyl area (year, month)		
1986, April-May	415	7.5
1986, June-December	1513	27.2
1987-1990	3575	64.3
Unknown	59	1.1
Duration of stay in the Chernobyl area (days)		
<30	362	6.5
30-89	2913	52.4
90-149	1272	22.9
150-209	670	12.0
≥210	286	5.1
Unknown	59	1.1
Documented external radiation dose (mSv)		
<100	2174	39.1
≥100	2020	36.3
Unknown	1368	24.6

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external radiation dose of 100 mSv or higher (Table 1). Among the 915 cleanup workers who died before 2001, 256 (28%) had documented radiation doses equal to or exceeding 100 mSv, 319 (35%) had recorded doses below 100 mSv, while the status of 340 workers regarding their radiation exposure remained unknown.

During 20 years of the follow-up period, 1922 deaths occurred, yielding an overall SMR of 1.07 (95% CI, 1.03-1.12) (Table 2).

Slightly elevated mortality risks were observed for all malignant neoplasms (SMR 1.15, 95% CI, 1.06-1.26), all circulatory diseases (SMR 1.09, 95% CI, 1.02-1.18), and ischemic heart disease (SMR 1.12, 95% CI, 1.02-1.23) (Table 2). For cerebrovascular diseases, the risk of death was higher in the cohort of cleanup workers compared with the Lithuanian male population (SMR 1.46, 95% Cl. 1.22-1.74) (Table 2). Death rates attributed to hypertension and acute myocardial infarction were elevated but not statistically significant (SMR 1.37, 95% CI, 0.99-1.89 and SMR 1.24, 95% CI, 0.97-1.57, respectively) (Table 2). Furthermore, increased mortality risks were observed for alcohol-related (SMR 1.24, 95% CI, 1.06-1.47), radiation-related (SMR 1.23, 95% CI, 1.09-1.38), and smoking-related cancer sites (SMR 2.70, 95% CI, 2.44-2.99) (Table 2).

We did not find any increase in mortality risk from all alcoholrelated diseases (ICD-10 codes F10, G31.2, K70, K86.0, and X45) (Table 2). The risk of suicide in the cohort was also not elevated in comparison to the general male population.

No major difference in mortality risk was observed between low and moderate dose groups (Table 3). For all outcomes, including the death from malignant neoplasms, the risk was higher in the lower radiation dose group, with an exception for hypertensive disease, where the risk of death was higher in the group with the dose above 100 mSv (SMR 1.68, 95% Cl. 1.03-2.74) compared with the group with the dose below 100 mSv (SMR 1.40, 95% CI, 0.84-2.32). Notably, no excess in mortality from radiation-related cancers was found in the documented dose group above 100 mSv (SMR 1.0, 95% CI, 0.79-1.25), while among the group of <100 mSv, the SMR was 1.39 (95% CI, 1.16-1.66).

DISCUSSION

During the 20-year observation period, the overall mortality in the Lithuanian cleanup workers' cohort was slightly elevated compared with the general male population (SMR 1.07, 95% CI, 1.03-1.12). This is compatible with the findings in the Estonian cohort of cleanup workers with a longer follow-up period (1986-2020), where the allcause SMR was 1.04 (95% CI, 0.99-1.09).5 In the Latvian cohort, observed over a shorter period (1999-2009), overall mortality did not differ from the general population (SMR 1.00, 95% CI, 0.93-1.07).²⁹

During the first follow-up period from 1987 to 1998, mortality risk for all causes in the Russian cohort was significantly lower than that in the general population (SMR 0.85, 95% CI, 0.82-0.87).³⁰ The updated mortality follow-up (from 1992 to 2008) of the Russian cohort yielded overall mortality rates similar to the general population.31

We observed a statistically significant excess mortality from all cancers, as well as from groups of smoking-related, alcohol-related, and radiation-related cancer sites combined. In our cancer incidence study, we also reported slightly elevated risks of alcohol-related cancer sites with the lower CI limit below unity (SIR 1.16, 95% CI, 0.99-1.37).²⁶ The observed significant increase in mortality from the category of smoking-related cancers (SMR 2.70, 95% CI, 2.44-2.99) indicates that other risk factors such as smoking habits and lifestyle, rather than radiation, could have contributed to the increased overall mortality. According to the results of a systematic analysis of smoking habits in Lithuania which started in the 1990s, the overall smoking prevalence in the Lithuanian population remains very high, although among men it declined from 44% in 1994 to 33% in 2012.32

Our findings regarding mortality from all cancers and radiationrelated cancers are similar to the observations from the Estonian cohort (SMR 1.16, 95% CI, 1.03-1.28; SMR 1.20, 95% CI, 1.03-1.36, respectively).⁵ The Lithuanian cohort had a lower alcohol-related cancer mortality rate (SMR 1.24, 95% Cl. 1.06-1.47) compared with the Estonian cohort (SMR 1.56, 95% CI, 1.26-1.86).5 In contrast, in the Estonian cohort, the excess mortality from smoking-related cancers (SMR 1.20, 95% CI, 1.06-1.35)⁵ was less pronounced than in the Lithuanian cohort (SMR 2.70. 95% Cl. 2.44-2.99). The mortality from all solid cancers among Russian cleanup workers was lower compared with the mortality in Russian men (SMR 0.95, 95% CI, 0.92-0.99).³³ In Latvia, no excess deaths were reported due to malignant neoplasms either (SMR 0.91, 95% CI, 0.76-1.08).^{29,34} While cancer registration practices are compatible between Lithuania and Estonia, our results are difficult to compare with those observed in the Russian Federation. In the Russian Federation, cancer incidence and mortality data on Chernobyl cleanup workers are collected in all administrative regions by the Russian National Medical and Dosimetric Registry (RNMDR); the process is different from the data collection for the general population. 30,31 In Latvia, due to the changes in the Latvian health administration system, cancer registration underwent different reorganizations since 2006, and the data completeness differs depending on the time period.³⁵

We could not find an association between the documented external radiation dose and the increased risk of death from all cancers combined and from the radiation-related cancer sites combined. This is not surprising because it is difficult to evaluate the validity of the cleanup workers' documented doses for a variety of reasons, such as inadequate monitoring due to the lack of individual dosimeters, uncalibrated and non-validated dosimeters, and different recording practices used by different organizations that sent cleanup workers to Chernobyl, and so on.³⁶

In our cohort, we found a modest excess of deaths from all diseases of the circulatory system, and from hypertensive diseases, ischemic heart diseases, acute myocardial infarction, and cerebrovascular diseases, separately. Mortality follow-up of the Estonian cohort did not show any differences in the risk of death from circulatory or ischemic heart diseases between the cleanup workers and the Estonian male population. 5,20 Among Latvian cleanup workers,

TABLE 2 Observed (OBS) and expected (EXP) number of deaths and standardized mortality ratio (SMR) with 95% confidence interval (CI) in the Lithuanian cohort of Chernobyl cleanup workers by cause of death, 2001–2020.

Causes of death	ICD-10	OBS	EXP	SMR	95% CI	
All causes	A00-Y98	1922	1790.16	1.07	1.03	1.12
Certain infectious and parasitic diseases	A00-B99	54	47.93	1.13	0.86	1.47
Tuberculosis	A15-A19	33	26.14	1.26	0.90	1.78
Respiratory tuberculosis	A15-A16	23	20.34	1.13	0.75	1.70
Miliary tuberculosis	A19	10	5.64	1.77	0.95	3.30
Sepsis	A40-A41	11	9.51	1.16	0.64	2.09
Malignant neoplasms:	C00-C97	478	414.23	1.15	1.06	1.26
Upper aerodigestive tract	C01-C14, C32	70	48.56	1.44	1.14	1.82
Digestive organs	C15-C26	143	126.99	1.13	0.96	1.33
Trachea, bronchus, lung	C33-C34	126	111.75	1.13	0.95	1.34
Brain	C71	9	12.11	0.74	0.39	1.43
Thyroid gland	C73	1	0.81	1.23	0.17	8.77
Leukemia	C91-C95	11	9.46	1.16	0.64	2.10
Alcohol-related sites	C01-C15, C18-C22, C32	143	114.96	1.24	1.06	1.47
Smoking-related sites	C01-C16, C18-C22, C25, C30-C34, C64-C68, C92	376	139.05	2.70	2.44	2.99
Radiation-related sites	C07-C08, C15, C16, C18, C33-C34, C40-C41, C44, C64-C68, C70-C73, C91-C95 (except C91.1)	266	216.65	1.23	1.09	1.38
Diseases of the blood and blood-forming organs	D50-D89	2	0.94	2.13	0.53	8.50
Endocrine, nutritional, and metabolic diseases	E00-E89	10	15.39	0.65	0.35	1.21
Mental and behavioral disorders	F00-F99	3	5.33	0.56	0.18	1.74
Alcohol-related mental diseases	F10	3	3.37	0.89	0.29	2.76
Diseases of the nervous system	G00-G99	17	26.46	0.64	0.40	1.03
Degeneration of the nervous system due to alcohol	G31.2	3	2.90	1.03	0.33	3.20
Diseases of the eye (adnexa) and ear	H00-H95	0	0.11	-	-	-
Diseases of the circulatory system	100-199	744	680.24	1.09	1.02	1.18
Hypertensive diseases	I10-I15	37	27.02	1.37	0.99	1.89
Ischemic heart diseases	120-125	464	413.37	1.12	1.02	1.23
Acute myocardial infarction	121	67	54.10	1.24	0.97	1.57
Cerebrovascular diseases	160-169	118	81.05	1.46	1.22	1.74
Diseases of the respiratory system	J00-J99	80	74.00	1.08	0.87	1.35
Pneumonia	J12-J18	43	35.61	1.21	0.90	1.63
Lower respiratory diseases	J40-J47	29	31.24	0.93	0.65	1.34
Diseases of the digestive system	K00-K93	134	134.46	1.00	0.84	1.18
Peptic ulcer	K25-K27	7	13.78	0.51	0.24	1.07
Diseases of liver	K70-K76	92	90.22	1.02	0.83	1.25
Alcohol-related liver diseases	K70	44	43.45	1.01	0.75	1.36
Fibrosis and cirrhosis of the liver	K74	37	35.47	1.04	0.76	1.44
Alcohol-induced pancreatitis	K86.0	0	0.88	-	-	-
Diseases of the skin and subcutaneous tissue	L00-L99	0	1.98	-	_	_
Diseases of the musculoskeletal system	M00-M99	2	3.43	0.58	0.15	2.33
Diseases of the genitourinary system	N00-N99	7	8.88	0.79	0.38	1.65
Findings not elsewhere classified	R00-R99	49	37.41	1.31	0.99	1.73
External causes	V00-Y89	335	334.42	1.00	0.90	1.11

Causes of death	ICD-10	OBS	EXP	SMR	95% CI	
Accidental poisoning	X40-X49	52	49.27	1.06	0.80	1.39
Accidental poisoning by and exposure to alcohol	X45	32	34.25	0.93	0.66	1.32
Suicide	X60-X84	87	86.73	1.00	0.81	1.24
Event of undetermined intent	Y10-Y34	22	27.11	0.81	0.53	1.23
Alcohol-related diseases	F10, G31.2, G62.1, I42.6, K70, K86.0, X45	98	101.61	0.96	0.79	1.18

Documented external radiation dose (mSv)	OBS	EXP	SMR	95% CI	
100-199 Diseases of the circulatory system					
<100	318	265.53	1.20	1.07	1.34
≥100	252	236.80	1.06	0.94	1.20
Unknown	174	177.91	0.98	0.84	1.13
I10-I15 Hypertensive diseases					
<100	15	10.73	1.40	0.84	2.32
≥100	16	9.55	1.68	1.03	2.74
Unknown	6	6.74	0.89	0.40	1.98
120-125 Ischemic heart diseases					
<100	196	161.33	1.21	1.06	1.40
≥100	150	143.07	1.05	0.89	1.23
Unknown	118	108.98	1.08	0.90	1.30
I21 Acute myocardial infarction					
<100	27	21.36	1.26	0.87	1.84
≥100	17	18.93	0.90	0.56	1.44
Unknown	23	13.81	1.67	1.11	2.51
160-169 Cerebrovascular diseases					
<100	51	31.17	1.64	1.24	2.15
≥100	40	27.58	1.45	1.06	1.98
Unknown	27	22.30	1.21	0.83	1.77
C00-C97 Malignant neoplasms					
<100	223	164.62	1.35	1.19	1.54
≥100	135	144.24	0.94	0.79	1.11
Unknown	120	105.36	1.14	0.95	1.36
Radiation-related cancer sites					
<100	120	86.54	1.39	1.16	1.66
≥100	75	75.29	1.00	0.79	1.25
Unknown	71	54.99	1.29	1.02	1.63

TABLE 3 The observed (OBS) and expected (EXP) number of selected causes of death and standardized mortality ratios (SMR) with 95% confidence interval (CI) in the Lithuanian cohort of Chernobyl cleanup workers by documented external radiation dose, 2001-2020.

mortality due to cardiovascular diseases was slightly lower (SMR 0.94, 95% CI, 0.84–1.06) compared with the general male population.²⁹

We did not find a positive association between the official radiation dose and the risk of death from circulatory diseases, except for hypertension. However, the latter observation was based on a small number of cases (15 cases with radiation dose <100 mSv and 16 cases with radiation dose ≥100 mSv). A large study of the Russian cohort of cleanup workers demonstrated a statistically significant radiation dose response for mortality from circulatory diseases, particularly from

ischemic heart disease (ERR/Gy 0.41, 95% CI, 0.05-0.78) and from cerebrovascular diseases (ERR/Gy 0.45, 95% CI, 0.11-0.8). 16 These findings should be interpreted with caution since other important risk factors for circulatory diseases, such as overweight, alcohol consumption, or smoking, were not considered. During 53 years of follow-up of the Japanese Life Span Study cohort, the excess relative risk per Gy for heart disease was 14% (95% CI, 6%-23%, p < .001).37 However, the dose-response effect over the dose range of up to 0.5 Gy was not statistically significant.³⁷ The underlying biological

mechanisms implicated in low-dose radiation-related risks of circulatory diseases are still unknown.^{38,39} The evidence from low-dose studies is still inconclusive, requiring higher quality studies with more statistical power and availability of information on key confounders, such as lifestyle, as well as a precise diagnostic criterion of studied outcomes.38

In contrast to the Estonian study,^{5,20} the suicide rate in the Lithuanian cohort was not higher than in the general male population, which is among the highest in the world.⁴⁰ It is somewhat unexpected, given the recognized psychosocial problems, including depression and post-traumatic stress disorder (PTSD), among Chernobyl cleanup workers.^{21,24} We can only hypothesize that differences between the general male population and the members of the cohort of cleanup workers in education, ethnicity, and affiliation to religion, that is, the important determinants of suicide risk.^{23,41} are not the same in Estonia and Lithuania and could explain the observed contrast.

The strengths of our study include the availability of high-quality vital status and cause-of-death data from the population-based Cancer Registry, the Central Population Register, and the Causes of Death Registry. An additional strength of the study is the comprehensive comparison of mortality rates between the cohort and the general population, which includes all relevant causes of death. The unique PID facilitated linkage between the registries and the cohort of cleanup workers and reassured the high completeness of mortality follow-up from 2001 onwards. The current study is a result of the latest follow-up of the Lithuanian cohort of cleanup workers from which the data were used for previous analyses, individually and jointly with other Baltic cohorts. 7,26,42,43

The significant limitation for studying effects of low-dose radiation is the low statistical power of our study due to the small size of the cohort and absence of reliable individual radiation doses because of inadequate or non-existent monitoring. 36,44 This limited our ability to identify indications of an association between the external radiation received during Chernobyl cleanup and mortality from cancer and non-cancer diseases. Since most of the cleanup workers were military reservists or in regular army service, they might have been healthier than other males in the general population. Our estimates of mortality risks therefore can be attenuated because of the "healthy worker effect."45

The absence of detailed mortality data between 1986 and 2000 due to the changes in Lithuania's data collection and protection laws is another serious limitation of our study. However, the studies of nuclear workers and Japanese atomic bomb survivors have shown that most of the solid cancers and circulatory diseases have a minimum 5-year latent period following exposure to radiation and require decades of mortality follow-up.46 In addition, proportions of the cleanup workers with documented low or moderate external doses were comparable between the two groups (those who died before 2001 and those who died 2001 or later). The study has additional limitations, such as the exclusion of cleanup workers who were lost to follow-up and those who moved abroad. However, a major selection bias can be reasonably ruled out in our study because the selection process was unlikely

associated with both the exposure (radiation dose) and the outcome (cause-specific mortality). Specifically:

- The absence of cause of death data before 2001 affected individuals regardless of their radiation dose level, as confirmed by the dose distribution analyses showing no systematic differences between included and excluded groups (not shown).
- There is no evidence to suggest that selection was related to the diseases under study, as exclusion was primarily due to other reasons (e.g., incomplete records, emigration) rather than health status.

There are also other limitations, such as the lack of information regarding potential confounding factors (socio-economic status, lifestyle factors) and the absence of reliable individual doses of external exposure to more precisely evaluate possible associations between the radiation dose and mortality.

Studies of the Japanese atomic bomb survivors and workers in the nuclear industry have demonstrated the importance of continuing follow-up of exposed cohorts through decades after exposure occurred. Now, 39 years after the accident, the time lag is sufficient to detect health effects with potentially longer latency. Since 65% of the members of the Lithuanian cohort were still alive on 1 January 2021, it is important to assure the update of the follow-up of this well-defined cohort of the Chernobyl cleanup workers.

The pooling of coherent and good quality data from the Baltic cohorts could help to increase the limited statistical power of individual cohorts, if emerging challenges to conduct health research by European Data Protection Law and its national interpretations can be overcome and funding can be sought.

5 **CONCLUSIONS**

In addition to serving as a scientific basis for health and radiation protection authorities, the continuous research into the long-term mortality patterns of cancer and non-cancer diseases among the Chernobyl cleanup workers is a reliable source of information about the longterm health impact of the Chernobyl accident for the cleanup workers themselves and for the general public. The cohort study of Chernobyl cleanup workers demonstrated that almost four decades after the Chernobyl accident, the overall mortality among the Chernobyl cleanup workers from Lithuania was slightly elevated compared with the general male population, as was the mortality from all cancer types. The highest risk was observed for smoking-related cancers. Modest increases in mortality from cerebrovascular and cardiovascular diseases were also observed. However, we could not find evidence that those increases were positively associated with higher recorded doses received during the cleanup activities. Other factors, such as smoking, alcohol abuse, diet/obesity, and socio-economic status, along with Chornobyl NPP accident-related ionizing radiation, may lead to an increased risk of cancer. Our findings complement the evidence-based conclusions from analyses concerning the long-term

health effects experienced by individuals subjected to low and moderate doses of external radiation.

AUTHOR CONTRIBUTIONS

Rita Steponaviciene: Writing – review and editing; writing – original draft; formal analysis; conceptualization. Ausrele Kesminiene: Writing – review and editing; writing – original draft; validation; supervision; methodology; investigation; conceptualization. Auguste Kaceniene: Writing – review and editing; investigation; formal analysis; data curation. Giedre Smailyte: Writing – review and editing; supervision; methodology; investigation.

CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest.

DATA AVAILABILITY STATEMENT

Only publicly available data were used in this study, and data sources and handling of these data are described in Section 2. Further information is available from the corresponding author upon request.

ETHICS STATEMENT

This study was approved by the Regional Ethical Committee (No 158200-17-929-432, 4 July 2017).

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