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Non-cancer morbidity among Estonian Chernobyl cleanup workers: a register-based cohort study

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ABSTRACT

Objective: To examine non-cancer morbidity in the Estonian Chernobyl cleanup workers cohort in comparison to the unexposed population controls with special attention to radiation-related diseases and mental health disorders.

Design: Register-based cohort study.

Setting: Estonia.

Participants: A total of 3680 cleanup workers (exposed cohort) and 7631 population controls (unexposed cohort) were followed 2004–2012 through the Population Registry and Health Insurance Fund database.

Methods: Morbidity in the exposed cohort compared to the unexposed controls was estimated in terms of rate ratio (RR) with 95% confidence intervals (CI) using Poisson regression models.

Results: Elevated morbidity in the exposed cohort was found for diseases of the nervous system, digestive system, musculoskeletal system, ischemic heart disease, and for external causes. The most salient excess risk was observed for thyroid diseases (RR=1.69; 95% CI 1.38–2.07), intentional self-harm (RR=1.47; 95% CI 1.04–2.09), and selected alcohol-related diagnoses (RR=1.25; 95% CI 1.12–1.39). No increase in morbidity for stress reactions, depression, headaches or sleep disorders was detected.

Conclusions: No obvious excess morbidity consistent with biological effects of radiation was seen in the exposed cohort, with the possible exception of benign thyroid diseases. Increased alcohol-induced morbidity reflects alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported. The future challenge will be to study mental and physical co-morbidities in the Chernobyl cleanup workers cohort.

ARTICLE SUMMARY

Article focus

- Psychological aftermath of the accident at the Chernobyl nuclear power station has been acknowledged as the major long-term public health concern in the exposed populations (including cleanup workers), but the number of publications on this issue is limited.
- Earlier studies of Estonian cleanup workers revealed higher incidence of alcohol-related cancers and excess of suicide.

Key messages

- No obvious excess morbidity consistent with biological effects of radiation was found in the cleanup workers cohort, with the possible exception of benign thyroid diseases.
- Increased alcohol-induced morbidity in the cleanup workers cohort reflects alcohol abuse, and could underlie some of the higher morbidity rates.
- It is important to study and treat mental and physical co-morbidities in the Chernobyl cleanup workers cohorts.

Strengths and limitations of this study

- Morbidity information provided in this study was obtained from population-based registries via electronic record linkages using personal identification number as the key variable.
- This study was limited to morbidity cases in 2004–2012, no prior information was available.
- The documented radiation doses were not entirely reliable.

INTRODUCTION

In the aftermath of the accident at the Chernobyl nuclear power station in April, 1986, about 600,000 men from throughout the former Soviet Union were commissioned to the area to clean up the environment.[1] Among them were nearly 5000 (mostly) military reservists from Estonia who worked in the contaminated area for three months on average; their mean received cumulative whole-body radiation dose was 0.1 Gy.[2]

Epidemiological evidence of non-cancer disease risk in the cohorts exposed to ionizing radiation is mainly based on mortality since administratively registered death records are available and easy to use for linkages. Dose-dependent risk of death for the broad categories of the circulatory, respiratory and digestive systems has been found among atomic-bomb survivors,[3] but not in other environmentally exposed populations,[4] or in nuclear industry workers.[5] Most of these studies focused on circulatory diseases, the major cause of death in developed countries. Excess mortality from stroke and heart disease was observed in atomic-bomb survivors; however the association below dose of 0.5 Gy was not significant.[6]

A few studies have reported morbidity outcomes. The most informative non-cancer disease incidence study in atomic-bomb survivors found significant radiation effects for thyroid diseases, liver disease, cataract, and calculus of the kidney and ureter.[7] The morbidity study of Mayak nuclear weapons facility workers demonstrated an increasing dose-related trend for cerebrovascular diseases [8] and ischemic heart disease,[9] but did not provide information on risk at doses below 0.2 Gy. Analyses of non-cancer morbidity in a cohort of Russian Chernobyl cleanup workers have shown dose-dependent excess (per 1 Gy) for endocrine and metabolic diseases, mental disorders, diseases of the nervous system, diseases of the digestive system, cerebrovascular diseases, hypertension, and ischemic heart disease.[10, 11] However, risk estimates at low doses still remain uncertain.[12]

Although the psychological aftermath of the Chernobyl accident has been acknowledged as the major long-term public health problem in the exposed populations,[1, 13] the mental health of cleanup workers has only been assessed in small-scale studies in Ukraine.[14–15] There is an urgent need to examine mental health along with somatic diseases when considering the health of cleanup workers.[15]

An updated analysis of mortality and cancer incidence in the Estonian Chernobyl cohort revealed higher incidence of alcohol-related cancers and excess of suicide.[2] Suicide risk has been persistently elevated since the beginning of follow-up.[16, 17] The current research provides the first overview of morbidity other than cancer in the Estonian cohort of Chernobyl cleanup workers with special attention to radiation-related diseases and mental health disorders.

METHODS

Sample and follow-up

The Estonian cohort of Chernobyl cleanup workers (exposed cohort) includes 4831 men recruited in 1986–1991 to the area by the Soviet authorities for decontamination, building and other related activities. Detailed information on the assembly and description of the cohort is given elsewhere.[18] To examine morbidity in this cohort, we used data from the Estonian Health Insurance Fund (EHIF) database available since January 2004. Thus, for the morbidity analyses we identified all cohort members aged 35–69 years and living in Estonia on January 1, 2004 (3680 men). An unexposed population-based comparison cohort was selected corresponding to the age distribution of the exposed cohort. A random sample stratified by 5-year age groups with the exposed to unexposed ratio of 1:2 and 5% extra men in each age group was extracted from the Estonian Population Registry (EPR). After excluding 87 men who had worked in the Chernobyl area, 7631 men remained in the unexposed cohort (Table 1).

The cohort of cleanup workers was linked to the EPR to update vital status (emigration or death with corresponding date), ethnicity and education. Each person in both cohorts was followed up from January 1, 2004 until death, emigration or December 31, 2012 (whichever date came first). From the EHIF database, we obtained dates and ICD-10 codes for each contact with a health provider. All linkages were performed using the unique personal identification number (assigned to all permanent residents of Estonia) as the key variable. EHIF manages the mandatory universal health insurance system that is based on solidarity and covers 95% of the Estonian population.[19] All employees and self-employed persons contribute 13% of their wages, some groups of the population are financed by the State (e.g. registered unemployed, Chernobyl veterans), and some groups are insured without contribution (e.g. children, students, pensioners). People without coverage from the above mentioned sources can pay the tax voluntarily.

Health care contacts were identified from the EHIF database for 2004–2012 using the first occurrence of the three-digit ICD-10 code. All diseases (except cancer, ICD-10 C00–C97), external causes of morbidity, and examinations or counseling were considered. Four-digit codes were taken separately only for some alcohol-induced diseases. A combined category of alcohol-induced diagnoses included mental disorders due to alcohol (F10), degeneration of the nervous system due to alcohol (G31.2), alcoholic cardiomyopathy (I42.6), alcoholic liver disease (K70), alcohol-induced pancreatitis (K86.0), accidental poisoning by alcohol (X45), intentional self-poisoning by alcohol (X65), and poisoning by alcohol, undetermined intent (Y15). The accuracy of the diagnosis was the responsibility of the physician issuing the invoice to EHIF for ambulatory or hospital care.

Morbidity measures and statistical analysis

We estimated morbidity in the cleanup workers cohort by means of rate ratio (RR) with 95% confidence intervals (CI) using Poisson regression models with the logarithm of the person-years at risk (summed by five-year age groups) as the offset.[20] At first, we performed analysis comparing the exposed cohort with the unexposed cohort (external analysis) to obtain an overview of morbidity rate ratios. Diagnoses were grouped into broad categories with selected specific diagnoses (Table 2). Analyses were adjusted for age at diagnosis by five-year age groups.

Additionally, analysis was done between different subgroups within the exposed cohort (internal analysis) to assess possible effects of year of arrival to Chernobyl area (1986; 1987–1991), duration of stay (<92; ≥92 days), documented whole-body radiation dose (<5.0; 5.0–9.9; ≥10.0 cGy), education (higher or secondary; basic or less), and ethnicity (Estonian; non-Estonian (mainly Russians)) on morbidity risk. We used year of arrival and duration of stay as proxy variables for radiation exposure estimates for two reasons – radiation doses documented in military passports were unreliable,[18] and for 15% of the cohort members the dose was not recorded. Ethnicity and educational level were included in the analysis as surrogates for health behavior. Smoking and heavy alcohol consumption are more prevalent in less educated men in Estonia.[21, 22] Although population-based health (behavior) prevalence studies do not report differences in smoking and drinking habits between Estonians and non-Estonians,[21, 22] mortality is higher in non-Estonians than in Estonians,[23] particularly alcohol-related mortality.[24]

Analyses within the exposed cohort focused on disease risks previously reported in atomic-bomb survivors and Chernobyl cleanup workers (Table 3). The first set of models included the year of arrival in the Chernobyl area, duration of stay, age at diagnosis, education and ethnicity. One hundred and seventy four subjects with missing information for any characteristic were excluded from the analysis. In the second set of models we included documented radiation dose; due to unrecorded values, an additional 452 subjects were excluded.

We used Visual FoxPro 6.0 (Microsoft Corporation, Redmond, WA, USA) for database management, and Stata 12 (StataCorp LP, College Station, TX, USA) for statistical modeling.

RESULTS

Description of the exposed and unexposed cohorts

We followed 3680 exposed and 7631 unexposed men from January 1, 2004 until December 31, 2012 (Table 1). The exposed and unexposed cohorts contributed 30,674 and 65,112 person-years, respectively. Mean age at the start of follow-up was 48 years in both cohorts. During the follow-up, 12.9% of the exposed cohort and 10.5% of the unexposed cohort died. The proportions of non-Estonians (mainly Russians) and less educated persons were higher in the exposed cohort, although educational level was unknown for the 16.4% of the subjects in the unexposed cohort. Two-thirds of the cleanup workers entered the Chernobyl area in 1986; the mean and median durations of the mission were 102 and 92 days, respectively (range: 1–833 days). The cohort was exposed to low-level whole-body radiation with the mean and median documented radiation doses of 9.9 and 8.9 cGy, respectively (range: 0.0–54.5 cGy).

Nearly all men had at least one record in the EHIF database (93.6% of the exposed and 95.3% of the unexposed cohort). On average, members of both cohorts had 12 different diagnoses (three-digit ICD-10 codes). Men in the exposed cohort had their first health services contact on average half a year earlier than their unexposed counterparts (52.1 vs. 52.6 years of age).

(Insert Table 1 here)

Morbidity in the exposed cohort in relation to the unexposed cohort (external analysis)

In the external analysis (Table 2), we observed a very small increase of borderline significance in all-disease risk among Chernobyl cleanup workers (RR=1.01; 95% CI 1.00–1.03). From the non-cancer late effects that might be related to the Chernobyl accident (UNSCEAR 2011), we found significantly elevated morbidity for diseases of thyroid gland (RR=1.69; 95% CI 1.38–2.07) and ischemic heart disease (RR=1.09; 95% CI 1.00–1.18). There was no evidence for excess cataract cases in the exposed cohort. Stress reactions, depression, severe headaches and sleep disorders were not diagnosed more frequently in the exposed cohort than in the reference cohort.

Increased morbidity was apparent for the broad categories of diseases of the nervous system, digestive system, musculoskeletal system, and alcohol-induced diagnoses. Morbidity from external causes in the exposed cohort exceeded that in the unexposed cohort (RR=1.07; 95% CI 1.03–1.11). Significantly higher morbidity was registered for falls, intentional self-harm and exposure to excessive cold. Cleanup workers did not undergo medical observations for suspected diseases (ICD-10 Z03) more frequently than unexposed men (RR=1.06; 95% CI 0.94–1.19).

(Insert Table 2 here)

Differences between subgroups in the exposed cohort (internal analysis)

Internal analysis revealed more depressive disorders and stress reactions (RR=1.27; 95% CI 1.00–1.62), and severe headaches (RR=1.69; 95% CI 1.10–2.60) among cleanup workers who entered the area shortly after the accident than in those arriving later (Table 3). Higher thyroid diseases morbidity was not related to year of arrival in the contaminated area. Longer mission did not increase the morbidity of any disease. Acute myocardial infarction, cerebrovascular diseases, diseases of liver, calculus of kidney and ureter, headaches, and alcohol-induced morbidity occurred more frequently among non-Estonians, while mental disorders were more frequent among Estonians. Less educated cleanup workers had higher risk for diseases of the nervous system, cerebrovascular diseases, intentional self-harm, and alcohol-induced morbidity, and lower risk for in situ and benign neoplasms.

Including education and ethnicity in the model did not alter markedly the point estimates of RR for year of arrival or duration of stay. Higher documented radiation dose (5.0–9.9 or ≥10.0 vs. <5.0 cGy) was not associated with higher morbidity of thyroid diseases (RR=0.92; 95% CI 0.60–1.40; 0.92; 0.60–1.40, respectively), cataract (RR=1.26; 95% CI 0.80–1.98; 1.13; 0.70–1.83, respectively), or any of the other selected diseases.

(Insert Table 3 here)

DISCUSSION

The first non-cancer morbidity analysis of the Estonian cohort of Chernobyl cleanup workers revealed elevated morbidity for diseases of the nervous system, digestive system, musculoskeletal system, ischemic heart disease, and for external causes. The most salient excess risk was observed for thyroid diseases, and as expected, for intentional self-harm and selected alcohol-induced diagnoses.

Limitations

First, this study was limited to morbidity cases in 2004–2012. We had no information about morbidity prior to this time period. Thus, it was not possible to specify incident cases or assess early effects of exposure. Among given diseases there could be suspicions or preliminary diagnoses unconfirmed afterwards. We are aware of the possibility of diagnostic errors associated with the use of an reimbursement-administrative database. A small number of cases might have been diagnosed by commercial health care providers and not reported to the EHIF. However, because of universal health insurance, these limitations would be expected to affect the exposed and unexposed cohorts in a similar fashion (non-differential misclassification).

Second, the documented radiation doses are not entirely accurate, and there could be incorrect readings in both directions as discussed elsewhere.[2, 18] Although no correlation was observed between individual doses from military passports (lists) and the biodosimetry estimates for the sub-cohort of cleanup workers, it is estimated that the cohort was exposed to low-dose radiation around 0.1 Gy on average.[25, 26] A similar dose level was reported for Latvian and Lithuanian Chernobyl cleanup workers.[27] Thus, we used year of arrival and duration of stay as proxy variables for radiation exposure. Given these limitations, our conclusions are duly tempered.

Possible radiation effects?

Thyroid diseases have been under close surveillance after the Chernobyl accident since radioiodine (mainly ^{131}I with a half-life of eight days) released during the explosion is concentrated in the thyroid gland. Ron and Brenner [28] summarized the evidence of benign thyroid diseases after radiation exposure. They concluded that associations have been weak and elevated risk occurred mainly in subjects with high doses, exposed at young ages, and in women. Keeping in mind that the cohort of cleanup workers includes only adult men who were exposed to low doses, we cannot attribute the thyroid findings to radiation. This interpretation is supported by the lack of general increase in thyroid diseases in the exposed cohort as well as lack of more pronounced excess among the early entrants or subjects with the highest documented radiation doses. During thyroid screening among the Estonian cleanup workers in 1995, no clear correlation was found between the prevalence of thyroid nodules and the year of arrival or recorded radiation dose.[29]

High radiation doses increase the risk of circulatory diseases, but less is known about the effect of low or moderate doses (<0.5 Gy). Difficulty in estimating dose-response at low dose levels is due to paucity of large cohorts with high-quality data on doses and confounders.[30] As the Estonian cohort of cleanup workers is small and with low average radiation dose, we cannot attribute the small increase in ischemic heart disease morbidity seen in the cohort to biological effects of radiation exposure. This conclusion is also supported by the mortality analyses, where no excess deaths from circulatory diseases were found.[2]

An increased risk of cataract, observed in atomic-bomb survivors [7] and Ukrainian cleanup workers,[31] did not emerge in the Estonian cohort. Although cataract has been conventionally regarded as a late deterministic effect of radiation with a threshold dose of 0.5 Gy, recent studies have suggested a need to lower this dose limit and reconsider the threshold model.[30, 32] Nevertheless, it is unlikely that radiation-related cataracts will be detectable among the Estonian cleanup workers in the future, given the low dose level.

Mental and neurological disorders

Natural or man-made disasters can inflict psychological consequences to the affected populations. Radiation events evoke images of the bombings of Hiroshima and Nagasaki, and mental health effects such as post-traumatic stress, depression, anxiety, and somatization can be long-lasting.[33] After the Chernobyl accident, the mental health of the local population and cleanup workers was considered to be the main public health concern.[1, 13] Cleanup workers were exposed not only to radiation, but also to the lack of protective gear and to the poor living conditions, sometimes doing meaningless jobs, and drinking large amounts of alcohol (mainly home-distilled).[18, 34] Misleading or no information about the possible long-term health effects generated rumors and misapprehensions, and radiation fears were exaggerated.[35, 36] The situation bred profound mistrust of all authorities. One of the most difficult lessons from Chernobyl has been to gain the public's trust and to deliver scientific information about the radiation risks, as there exists an insuperable gap between the experts' and public's perceptions about radiation.[37–39]

To date, the persistently elevated suicide risk in the Estonian cohort has been the definitive indication of psychological impairment as a result of working as a Chernobyl cleanup worker.[2] However, the current morbidity analyses showed a mixed pattern of mental and neurological disorders. Based on the results from a study of Ukrainian cleanup workers,[14] we expected higher rates of depression, anxiety, post-traumatic stress disorder, and headaches. Yet, there was no overall increase of mental disorders as a group (RR=1.00), or of physician-diagnosed depression or anxiety. During the follow-up period, the cleanup workers used health care services significantly less frequently for stress reactions than the unexposed cohort. No excess of severe headaches or sleep disorders was found among cleanup workers. However, depression and stress reactions, and severe headaches were more frequent in the early entrants. Elevated morbidity due to intentional self-harm is also an indicator of psychological distress. This finding is consistent with the increased suicide rate in the cohort,[2] which is strongly related to alcohol dependence among middle-aged men in Estonia.[40]

Excess morbidity emerged for alcohol-induced diseases – mental disorders due to alcohol and degeneration of nervous system due to alcohol. Morbidity from alcohol-induced diagnoses as a group was 25% higher among cleanup workers than in the unexposed cohort. Considering common alcohol abuse among men in Estonia (especially with lower educational level),[22] it is not surprising that cleanup workers used alcohol to cope with stressful situation, and still do. Higher morbidity due to excessive cold is most likely attributable to homelessness and suggests that periods of homelessness were more common in cleanup workers than in men in the comparison cohort. Results of our study demonstrate that the men with Estonian ethnicity and/ or higher educational level coped better with Chernobyl consequences including alcohol abuse.

Although Ukrainian cleanup workers had more mental disorders than controls, no excess of alcoholism was observed.[14] This illustrates how analysis of similar cohorts with different design and risk measures can produce entirely opposite results. Very likely, mental disorders other than alcoholism were under-diagnosed in the Estonian cohort, and the prevalence of alcohol problems was underestimated in the Ukrainian cohort. It is common that people do not seek professional help for mental health problems.[33] Untreated mental disorders can manifest as unexplained physical complaints such as headache or back pain, or they are risk factors for somatic diseases (e.g. thyroid diseases or diseases of the digestive system).[41, 42] Thus, it is important to pay attention to both mental and somatic diseases of Chernobyl cleanup workers simultaneously.

CONCLUSIONS

No obvious excess morbidity consistent with biological effects of radiation was seen in the exposed cohort, with the possible exception of benign thyroid diseases. Increased alcohol-induced morbidity reflects alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported. The future challenge will be to study mental and physical co-morbidities in the Chernobyl cleanup workers cohort.

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Contributors KR and MR designed the study. KR performed the statistical analyses and drafted the manuscript. EB, TH, AA, AU and MR contributed to the interpretation of the results and revised critically the manuscript. MR supervised the whole process. All authors have seen and approved the final version of the manuscript.

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Competing interests None.

Ethics approval The study was approved by the Tallinn Medical Ethics Committee (no. 1939, February 11, 2010), and by the Estonian Data Protection Inspectorate (no. 2.2-3/10/120r, April 9, 2010).

Data sharing statement No additional data are available.

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Table 1 Characteristics of the Estonian cohort of Chernobyl cleanup workers (exposed cohort) and the unexposed population cohort

Characteristic	Exposed cohort		Unexposed cohort	
	No.	(%)	No.	(%)
Total	3680	(100)	7631	(100)
Vital status on December 31, 2012				
Living in Estonia	3132	(85.1)	6795	(89.0)
Dead	474	(12.9)	798	(10.5)
Emigrated	74	(2.0)	38	(0.5)
Age at start of follow-up (full years)				
35–44	1265	(34.4)	2645	(34.7)
45–54	1850	(50.3)	3738	(49.0)
55–64	536	(14.6)	1186	(15.5)
≥65	29	(0.8)	62	(0.8)
Person-years in an age group (2004–2012)				
35–44	4718.4	(15.4)	9416.1	(14.5)
45–54	15,513.5	(50.6)	32,825.3	(50.4)
55–64	9303.9	(30.3)	20,126.9	(30.9)
≥65	1138.6	(3.7)	2743.5	(4.2)
Total	30,674.4	(100)	65,111.8	(100)
Ethnicity				
Estonian	2036	(55.3)	4690	(61.5)
Non-Estonian	1643	(44.6)	2848	(37.3)
Unknown	1	(0.0)	93	(1.2)
Education				
Higher	322	(8.8)	1159	(15.2)
Secondary	2446	(66.5)	4017	(52.6)
Basic or less	824	(22.4)	1200	(15.7)
Unknown	88	(2.4)	1255	(16.4)
Time of arrival in the Chernobyl area				
1986, April–May	1154	(31.4)		
1986, June–December	1128	(30.7)		
1986, month unknown	13	(0.4)		
1987	820	(22.3)		
1988	417	(11.3)		
1989–1991	67	(1.8)		
Unknown	81	(2.2)		
Duration of stay in the Chernobyl area (days)				
<30	220	(6.0)		
30–89	1487	(40.4)		
90–149	1163	(31.6)		
150–209	648	(17.6)		
≥210	60	(1.6)		
Unknown	102	(2.8)		
Documented dose (cGy)				
<5.0	810	(22.0)		
5.0–9.9	1022	(27.8)		
10.0–14.9	555	(15.1)		
15.0–19.9	519	(14.1)		
20.0–24.9	195	(5.3)		
≥25.0	21	(0.6)		
Unknown	558	(15.2)		

Table 2 Number of morbidity cases and age-adjusted morbidity rate ratios* (RR) with 95% confidence intervals (CI) in the Estonian cohort of Chernobyl cleanup workers (exposed cohort) in relation to the unexposed population cohort, 2004–2012

ICD-10	Diagnosis/ external cause of morbidity	No. of cases		RR (95% CI)
		Exposed cohort	Unexposed cohort	
A00–R99, V01–Z99	All diagnoses and external causes	41,370	86,441	1.02 (1.01–1.03)
A00–R99, except C00–C97	All diseases, except cancer	31,757	66,799	1.01 (1.00–1.03)
A00–B99	Infectious diseases	1338	3022	0.94 (0.88–1.00)
A15–A16	Respiratory tuberculosis	41	73	1.19 (0.81–1.74)
D00–D48	In situ and benign neoplasms	517	1060	1.04 (0.94–1.16)
D50–D89	Diseases of the blood and blood-forming organs	97	195	1.07 (0.84–1.36)
E00–E90	Endocrine, nutritional and metabolic diseases	806	1754	0.98 (0.90–1.07)
E00–E07	Diseases of thyroid gland	167	211	1.69 (1.38–2.07)
F00–F99	Mental disorders	1380	2918	1.00 (0.94–1.07)
F10	Mental disorders due to alcohol	328	570	1.21 (1.06–1.39)
F32–F33	Depressive disorders	290	633	0.97 (0.84–1.11)
F41	Anxiety disorders	119	275	0.91 (0.74–1.13)
F43	Stress reactions	55	162	0.72 (0.53–0.97)
G00–G99	Diseases of the nervous system	1352	2550	1.13 (1.06–1.21)
G31.2	Degeneration of nervous system due to alcohol	48	68	1.51 (1.04–2.18)
G40	Epilepsy	148	223	1.40 (1.14–1.73)
G43–G44	Migraine and other headache	125	256	1.03 (0.83–1.28)
G50–G59	Nerve, nerve root and plexus disorders	447	829	1.15 (1.02–1.29)
F51, G47	Sleep disorders	267	529	1.08 (0.93–1.25)
H00–H59	Diseases of the eye	2004	4592	0.93 (0.89–0.98)
H25–H26, H28	Cataract	155	449	0.77 (0.64–0.92)
H40, H42	Glaucoma	109	247	0.96 (0.77–1.20)
H60–H95	Diseases of the ear	1228	2707	0.97 (0.91–1.04)
I00–I99	Diseases of the circulatory system	4432	9477	1.00 (0.97–1.04)
I10–I15	Hypertensive diseases	1936	4210	0.98 (0.93–1.04)
I20–I25	Ischemic heart disease	773	1537	1.09 (1.00–1.18)
I21	Acute myocardial infarction	104	214	1.05 (0.83–1.33)
I60–I69	Cerebrovascular diseases	291	606	1.05 (0.91–1.20)
J00–J99	Diseases of the respiratory system	4699	10,079	0.99 (0.95–1.02)
J30–J39	Diseases of upper respiratory tract	592	1431	0.87 (0.79–0.96)
J40–J47	Lower respiratory diseases	580	1130	1.10 (1.00–1.22)
K00–K93	Diseases of the digestive system	3179	6068	1.11 (1.07–1.16)
K20–K31	Diseases of oesophagus, stomach and duodenum	1415	2648	1.14 (1.06–1.21)
K25–K27	Peptic ulcer	464	857	1.15 (1.02–1.28)
K70–K77	Diseases of liver	194	357	1.16 (0.97–1.38)
K70	Alcoholic liver disease	68	117	1.23 (0.91–1.66)
K85–K86	Diseases of pancreas	128	213	1.27 (1.02–1.58)
K86.0	Alcohol-induced pancreatitis	25	41	1.27 (0.77–2.09)
L00–L99	Diseases of the skin	1793	3730	1.02 (0.97–1.08)
M00–M99	Diseases of the musculoskeletal system	6296	12,623	1.06 (1.03–1.09)
M15–M19	Arthrosis	925	1881	1.06 (0.98–1.14)
M54	Dorsalgia	1475	2817	1.11 (1.04–1.18)
N00–N99	Diseases of the genitourinary system	1518	3648	0.89 (0.84–0.95)
N20	Calculus of kidney and ureter	140	321	0.93 (0.76–1.14)
N40	Hyperplasia of prostate	418	1032	0.88 (0.79–0.99)
R00–R99	Findings, not elsewhere classified	1091	2297	1.01 (0.94–1.09)
V01–Y98	External causes of morbidity	5084	10,055	1.07 (1.03–1.11)
V01–V99	Transport accidents	171	423	0.85 (0.71–1.02)
W00–W19	Falls	2010	3817	1.11 (1.06–1.18)
W20–W49	Exposure to mechanical forces	1864	3799	1.03 (0.98–1.09)
X31	Excessive cold	26	32	1.74 (1.04–2.92)
X40–X49	Accidental poisoning	34	69	1.05 (0.69–1.58)
X60–X84	Intentional self-harm	53	76	1.47 (1.04–2.09)
Z00–Z99	Contact with health services	4135	8862	0.99 (0.96–1.03)
Z03	Medical observation for suspected disease	389	788	1.06 (0.94–1.19)

F10, G31.2, I42.6, K70, K86.0, X45, X65, Y15	Selected alcohol-induced diagnoses and external causes of morbidity	528	896	1.25 (1.12–1.39)

* Adjusted for age at diagnosis

Table 3 Adjusted morbidity rate ratios* (RR) with 95% confidence intervals (CI) by exposure for selected diagnoses and external causes of morbidity in the Estonian cohort of Chernobyl cleanup workers (exposed cohort), 2004–2012

ICD-10	Diagnosis/ external cause of morbidity	Year of arrival 1986†	Duration of stay ≥92 days‡	Ethnicity Non-Estonian§	Education Basic or less¶
D00–D48	In situ and benign neoplasms	1.15 (0.95–1.39)	0.77 (0.64–0.92)	1.09 (0.91–1.30)	0.76 (0.61–0.96)
E00–E07	Diseases of thyroid gland	0.94 (0.68–1.31)	1.00 (0.73–1.38)	0.85 (0.62–1.17)	0.82 (0.55–1.22)
F00–F99	Mental disorders	1.08 (0.96–1.21)	0.85 (0.76–0.95)	0.82 (0.74–0.92)	1.11 (0.97–1.27)
F32–F33, F43	Depressive disorders and stress reactions	1.27 (1.00–1.62)	0.72 (0.58–0.90)	0.53 (0.41–0.67)	0.88 (0.66–1.17)
G00–G99	Diseases of the nervous system	1.01 (0.90–1.13)	0.93 (0.83–1.04)	0.97 (0.87–1.09)	1.20 (1.05–1.37)
G43–G44	Migraine and other headache	1.69 (1.10–2.60)	0.79 (0.55–1.14)	1.48 (1.03–2.12)	0.97 (0.59–1.58)
H25–H26, H28	Cataract	1.07 (0.77–1.49)	1.05 (0.76–1.45)	1.29 (0.93–1.77)	0.93 (0.65–1.33)
H40, H42	Glaucoma	1.26 (0.83–1.89)	0.78 (0.52–1.15)	1.20 (0.81–1.78)	0.80 (0.51–1.27)
I10–I15	Hypertensive diseases	1.03 (0.94–1.14)	0.92 (0.84–1.01)	1.07 (0.98–1.17)	0.99 (0.88–1.11)
I20–I25	Ischemic heart disease	1.15 (0.99–1.34)	0.81 (0.70–0.94)	1.12 (0.97–1.30)	1.10 (0.93–1.30)
I21	Acute myocardial infarction	1.11 (0.74–1.68)	0.94 (0.63–1.39)	1.53 (1.03–2.26)	1.17 (0.74–1.83)
I60–I69	Cerebrovascular diseases	1.11 (0.86–1.42)	1.03 (0.81–1.42)	1.65 (1.30–2.11)	1.61 (1.25–2.08)
K70–K77	Diseases of liver	1.13 (0.82–1.54)	1.13 (0.84–1.51)	1.42 (1.07–1.90)	1.12 (0.79–1.58)
N20	Calculus of kidney and ureter	1.08 (0.74–1.57)	0.88 (0.62–1.26)	1.99 (1.39–2.85)	0.73 (0.45–1.19)
X60–X84	Intentional self-harm	1.27 (0.68–2.36)	0.77 (0.43–1.37)	1.43 (0.82–2.52)	2.73 (1.48–5.05)
F10, G31.2, I42.6, K70, K86.0, X45, X65, Y15	Selected alcohol-induced diagnoses and external causes of morbidity	0.92 (0.76–1.11)	0.98 (0.82–1.17)	1.37 (1.15–1.63)	1.76 (1.44–2.15)

* Models include age at diagnosis, year of arrival, duration of stay, ethnicity, and education
† 1987–1991 as the reference category
‡ <92 days as the reference category
§ Estonian as the reference category
¶ Higher/ secondary as the reference category

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	7-8
		(*d*) If applicable, explain how loss to follow-up was addressed	no losses (Table 1)
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8, Table 1
		(b) Give reasons for non-participation at each stage	5-6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	8, Table 1
		(c) Summarise follow-up time (eg, average and total amount)	8, Table 1
Outcome data	15*	Report numbers of outcome events or summary measures over time	8, Table 2
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-10, Table 2-3
		(*b*) Report category boundaries when continuous variables were categorized	8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-10, Table 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations			10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			14-15
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Non-cancer morbidity among Estonian Chernobyl cleanup workers: a register-based cohort study

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Non-cancer morbidity among Estonian Chernobyl cleanup workers: a register-based cohort study

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ABSTRACT

Objective: To examine non-cancer morbidity in the Estonian Chernobyl cleanup workers cohort compared to the population sample with special attention to radiation-related diseases and mental health disorders.

Design: Register-based cohort study.

Setting: Estonia.

Participants: An exposed cohort of 3680 men (cleanup workers) and an unexposed cohort of 7631 men (population sample) were followed 2004–2012 through the Population Registry and Health Insurance Fund database.

Methods: Morbidity in the exposed cohort compared to the unexposed controls was estimated in terms of rate ratio (RR) with 95% confidence intervals (CI) using Poisson regression models.

Results: Elevated morbidity in the exposed cohort was found for diseases of the nervous system, digestive system, musculoskeletal system, ischemic heart disease, and for external causes. The most salient excess risk was observed for thyroid diseases (RR=1.69; 95% CI 1.38–2.07), intentional self-harm (RR=1.47; 95% CI 1.04–2.09), and selected alcohol-related diagnoses (RR=1.25; 95% CI 1.12–1.39). No increase in morbidity for stress reactions, depression, headaches or sleep disorders was detected.

Conclusions: No obvious excess morbidity consistent with biological effects of radiation was seen in the exposed cohort, with the possible exception of benign thyroid diseases. Increased alcohol-induced morbidity may reflect alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported. The future challenge will be to study mental and physical co-morbidities in the Chernobyl cleanup workers cohort.

ARTICLE SUMMARY

Article focus

- There is limited information about the impact of the Chernobyl accident on the non-cancer morbidity among the cleanup workers. Earlier studies of Estonian cleanup workers revealed an excess of suicide.
- This study provides insight into non-cancer morbidity in the cohort of Estonian cleanup workers with emphasis on radiation-related diseases and mental health disorders.

Key messages

- No obvious excess morbidity consistent with biological effects of radiation was found in the cleanup workers cohort, with the possible exception of benign thyroid diseases.
- Increased alcohol-induced morbidity in the cleanup workers cohort may reflect alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported.

Strengths and limitations of this study

- Morbidity information provided in this study was obtained from population-based registries via electronic record linkages using personal identification number as the key variable.
- Limitations of the study are as follows: relatively short follow-up; the probable presence of tentative and preliminary diagnoses in the health insurance database; the documented radiation doses were not entirely reliable; the small size of the cohort; probable overestimation of findings due to multiple comparisons.

INTRODUCTION

In the aftermath of the accident at the Chernobyl nuclear power station in April, 1986, about 600,000 men from throughout the former Soviet Union were commissioned to the area to clean up the environment.[1] Among them were nearly 5000 (mostly) military reservists from Estonia who worked in the contaminated area for three months on average; their mean received cumulative whole-body radiation dose was 0.1 Gy.[2]

Epidemiological evidence of non-cancer disease risk in the cohorts exposed to ionizing radiation is mainly based on mortality since administratively registered death records are available and easy to use for linkages. Most of these studies have focused on circulatory diseases, the major cause of death in developed countries. Excess mortality from all circulatory diseases, stroke and heart disease was observed in atomic-bomb survivors; however the association below dose of 0.5 Gy was not significant.[3] Follow-up of nuclear industry workers from 15 countries resulted with no significant findings for a dose-dependent rise in mortality from circulatory diseases.[4] Elevated risk of death for the broad categories of the respiratory and digestive systems has been found among atomic-bomb survivors,[5] but not in other environmentally exposed populations [6] or in nuclear industry workers.[4]

A few studies have reported morbidity outcomes. The most informative non-cancer disease incidence study in atomic-bomb survivors found significant radiation effects for thyroid diseases, liver disease, cataract, and calculus of the kidney and ureter.[7] The morbidity study of Mayak nuclear weapons facility workers demonstrated an increasing dose-related trend for cerebrovascular diseases [8] and ischemic heart disease,[9] but did not provide information on risk at doses below 0.2 Gy. A meta-analysis by Little et al. [10] combining morbidity and mortality studies of occupationally and environmentally exposed populations with mean dose below 0.5 Gy, demonstrated significantly increased dose-

dependent risk for ischemic heart disease, cerebrovascular diseases and other circulatory diseases.

Analyses of non-cancer morbidity in a cohort of Russian Chernobyl cleanup workers have shown dose-dependent excess (per 1 Gy) for endocrine and metabolic diseases, mental disorders, diseases of the nervous system, diseases of the digestive system, cerebrovascular diseases, hypertension, and ischemic heart disease.[11, 12] However, risk estimates at low doses still remain uncertain.[13]

Although the psychological aftermath of the Chernobyl accident has been acknowledged as the major long-term public health problem in the exposed populations,[1, 14] the mental health of cleanup workers has only been assessed in small-scale studies in Ukraine.[15–16] There is an urgent need to examine mental health along with somatic diseases when considering the health of cleanup workers.[16]

An updated analysis of mortality and cancer incidence in the Estonian Chernobyl cohort revealed higher incidence of alcohol-related cancers and excess of suicide.[2] Suicide risk has been persistently elevated since the beginning of follow-up.[17, 18] The current research provides the first overview of morbidity other than cancer in the Estonian cohort of Chernobyl cleanup workers with special attention to radiation-related diseases and mental health disorders.

METHODS

Sample and follow-up

The Estonian cohort of Chernobyl cleanup workers (exposed cohort) includes 4831 men recruited in 1986–1991 to the Chernobyl area by the Soviet authorities for decontamination, building and other related activities. The "Chernobyl area" here denotes the 30-km zone (an area of 30-km radius from the nuclear power station) and territories outside, where the

workers were engaged with different activities during their mission period. Detailed information on the assembly and description of the cohort is given elsewhere.[19] To examine morbidity in this cohort, we used data from the Estonian Health Insurance Fund (EHIF) database available since January 2004. Thus, for the morbidity analyses we identified all cohort members aged 35–69 years and living in Estonia on January 1, 2004. Altogether, of 4831 men in the initial cohort, 1129 were excluded because of loss in follow-up (21), death (602) and emigration (506). In addition, we did not include men aged under 35 (9) and over 69 years (13) to have more homogeneous age group. This left just 3680 cleanup workers in the study. An unexposed population-based comparison cohort was selected corresponding to the age distribution of the exposed cohort. A random sample stratified by 5-year age groups with the exposed to unexposed ratio of 1:2 and 5% extra men in each age group was extracted from the Estonian Population Registry (EPR). After excluding 87 men who had worked in the Chernobyl area, 7631 men remained in the unexposed cohort.

The cohort of cleanup workers was linked to the EPR to update vital status (emigration or death with corresponding date), ethnicity and education. Each person in both cohorts was followed up from January 1, 2004 until death, emigration or December 31, 2012 (whichever date came first). From the EHIF database, we obtained dates and ICD-10 codes for each contact with a health provider. All linkages were performed using the unique personal identification number (assigned to all permanent residents of Estonia) as the key variable. EHIF manages the mandatory universal health insurance system that is based on solidarity and covers 95% of the Estonian population.[20] All employees and self-employed persons contribute 13% of their wages, some groups of the population are financed by the State (e.g. registered unemployed, Chernobyl veterans), and some groups are insured without contribution (e.g. children, students, pensioners). People without coverage from the above mentioned sources can pay the tax voluntarily.

Health care contacts were identified from the EHIF database for 2004–2012 using the first occurrence of the three-digit ICD-10 code. If the contact involved multiple diagnoses, the first occurrence of each of them was separately counted. All diseases (except cancer, ICD-10 C00–C97), external causes of morbidity, and examinations or counseling were considered. Four-digit codes were taken separately only for some alcohol-induced diseases. A combined category of alcohol-induced diagnoses included mental disorders due to alcohol (F10), degeneration of the nervous system due to alcohol (G31.2), alcoholic cardiomyopathy (I42.6), alcoholic liver disease (K70), alcohol-induced pancreatitis (K86.0), accidental poisoning by alcohol (X45), intentional self-poisoning by alcohol (X65), and poisoning by alcohol, undetermined intent (Y15). The accuracy of the diagnosis was the responsibility of the physician issuing the invoice to EHIF for ambulatory or hospital care.

Morbidity measures and statistical analysis

We estimated morbidity in the cleanup workers cohort by means of rate ratio (RR) with 95% confidence intervals (CI) using the Poisson regression models with the logarithm of the person-years at risk (summed by five-year age groups) as the offset.[21] At first, we performed analysis comparing the exposed cohort with the unexposed cohort (external analysis) to obtain an overview of morbidity rate ratios. Diagnoses were grouped into broad categories with selected specific diagnoses. Analyses were adjusted for age at diagnosis by five-year age groups.

Additionally, analysis was done between different subgroups within the exposed cohort (internal analysis) to assess possible effects of year of arrival in the Chernobyl area (1986; 1987–1991), duration of stay (<92; ≥92 days), documented cumulative whole-body radiation dose (<5.0; 5.0–9.9; ≥10.0 cGy), education (higher or secondary; basic or less), and ethnicity (Estonian; non-Estonian (mainly Russians)) on morbidity risk. As described elsewhere, [1, 22, 23] the cleanup workers were dominantly exposed to γ-radiation released mainly by ^{131}I, ^{134}Cs and ^{137}Cs. Received radiation doses were measured by individual or group dosimeters, or estimated by work area measurements. The readings were documented in the workers' military passports/ records. Considering, that documented doses were unreliable,[19] and not recorded for 15.2% of the cohort members, we used the year of arrival and duration of stay as proxy variables for radiation exposure.

Ethnicity and educational level were included in the analysis as surrogates for health behavior. The prevalence of alcohol consumption at least once a week (28.5%) and current smoking (69.0%) among the cleanup workers was studied in a postal questionnaire survey conducted in 1992–1993,[19] but not included in current analyses due to small cohort size and lack of longitudinal data on these factors of health behavior.

Analyses within the exposed cohort focused on disease risks previously reported in atomic-bomb survivors and Chernobyl cleanup workers.[7, 11, 12] The first set of models included the year of arrival in the Chernobyl area, duration of stay, age at diagnosis, education and ethnicity. One hundred and seventy four subjects with missing information for any characteristic were excluded from the analysis. In the second set of models we included documented radiation dose; due to unrecorded values, an additional 452 subjects were excluded.

We used Visual FoxPro 6.0 (Microsoft Corporation, Redmond, WA, USA) for database management, and Stata 12 (StataCorp LP, College Station, TX, USA) for statistical modeling.

RESULTS

Description of the exposed and unexposed cohorts

We followed 3680 exposed and 7631 unexposed men from January 1, 2004 until December 31, 2012 (Table 1). The exposed and unexposed cohorts contributed 30,674 and 65,112 person-years, respectively. Mean age at the start of follow-up was 48 years in both cohorts. During the follow-up, 12.9% of the exposed cohort and 10.5% of the unexposed cohort died. The proportions of non-Estonians (mainly Russians) and less educated persons were higher in the exposed cohort, although educational level was unknown for the 16.4% of the subjects in the unexposed cohort. Two-thirds of the cleanup workers entered the Chernobyl area in 1986; the mean and median durations of the mission were 102 and 92 days, respectively (range: 1–833 days). The cohort was exposed to low-level whole-body radiation with the mean and median documented radiation doses of 9.9 and 8.9 cGy, respectively (range: 0.0–54.5 cGy).

Nearly all men had at least one record in the EHIF database (93.6% of the exposed and 95.3% of the unexposed cohort). On average, members of both cohorts had 12 different diagnoses (three-digit ICD-10 codes). Men in the exposed cohort had their first health services contact on average half a year earlier than their unexposed counterparts (52.1 vs. 52.6 years of age).

(Insert Table 1 here)

Morbidity in the exposed cohort in relation to the unexposed cohort (external analysis)

In the external analysis (Table 2), we observed a very small increase of borderline significance in all-disease risk among Chernobyl cleanup workers (RR=1.01; 95% CI 1.00–1.03). From the non-cancer late effects that might be related to the Chernobyl accident (UNSCEAR 2011), we found significantly elevated morbidity for diseases of thyroid gland (RR=1.69; 95% CI 1.38–2.07) and ischemic heart disease (RR=1.09; 95% CI 1.00–1.18). There was evidence of lower occurrence of cataract in the exposed cohort. Stress reactions, depression, severe headaches and sleep disorders were not diagnosed more frequently in the exposed cohort than in the reference cohort.

Increased morbidity was apparent for the broad categories of diseases of the nervous system, digestive system, musculoskeletal system, and alcohol-induced diagnoses. Morbidity from external causes in the exposed cohort exceeded that in the unexposed cohort (RR=1.07; 95% CI 1.03–1.11). Significantly higher morbidity was registered for falls, intentional self-harm and exposure to excessive cold. Cleanup workers did not undergo medical observations for suspected diseases (ICD-10 Z03) more frequently than unexposed men (RR=1.06; 95% CI 0.94–1.19). Additional adjustments for ethnicity and education (rate ratios not presented) did not materially alter these results.

(Insert Table 2 here)

Differences between subgroups in the exposed cohort (internal analysis)

Internal analysis revealed more depressive disorders and stress reactions (RR=1.27; 95% CI 1.00–1.62), and severe headaches (RR=1.69; 95% CI 1.10–2.60) among cleanup workers who entered the area shortly after the accident than in those arriving later (Table 3). Higher thyroid diseases morbidity was not related to year or month (April-May versus June-December, 1986) of arrival in the contaminated area. Longer mission did not increase the morbidity of any disease. Acute myocardial infarction, cerebrovascular diseases, diseases of liver, calculus of kidney and ureter, headaches, and alcohol-induced morbidity occurred more frequently among non-Estonians, while mental disorders were more frequent among Estonians. Less educated cleanup workers had higher risk for diseases of the nervous system, cerebrovascular diseases, intentional self-harm, and alcohol-induced morbidity, and lower risk for in situ and benign neoplasms.

Including education and ethnicity in the model did not alter markedly the crude point estimates of RR for year of arrival or duration of stay (rate ratios not presented). Higher documented radiation dose (5.0–9.9 or ≥10.0 vs. <5.0 cGy) was not associated with higher morbidity of thyroid diseases (RR=0.92; 95% CI 0.60–1.40; 0.92; 0.60–1.40, respectively), cataract (RR=1.26; 95% CI 0.80–1.98; 1.13; 0.70–1.83, respectively), or any of the other selected diseases.

(Insert Table 3 here)

DISCUSSION

The first non-cancer morbidity analysis of the Estonian cohort of Chernobyl cleanup workers revealed elevated morbidity for diseases of the nervous system, digestive system, musculoskeletal system, ischemic heart disease, and for external causes. The most salient excess risk was observed for thyroid diseases, and as expected, for intentional self-harm and selected alcohol-induced diagnoses.

Limitations

First, this study was limited to morbidity cases in 2004–2012. We had no information about morbidity prior to this time period. Thus, it was not possible to specify incident cases or assess early effects of exposure.

Second, among given diseases there could be tentative and preliminary diagnoses unconfirmed afterwards. We are aware of the possibility of diagnostic errors, upcoding and unbundling of codes associated with the use of an reimbursement-administrative database, originally created not for research purposes, but proved to be an important source for medical studies in Estonia.[24–26] A small number of cases might have been diagnosed by commercial health care providers and not reported to the EHIF. However, because of universal health insurance, these limitations would be expected to affect the exposed and unexposed cohorts in a similar fashion**.** This kind of non-differential misclassification of disease or of disease status probably either does not bias the rate ratio or biases it towards the null. The same may be said in a hypothetical situation when the validity of diagnoses in the EHIF will be almost perfect. In the last case as the most important, the number and heterogeneity of diagnostic entries would be reduced, and the accuracy of measurements improved.

Third, the documented radiation doses are not entirely accurate, and there could be incorrect readings in both directions as discussed elsewhere.[2, 19] Although no correlation was observed between individual doses from military passports (lists) and the biodosimetry estimates for the sub-cohort of cleanup workers, it is estimated that the cohort was exposed to low-dose radiation around 0.1 Gy on average.[22, 27] A similar dose level was reported for Latvian and Lithuanian Chernobyl cleanup workers.[28] Thus, we used year of arrival and duration of stay as proxy variables for radiation exposure. Given these limitations, our conclusions are duly tempered.

Fourth, the small size of the cohort has reduced the power of analysis. In addition, because of multiple comparisons, it is possible that some statistically significant findings could be due to chance.

Possible radiation effects?

Thyroid diseases have been under close surveillance after the Chernobyl accident since radioiodine (mainly ^{131}I with a half-life of eight days) released during the explosion is concentrated in the thyroid gland. Ron and Brenner [29] summarized the evidence of benign thyroid diseases after radiation exposure. They concluded that associations have been weak and elevated risk occurred mainly in subjects with high doses, exposed at young ages, and in women. Keeping in mind that the cohort of cleanup workers includes only adult men who were exposed to low doses, we cannot attribute the thyroid findings to radiation. This interpretation is supported by the lack of excess among the early entrants or subjects with the highest documented radiation doses. At the same time, we cannot exclude the possibility that a higher rate ratio among the cleanup workers is caused by close medical attention sought by them. During thyroid screening among the Estonian cleanup workers in 1995, no clear correlation was found between the prevalence of thyroid nodules and the year of arrival or recorded radiation dose.[30] Moreover, these whole-body external doses have little relevance to thyroid diseases because they are not thyroid doses.

High radiation doses increase the risk of circulatory diseases, but less is known about the effect of low or moderate doses (<0.5 Gy). Difficulty in estimating dose-response at low dose levels is due to paucity of large cohorts with high-quality data on doses and confounders.[10, 31] As the Estonian cohort of cleanup workers is small and with low average radiation dose, we cannot attribute the small increase in ischemic heart disease morbidity seen in the cohort to biological effects of radiation exposure. This conclusion is also supported by the mortality analyses, where no excess deaths from circulatory diseases were found.[2]

An increased risk of cataract, observed in atomic-bomb survivors [7] and Ukrainian cleanup workers,[31] did not emerge in the Estonian cohort. An observed statistically significant deficit of cataract cases may be an occasional finding without any epidemiological relevance. Although cataract has been conventionally regarded as a late deterministic effect of radiation with a threshold dose of 0.5 Gy, recent studies have suggested a need to lower this dose limit and reconsider the threshold model.[31- 33] Nevertheless, it is unlikely that radiation-related cataracts will be detectable among the Estonian cleanup workers in the future, given the low dose level.

Mental and neurological disorders

Natural or man-made disasters can inflict psychological consequences to the affected populations. Radiation events evoke images of the bombings of Hiroshima and Nagasaki, and mental health effects such as post-traumatic stress, depression, anxiety, and somatization can be long-lasting.[34] After the Chernobyl accident, the mental health of the local population

and cleanup workers was considered to be the main public health concern.[1, 14] Cleanup workers were exposed not only to radiation, but also to the lack of protective gear and to the poor living conditions, sometimes doing meaningless jobs, and drinking large amounts of alcohol (mainly home-distilled).[19, 35] Misleading or no information about the possible long-term health effects generated rumors and misapprehensions, and radiation fears were exaggerated.[36, 37] The situation bred profound mistrust of all authorities. One of the most difficult lessons from Chernobyl has been to gain the public's trust and to deliver scientific information about the radiation risks, as there exists an insuperable gap between the experts' and public's perceptions about radiation.[38–40]

To date, the persistently elevated suicide risk in the Estonian cohort has been the definitive indication of psychological impairment as a result of working as a Chernobyl cleanup worker.[2] However, the current morbidity analyses showed a mixed pattern of mental and neurological disorders. Based on the results from a study of Ukrainian cleanup workers,[15] we expected higher rates of depression, anxiety, post-traumatic stress disorder, and headaches. Yet, there was no overall increase of mental disorders as a group (RR=1.00), or of physician-diagnosed depression or anxiety. During the follow-up period, the cleanup workers used health care services significantly less frequently for stress reactions than the unexposed cohort. No excess of severe headaches or sleep disorders was found among cleanup workers. However, depression and stress reactions, and severe headaches were more frequent in the early entrants. Elevated morbidity due to intentional self-harm is also an indicator of psychological distress. This finding is consistent with the increased suicide rate in the cohort,[2] which is strongly related to alcohol dependence among middle-aged men in Estonia.[41]

Smoking and heavy alcohol consumption are more prevalent in less educated men in Estonia.[42, 43] Although population-based health (behavior) prevalence studies do not

report differences in smoking and drinking habits between Estonians and non-Estonians,[42, 43] mortality is higher in non-Estonians,[44] particularly alcohol-related mortality.[45]

Excess morbidity emerged for alcohol-induced diseases – mental disorders due to alcohol and degeneration of nervous system due to alcohol. Morbidity from alcohol-induced diagnoses as a group was 25% higher among cleanup workers than in the unexposed cohort. Considering common alcohol abuse among men in Estonia (especially with lower educational level),[43] it is not surprising that cleanup workers used alcohol to cope with stressful situation, and still do. Higher morbidity due to excessive cold is most likely attributable to homelessness and suggests that periods of homelessness were more common in cleanup workers than in men in the comparison cohort. Results of our study demonstrate that the men with Estonian ethnicity and/ or higher educational level coped better with Chernobyl consequences including alcohol abuse.

Although Ukrainian cleanup workers had more mental disorders than controls, no excess of alcoholism was observed.[15] This illustrates how analysis of similar cohorts with different design and risk measures can produce entirely opposite results. Very likely, mental disorders other than alcoholism were under-diagnosed in the Estonian cohort, and the prevalence of alcohol problems was underestimated in the Ukrainian cohort. It is common that people do not seek professional help for mental health problems.[34] Untreated mental disorders can manifest as unexplained physical complaints such as headache or back pain, or they are risk factors for somatic diseases (e.g. thyroid diseases or diseases of the digestive system).[46, 47] Thus, it is important to pay attention to both mental and somatic diseases of Chernobyl cleanup workers simultaneously.

CONCLUSIONS

No obvious excess morbidity consistent with biological effects of radiation was seen in the exposed cohort, with the possible exception of benign thyroid diseases. Increased alcohol-induced morbidity reflects alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported. The future challenge will be to study mental and physical co-morbidities in the Chernobyl cleanup workers cohort.

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Contributors KR and MR designed the study. KR performed the statistical analyses and drafted the manuscript. EB, TH, AA, AU and MR contributed to the interpretation of the results and revised critically the manuscript. MR supervised the whole process. All authors have seen and approved the final version of the manuscript.

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Table 1 Characteristics of the Estonian cohort of Chernobyl cleanup workers (exposed cohort) and the unexposed comparison cohort

Characteristic	Exposed cohort		Unexposed cohort	
	No.	(%)	No.	(%)
Total	3680	(100)	7631	(100)
Vital status on December 31, 2012				
Living in Estonia	3132	(85.1)	6795	(89.0)
Dead	474	(12.9)	798	(10.5)
Emigrated	74	(2.0)	38	(0.5)
Age at start of follow-up (full years)				
35–44	1265	(34.4)	2645	(34.7)
45–54	1850	(50.3)	3738	(49.0)
55–64	536	(14.6)	1186	(15.5)
≥65	29	(0.8)	62	(0.8)
Person-years in an age group (2004–2012)				
35–44	4718.4	(15.4)	9416.1	(14.5)
45–54	15,513.5	(50.6)	32,825.3	(50.4)
55–64	9303.9	(30.3)	20,126.9	(30.9)
≥65	1138.6	(3.7)	2743.5	(4.2)
Total	30,674.4	(100)	65,111.8	(100)
Ethnicity				
Estonian	2036	(55.3)	4690	(61.5)
Non-Estonian	1643	(44.6)	2848	(37.3)
Unknown	1	(0.0)	93	(1.2)
Education				
Higher	322	(8.8)	1159	(15.2)
Secondary	2446	(66.5)	4017	(52.6)
Basic or less	824	(22.4)	1200	(15.7)
Unknown	88	(2.4)	1255	(16.4)
Time of arrival in the Chernobyl area				
1986, April–May	1154	(31.4)		
1986, June–December	1128	(30.7)		
1986, month unknown	13	(0.4)		
1987	820	(22.3)		
1988	417	(11.3)		
1989–1991	67	(1.8)		
Unknown	81	(2.2)		
Duration of stay in the Chernobyl area (days)				
<30	220	(6.0)		
30–89	1487	(40.4)		
90–149	1163	(31.6)		
150–209	648	(17.6)		
≥210	60	(1.6)		
Unknown	102	(2.8)		
Documented dose (cGy)				
<5.0	810	(22.0)		
5.0–9.9	1022	(27.8)		
10.0–14.9	555	(15.1)		
15.0–19.9	519	(14.1)		
20.0–24.9	195	(5.3)		
≥25.0	21	(0.6)		
Unknown	558	(15.2)		

Table 2 Number of morbidity cases* and age-adjusted morbidity rate ratios† (RR) with 95% confidence intervals (CI) in the Estonian cohort of Chernobyl cleanup workers (exposed cohort) in relation to the unexposed comparison cohort, 2004–2012

ICD-10	Diagnosis/ external cause of morbidity	No. of cases		RR (95% CI)
		Exposed cohort	Unexposed cohort	
A00–R99, V01–Z99	All diagnoses and external causes	41,370	86,441	1.02 (1.01–1.03‡
A00–R99, except C00–C97	All diseases, except cancer	31,757	66,799	1.01 (1.00–1.03)
A00–B99	Infectious diseases	1338	3022	0.94 (0.88–1.00)
A15–A16	Respiratory tuberculosis	41	73	1.19 (0.81–1.74)
D00–D48	In situ and benign neoplasms	517	1060	1.04 (0.94–1.16)
D50–D89	Diseases of the blood and blood-forming organs	97	195	1.07 (0.84–1.36)
E00–E90	Endocrine, nutritional and metabolic diseases	806	1754	0.98 (0.90–1.07)
E00–E07	Diseases of thyroid gland	167	211	1.69 (1.38–2.07)‡
F00–F99	Mental disorders	1380	2918	1.00 (0.94–1.07)
F10	Mental disorders due to alcohol	328	570	1.21 (1.06–1.39)‡
F32–F33	Depressive disorders	290	633	0.97 (0.84–1.11)
F41	Anxiety disorders	119	275	0.91 (0.74–1.13)
F43	Stress reactions	55	162	0.72 (0.53–0.97)‡
G00–G99	Diseases of the nervous system	1352	2550	1.13 (1.06–1.21)‡
G31.2	Degeneration of nervous system due to alcohol	48	68	1.51 (1.04–2.18)‡
G40	Epilepsy	148	223	1.40 (1.14–1.73)‡
G43–G44	Migraine and other headache	125	256	1.03 (0.83–1.28)
G50–G59	Nerve, nerve root and plexus disorders	447	829	1.15 (1.02–1.29)‡
F51, G47	Sleep disorders	267	529	1.08 (0.93–1.25)
H00–H59	Diseases of the eye	2004	4592	0.93 (0.89–0.98)‡
H25–H26, H28	Cataract	155	449	0.77 (0.64–0.92)‡
H40, H42	Glaucoma	109	247	0.96 (0.77–1.20)
H60–H95	Diseases of the ear	1228	2707	0.97 (0.91–1.04)
I00–I99	Diseases of the circulatory system	4432	9477	1.00 (0.97–1.04)
I10–I15	Hypertensive diseases	1936	4210	0.98 (0.93–1.04)
I20–I25	Ischemic heart disease	773	1537	1.09 (1.00–1.18)
I21	Acute myocardial infarction	104	214	1.05 (0.83–1.33)
I60–I69	Cerebrovascular diseases	291	606	1.05 (0.91–1.20)
J00–J99	Diseases of the respiratory system	4699	10,079	0.99 (0.95–1.02)
J30–J39	Diseases of upper respiratory tract	592	1431	0.87 (0.79–0.96)‡
J40–J47	Lower respiratory diseases	580	1130	1.10 (1.00–1.22)
K00–K93	Diseases of the digestive system	3179	6068	1.11 (1.07–1.16)‡
K20–K31	Diseases of oesophagus, stomach and duodenum	1415	2648	1.14 (1.06–1.21)‡
K25–K27	Peptic ulcer	464	857	1.15 (1.02–1.28)‡
K70–K77	Diseases of liver	194	357	1.16 (0.97–1.38)
K70	Alcoholic liver disease	68	117	1.23 (0.91–1.66)
K85–K86	Diseases of pancreas	128	213	1.27 (1.02–1.58)‡
K86.0	Alcohol-induced pancreatitis	25	41	1.27 (0.77–2.09)
L00–L99	Diseases of the skin	1793	3730	1.02 (0.97–1.08)
M00–M99	Diseases of the musculoskeletal system	6296	12,623	1.06 (1.03–1.09)‡
M15–M19	Arthrosis	925	1881	1.06 (0.98–1.14)
M54	Dorsalgia	1475	2817	1.11 (1.04–1.18)‡
N00–N99	Diseases of the genitourinary system	1518	3648	0.89 (0.84–0.95)‡
N20	Calculus of kidney and ureter	140	321	0.93 (0.76–1.14)
N40	Hyperplasia of prostate	418	1032	0.88 (0.79–0.99)‡
R00–R99	Findings, not elsewhere classified	1091	2297	1.01 (0.94–1.09)
V01–Y98	External causes of morbidity	5084	10,055	1.07 (1.03–1.11)‡
V01–V99	Transport accidents	171	423	0.85 (0.71–1.02)
W00–W19	Falls	2010	3817	1.11 (1.06–1.18)‡
W20–W49	Exposure to mechanical forces	1864	3799	1.03 (0.98–1.09)
X31	Excessive cold	26	32	1.74 (1.04–2.92)‡
X40–X49	Accidental poisoning	34	69	1.05 (0.69–1.58)
X60–X84	Intentional self-harm	53	76	1.47 (1.04–2.09)‡
Z00–Z99	Contact with health services	4135	8862	0.99 (0.96–1.03)
Z03	Medical observation for suspected disease	389	788	1.06 (0.94–1.19)
F10, G31.2, I42.6, K70,	Selected alcohol-induced diagnoses and	528	896	1.25 (1.12–1.39)‡

K86.0, X45, X65, Y15	external causes of morbidity

* The first occurrence of the three-digit ICD-10 code in the study period was considered.
† Adjusted for age at diagnosis.
‡ $p<0.05$

Table 3 Adjusted morbidity rate ratios* (RR) with 95% confidence intervals (CI) by exposure for selected diagnoses and external causes of morbidity in the Estonian cohort of Chernobyl cleanup workers (3506 persons), 2004–2012

ICD-10	Diagnosis/ external cause of morbidity	Year of arrival 1986†	Duration of stay ≥92 days†	Ethnicity Non-Estonian†	Education Basic or less†
D00–D48	In situ and benign neoplasms	1.15 (0.95–1.39)	0.77 (0.64–0.92)‡	1.09 (0.91–1.30)	0.76 (0.61–0.96)‡
E00–E07	Diseases of thyroid gland	0.94 (0.68–1.31)	1.00 (0.73–1.38)	0.85 (0.62–1.17)	0.82 (0.55–1.22)
F00–F99	Mental disorders	1.08 (0.96–1.21)	0.85 (0.76–0.95)‡	0.82 (0.74–0.92)‡	1.11 (0.97–1.27)
F32–F33, F43	Depressive disorders and stress reactions	1.27 (1.00–1.62)	0.72 (0.58–0.90)‡	0.53 (0.41–0.67)‡	0.88 (0.66–1.17)
G00–G99	Diseases of the nervous system	1.01 (0.90–1.13)	0.93 (0.83–1.04)	0.97 (0.87–1.09)	1.20 (1.05–1.37)‡
G43–G44	Migraine and other headache	1.69 (1.10–2.60)‡	0.79 (0.55–1.14)	1.48 (1.03–2.12)‡	0.97 (0.59–1.58)
H25–H26, H28	Cataract	1.07 (0.77–1.49)	1.05 (0.76–1.45)	1.29 (0.93–1.77)	0.93 (0.65–1.33)
H40, H42	Glaucoma	1.26 (0.83–1.89)	0.78 (0.52–1.15)	1.20 (0.81–1.78)	0.80 (0.51–1.27)
I10–I15	Hypertensive diseases	1.03 (0.94–1.14)	0.92 (0.84–1.01)	1.07 (0.98–1.17)	0.99 (0.88–1.11)
I20–I25	Ischemic heart disease	1.15 (0.99–1.34)	0.81 (0.70–0.94)‡	1.12 (0.97–1.30)	1.10 (0.93–1.30)
I21	Acute myocardial infarction	1.11 (0.74–1.68)	0.94 (0.63–1.39)	1.53 (1.03–2.26)‡	1.17 (0.74–1.83)
I60–I69	Cerebrovascular diseases	1.11 (0.86–1.42)	1.03 (0.81–1.42)	1.65 (1.30–2.11)‡	1.61 (1.25–2.08)‡
K70–K77	Diseases of liver	1.13 (0.82–1.54)	1.13 (0.84–1.51)	1.42 (1.07–1.90)‡	1.12 (0.79–1.58)
N20	Calculus of kidney and ureter	1.08 (0.74–1.57)	0.88 (0.62–1.26)	1.99 (1.39–2.85)‡	0.73 (0.45–1.19)
X60–X84	Intentional self-harm	1.27 (0.68–2.36)	0.77 (0.43–1.37)	1.43 (0.82–2.52)	2.73 (1.48–5.05)‡
F10, G31.2, I42.6, K70, K86.0, X45, X65, Y15	Selected alcohol-induced diagnoses and external causes of morbidity	0.92 (0.76–1.11)	0.98 (0.82–1.17)	1.37 (1.15–1.63)‡	1.76 (1.44–2.15)‡

* Models include age at diagnosis, year of arrival, duration of stay, ethnicity, and education.
† The reference categories for these variables are as follows: year of arrival 1987–1991; duration of stay <92 days; ethnicity Estonian; education higher/ secondary.
‡ $p<0.05$.

Non-cancer morbidity among Estonian Chernobyl cleanup workers: a register-based cohort study

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ABSTRACT

Objective: To examine non-cancer morbidity in the Estonian Chernobyl cleanup workers cohort compared to the population sample with special attention to radiation-related diseases and mental health disorders.

Design: Register-based cohort study.

Setting: Estonia.

Participants: An exposed cohort of 3680 men (cleanup workers) and an unexposed cohort of 7631 men (population sample) were followed 2004–2012 through the Population Registry and Health Insurance Fund database.

Methods: Morbidity in the exposed cohort compared to the unexposed controls was estimated in terms of rate ratio (RR) with 95% confidence intervals (CI) using Poisson regression models.

Results: Elevated morbidity in the exposed cohort was found for diseases of the nervous system, digestive system, musculoskeletal system, ischemic heart disease, and for external causes. The most salient excess risk was observed for thyroid diseases (RR=1.69; 95% CI 1.38–2.07), intentional self-harm (RR=1.47; 95% CI 1.04–2.09), and selected alcohol-related diagnoses (RR=1.25; 95% CI 1.12–1.39). No increase in morbidity for stress reactions, depression, headaches or sleep disorders was detected.

Conclusions: No obvious excess morbidity consistent with biological effects of radiation was seen in the exposed cohort, with the possible exception of benign thyroid diseases. Increased alcohol-induced morbidity may reflect alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported. The future challenge will be to study mental and physical co-morbidities in the Chernobyl cleanup workers cohort.

ARTICLE SUMMARY

Article focus

- There is limited information about the impact of the Chernobyl accident on the non-cancer morbidity among the cleanup workers. Earlier studies of Estonian cleanup workers revealed an excess of suicide.
- This study provides insight into non-cancer morbidity in the cohort of Estonian cleanup workers with emphasis on radiation-related diseases and mental health disorders.

Key messages

- No obvious excess morbidity consistent with biological effects of radiation was found in the cleanup workers cohort, with the possible exception of benign thyroid diseases.
- Increased alcohol-induced morbidity in the cleanup workers cohort may reflect alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported.

Strengths and limitations of this study

- Morbidity information provided in this study was obtained from population-based registries via electronic record linkages using personal identification number as the key variable.
- Limitations of the study are as follows: relatively short follow-up; the probable presence of tentative and preliminary diagnoses in the health insurance database; the documented radiation doses were not entirely reliable; the small size of the cohort; probable overestimation of findings due to multiple comparisons.

INTRODUCTION

In the aftermath of the accident at the Chernobyl nuclear power station in April, 1986, about 600,000 men from throughout the former Soviet Union were commissioned to the area to clean up the environment.[1] Among them were nearly 5000 (mostly) military reservists from Estonia who worked in the contaminated area for three months on average; their mean received cumulative whole-body radiation dose was 0.1 Gy.[2]

Epidemiological evidence of non-cancer disease risk in the cohorts exposed to ionizing radiation is mainly based on mortality since administratively registered death records are available and easy to use for linkages. Most of these studies have focused on circulatory diseases, the major cause of death in developed countries. Excess mortality from all circulatory diseases, stroke and heart disease was observed in atomic-bomb survivors; however the association below dose of 0.5 Gy was not significant.[3] Follow-up of nuclear industry workers from 15 countries resulted with no significant findings for a dose-dependent rise in mortality from circulatory diseases.[4] Elevated risk of death for the broad categories of the respiratory and digestive systems has been found among atomic-bomb survivors,[5] but not in other environmentally exposed populations [6] or in nuclear industry workers.[4]

A few studies have reported morbidity outcomes. The most informative non-cancer disease incidence study in atomic-bomb survivors found significant radiation effects for thyroid diseases, liver disease, cataract, and calculus of the kidney and ureter.[7] The morbidity study of Mayak nuclear weapons facility workers demonstrated an increasing dose-related trend for cerebrovascular diseases [8] and ischemic heart disease,[9] but did not provide information on risk at doses below 0.2 Gy. A meta-analysis by Little et al. [10] combining morbidity and mortality studies of occupationally and environmentally exposed populations with mean dose below 0.5 Gy, demonstrated significantly increased dose-

dependent risk for ischemic heart disease, cerebrovascular diseases and other circulatory diseases.

Analyses of non-cancer morbidity in a cohort of Russian Chernobyl cleanup workers have shown dose-dependent excess (per 1 Gy) for endocrine and metabolic diseases, mental disorders, diseases of the nervous system, diseases of the digestive system, cerebrovascular diseases, hypertension, and ischemic heart disease.[11, 12] However, risk estimates at low doses still remain uncertain.[13]

Although the psychological aftermath of the Chernobyl accident has been acknowledged as the major long-term public health problem in the exposed populations,[1, 14] the mental health of cleanup workers has only been assessed in small-scale studies in Ukraine.[15–16] There is an urgent need to examine mental health along with somatic diseases when considering the health of cleanup workers.[16]

An updated analysis of mortality and cancer incidence in the Estonian Chernobyl cohort revealed higher incidence of alcohol-related cancers and excess of suicide.[2] Suicide risk has been persistently elevated since the beginning of follow-up.[17, 18] The current research provides the first overview of morbidity other than cancer in the Estonian cohort of Chernobyl cleanup workers with special attention to radiation-related diseases and mental health disorders.

METHODS

Sample and follow-up

The Estonian cohort of Chernobyl cleanup workers (exposed cohort) includes 4831 men recruited in 1986–1991 to the Chernobyl area by the Soviet authorities for decontamination, building and other related activities. The "Chernobyl area" here denotes the 30-km zone (an area of 30-km radius from the nuclear power station) and territories outside, where the

workers were engaged with different activities during their mission period. Detailed information on the assembly and description of the cohort is given elsewhere.[19] To examine morbidity in this cohort, we used data from the Estonian Health Insurance Fund (EHIF) database available since January 2004. Thus, for the morbidity analyses we identified all cohort members aged 35–69 years and living in Estonia on January 1, 2004. Altogether, of 4831 men in the initial cohort, 1129 were excluded because of loss in follow-up (21), death (602) and emigration (506). In addition, we did not include men aged under 35 (9) and over 69 years (13) to have more homogeneous age group. This left just 3680 cleanup workers in the study. An unexposed population-based comparison cohort was selected corresponding to the age distribution of the exposed cohort. A random sample stratified by 5-year age groups with the exposed to unexposed ratio of 1:2 and 5% extra men in each age group was extracted from the Estonian Population Registry (EPR). After excluding 87 men who had worked in the Chernobyl area, 7631 men remained in the unexposed cohort.

The cohort of cleanup workers was linked to the EPR to update vital status (emigration or death with corresponding date), ethnicity and education. Each person in both cohorts was followed up from January 1, 2004 until death, emigration or December 31, 2012 (whichever date came first). From the EHIF database, we obtained dates and ICD-10 codes for each contact with a health provider. All linkages were performed using the unique personal identification number (assigned to all permanent residents of Estonia) as the key variable. EHIF manages the mandatory universal health insurance system that is based on solidarity and covers 95% of the Estonian population.[20] All employees and self-employed persons contribute 13% of their wages, some groups of the population are financed by the State (e.g. registered unemployed, Chernobyl veterans), and some groups are insured without contribution (e.g. children, students, pensioners). People without coverage from the above mentioned sources can pay the tax voluntarily.

Health care contacts were identified from the EHIF database for 2004–2012 using the first occurrence of the three-digit ICD-10 code. If the contact involved multiple diagnoses, the first occurrence of each of them was separately counted. All diseases (except cancer, ICD-10 C00–C97), external causes of morbidity, and examinations or counseling were considered. Four-digit codes were taken separately only for some alcohol-induced diseases. A combined category of alcohol-induced diagnoses included mental disorders due to alcohol (F10), degeneration of the nervous system due to alcohol (G31.2), alcoholic cardiomyopathy (I42.6), alcoholic liver disease (K70), alcohol-induced pancreatitis (K86.0), accidental poisoning by alcohol (X45), intentional self-poisoning by alcohol (X65), and poisoning by alcohol, undetermined intent (Y15). The accuracy of the diagnosis was the responsibility of the physician issuing the invoice to EHIF for ambulatory or hospital care.

Morbidity measures and statistical analysis

We estimated morbidity in the cleanup workers cohort by means of rate ratio (RR) with 95% confidence intervals (CI) using the Poisson regression models with the logarithm of the person-years at risk (summed by five-year age groups) as the offset.[21] At first, we performed analysis comparing the exposed cohort with the unexposed cohort (external analysis) to obtain an overview of morbidity rate ratios. Diagnoses were grouped into broad categories with selected specific diagnoses. Analyses were adjusted for age at diagnosis by five-year age groups.

Additionally, analysis was done between different subgroups within the exposed cohort (internal analysis) to assess possible effects of year of arrival in the Chernobyl area (1986; 1987–1991), duration of stay (<92; ≥92 days), documented cumulative whole-body radiation dose (<5.0; 5.0–9.9; ≥10.0 cGy), education (higher or secondary; basic or less), and ethnicity (Estonian; non-Estonian (mainly Russians)) on morbidity risk. As described elsewhere, [1, 22, 23] the cleanup workers were dominantly exposed to γ-radiation released mainly by ^{131}I, ^{134}Cs and ^{137}Cs. Received radiation doses were measured by individual or group dosimeters, or estimated by work area measurements. The readings were documented in the workers' military passports/ records. Considering, that documented doses were unreliable,[19] and not recorded for 15.2% of the cohort members, we used the year of arrival and duration of stay as proxy variables for radiation exposure.

Ethnicity and educational level were included in the analysis as surrogates for health behavior. The prevalence of alcohol consumption at least once a week (28.5%) and current smoking (69.0%) among the cleanup workers was studied in a postal questionnaire survey conducted in 1992–1993,[19] but not included in current analyses due to small cohort size and lack of longitudinal data on these factors of health behavior.

Analyses within the exposed cohort focused on disease risks previously reported in atomic-bomb survivors and Chernobyl cleanup workers.[7, 11, 12] The first set of models included the year of arrival in the Chernobyl area, duration of stay, age at diagnosis, education and ethnicity. One hundred and seventy four subjects with missing information for any characteristic were excluded from the analysis. In the second set of models we included documented radiation dose; due to unrecorded values, an additional 452 subjects were excluded.

We used Visual FoxPro 6.0 (Microsoft Corporation, Redmond, WA, USA) for database management, and Stata 12 (StataCorp LP, College Station, TX, USA) for statistical modeling.

RESULTS

Description of the exposed and unexposed cohorts

We followed 3680 exposed and 7631 unexposed men from January 1, 2004 until December 31, 2012 (Table 1). The exposed and unexposed cohorts contributed 30,674 and 65,112 person-years, respectively. Mean age at the start of follow-up was 48 years in both cohorts. During the follow-up, 12.9% of the exposed cohort and 10.5% of the unexposed cohort died. The proportions of non-Estonians (mainly Russians) and less educated persons were higher in the exposed cohort, although educational level was unknown for the 16.4% of the subjects in the unexposed cohort. Two-thirds of the cleanup workers entered the Chernobyl area in 1986; the mean and median durations of the mission were 102 and 92 days, respectively (range: 1–833 days). The cohort was exposed to low-level whole-body radiation with the mean and median documented radiation doses of 9.9 and 8.9 cGy, respectively (range: 0.0–54.5 cGy).

Nearly all men had at least one record in the EHIF database (93.6% of the exposed and 95.3% of the unexposed cohort). On average, members of both cohorts had 12 different diagnoses (three-digit ICD-10 codes). Men in the exposed cohort had their first health services contact on average half a year earlier than their unexposed counterparts (52.1 vs. 52.6 years of age).

(Insert Table 1 here)

Morbidity in the exposed cohort in relation to the unexposed cohort (external analysis)

In the external analysis (Table 2), we observed a very small increase of borderline significance in all-disease risk among Chernobyl cleanup workers (RR=1.01; 95% CI 1.00–1.03). From the non-cancer late effects that might be related to the Chernobyl accident (UNSCEAR 2011), we found significantly elevated morbidity for diseases of thyroid gland (RR=1.69; 95% CI 1.38–2.07) and ischemic heart disease (RR=1.09; 95% CI 1.00–1.18). There was evidence of lower occurrence of cataract in the exposed cohort. Stress reactions, depression, severe headaches and sleep disorders were not diagnosed more frequently in the exposed cohort than in the reference cohort.

Increased morbidity was apparent for the broad categories of diseases of the nervous system, digestive system, musculoskeletal system, and alcohol-induced diagnoses. Morbidity from external causes in the exposed cohort exceeded that in the unexposed cohort (RR=1.07; 95% CI 1.03–1.11). Significantly higher morbidity was registered for falls, intentional self-harm and exposure to excessive cold. Cleanup workers did not undergo medical observations for suspected diseases (ICD-10 Z03) more frequently than unexposed men (RR=1.06; 95% CI 0.94–1.19). Additional adjustments for ethnicity and education (rate ratios not presented) did not materially alter these results.

(Insert Table 2 here)

Differences between subgroups in the exposed cohort (internal analysis)

Internal analysis revealed more depressive disorders and stress reactions (RR=1.27; 95% CI 1.00–1.62), and severe headaches (RR=1.69; 95% CI 1.10–2.60) among cleanup workers who entered the area shortly after the accident than in those arriving later (Table 3). Higher thyroid diseases morbidity was not related to year or month (April-May versus June-December, 1986) of arrival in the contaminated area. Longer mission did not increase the morbidity of any disease. Acute myocardial infarction, cerebrovascular diseases, diseases of liver, calculus of kidney and ureter, headaches, and alcohol-induced morbidity occurred more frequently among non-Estonians, while mental disorders were more frequent among Estonians. Less educated cleanup workers had higher risk for diseases of the nervous system, cerebrovascular diseases, intentional self-harm, and alcohol-induced morbidity, and lower risk for in situ and benign neoplasms.

Including education and ethnicity in the model did not alter markedly the crude point estimates of RR for year of arrival or duration of stay (rate ratios not presented). Higher documented radiation dose (5.0–9.9 or ≥10.0 vs. <5.0 cGy) was not associated with higher morbidity of thyroid diseases (RR=0.92; 95% CI 0.60–1.40; 0.92; 0.60–1.40, respectively), cataract (RR=1.26; 95% CI 0.80–1.98; 1.13; 0.70–1.83, respectively), or any of the other selected diseases.

(Insert Table 3 here)

DISCUSSION

The first non-cancer morbidity analysis of the Estonian cohort of Chernobyl cleanup workers revealed elevated morbidity for diseases of the nervous system, digestive system, musculoskeletal system, ischemic heart disease, and for external causes. The most salient excess risk was observed for thyroid diseases, and as expected, for intentional self-harm and selected alcohol-induced diagnoses.

Limitations

First, this study was limited to morbidity cases in 2004–2012. We had no information about morbidity prior to this time period. Thus, it was not possible to specify incident cases or assess early effects of exposure.

Second, among given diseases there could be tentative and preliminary diagnoses unconfirmed afterwards. We are aware of the possibility of diagnostic errors, upcoding and unbundling of codes associated with the use of an reimbursement-administrative database, originally created not for research purposes, but proved to be an important source for medical studies in Estonia.[24–26] A small number of cases might have been diagnosed by commercial health care providers and not reported to the EHIF. However, because of universal health insurance, these limitations would be expected to affect the exposed and unexposed cohorts in a similar fashion. This kind of non-differential misclassification of disease or of disease status probably either does not bias the rate ratio or biases it towards the null. The same may be said in a hypothetical situation when the validity of diagnoses in the EHIF will be almost perfect. In the last case as the most important, the number and heterogeneity of diagnostic entries would be reduced, and the accuracy of measurements improved.

Third, the documented radiation doses are not entirely accurate, and there could be incorrect readings in both directions as discussed elsewhere.[2, 19] Although no correlation was observed between individual doses from military passports (lists) and the biodosimetry estimates for the sub-cohort of cleanup workers, it is estimated that the cohort was exposed to low-dose radiation around 0.1 Gy on average.[22, 27] A similar dose level was reported for Latvian and Lithuanian Chernobyl cleanup workers.[28] Thus, we used year of arrival and duration of stay as proxy variables for radiation exposure. Given these limitations, our conclusions are duly tempered.

Fourth, the small size of the cohort has reduced the power of analysis. In addition, because of multiple comparisons, it is possible that some statistically significant findings could be due to chance.

Possible radiation effects?

Thyroid diseases have been under close surveillance after the Chernobyl accident since radioiodine (mainly ^{131}I with a half-life of eight days) released during the explosion is concentrated in the thyroid gland. Ron and Brenner [29] summarized the evidence of benign thyroid diseases after radiation exposure. They concluded that associations have been weak and elevated risk occurred mainly in subjects with high doses, exposed at young ages, and in women. Keeping in mind that the cohort of cleanup workers includes only adult men who were exposed to low doses, we cannot attribute the thyroid findings to radiation. This interpretation is supported by the lack of excess among the early entrants or subjects with the highest documented radiation doses**.** At the same time, we cannot exclude the possibility that a higher rate ratio among the cleanup workers is caused by close medical attention sought by them. During thyroid screening among the Estonian cleanup workers in 1995, no clear correlation was found between the prevalence of thyroid nodules and the year of arrival or recorded radiation dose.[30] Moreover, these whole-body external doses have little relevance to thyroid diseases because they are not thyroid doses.

High radiation doses increase the risk of circulatory diseases, but less is known about the effect of low or moderate doses (<0.5 Gy). Difficulty in estimating dose-response at low dose levels is due to paucity of large cohorts with high-quality data on doses and confounders.[10, 31] As the Estonian cohort of cleanup workers is small and with low average radiation dose, we cannot attribute the small increase in ischemic heart disease morbidity seen in the cohort to biological effects of radiation exposure. This conclusion is also supported by the mortality analyses, where no excess deaths from circulatory diseases were found.[2]

An increased risk of cataract, observed in atomic-bomb survivors [7] and Ukrainian cleanup workers,[31] did not emerge in the Estonian cohort. An observed statistically significant deficit of cataract cases may be an occasional finding without any epidemiological relevance. Although cataract has been conventionally regarded as a late deterministic effect of radiation with a threshold dose of 0.5 Gy, recent studies have suggested a need to lower this dose limit and reconsider the threshold model.[31, 33] Nevertheless, it is unlikely that radiation-related cataracts will be detectable among the Estonian cleanup workers in the future, given the low dose level.

Mental and neurological disorders

Natural or man-made disasters can inflict psychological consequences to the affected populations. Radiation events evoke images of the bombings of Hiroshima and Nagasaki, and mental health effects such as post-traumatic stress, depression, anxiety, and somatization can be long-lasting.[34] After the Chernobyl accident, the mental health of the local population

and cleanup workers was considered to be the main public health concern.[1, 14] Cleanup workers were exposed not only to radiation, but also to the lack of protective gear and to the poor living conditions, sometimes doing meaningless jobs, and drinking large amounts of alcohol (mainly home-distilled).[19, 35] Misleading or no information about the possible long-term health effects generated rumors and misapprehensions, and radiation fears were exaggerated.[36, 37] The situation bred profound mistrust of all authorities. One of the most difficult lessons from Chernobyl has been to gain the public's trust and to deliver scientific information about the radiation risks, as there exists an insuperable gap between the experts' and public's perceptions about radiation.[38–40]

To date, the persistently elevated suicide risk in the Estonian cohort has been the definitive indication of psychological impairment as a result of working as a Chernobyl cleanup worker.[2] However, the current morbidity analyses showed a mixed pattern of mental and neurological disorders. Based on the results from a study of Ukrainian cleanup workers,[15] we expected higher rates of depression, anxiety, post-traumatic stress disorder, and headaches. Yet, there was no overall increase of mental disorders as a group (RR=1.00), or of physician-diagnosed depression or anxiety. During the follow-up period, the cleanup workers used health care services significantly less frequently for stress reactions than the unexposed cohort. No excess of severe headaches or sleep disorders was found among cleanup workers. However, depression and stress reactions, and severe headaches were more frequent in the early entrants. Elevated morbidity due to intentional self-harm is also an indicator of psychological distress. This finding is consistent with the increased suicide rate in the cohort,[2] which is strongly related to alcohol dependence among middle-aged men in Estonia.[41]

Smoking and heavy alcohol consumption are more prevalent in less educated men in Estonia.[42, 43] Although population-based health (behavior) prevalence studies do not

report differences in smoking and drinking habits between Estonians and non-Estonians,[42, 43] mortality is higher in non-Estonians,[44] particularly alcohol-related mortality.[45]

Excess morbidity emerged for alcohol-induced diseases – mental disorders due to alcohol and degeneration of nervous system due to alcohol. Morbidity from alcohol-induced diagnoses as a group was 25% higher among cleanup workers than in the unexposed cohort. Considering common alcohol abuse among men in Estonia (especially with lower educational level),[43] it is not surprising that cleanup workers used alcohol to cope with stressful situation, and still do. Higher morbidity due to excessive cold is most likely attributable to homelessness and suggests that periods of homelessness were more common in cleanup workers than in men in the comparison cohort. Results of our study demonstrate that the men with Estonian ethnicity and/ or higher educational level coped better with Chernobyl consequences including alcohol abuse.

Although Ukrainian cleanup workers had more mental disorders than controls, no excess of alcoholism was observed.[15] This illustrates how analysis of similar cohorts with different design and risk measures can produce entirely opposite results. Very likely, mental disorders other than alcoholism were under-diagnosed in the Estonian cohort, and the prevalence of alcohol problems was underestimated in the Ukrainian cohort. It is common that people do not seek professional help for mental health problems.[34] Untreated mental disorders can manifest as unexplained physical complaints such as headache or back pain, or they are risk factors for somatic diseases (e.g. thyroid diseases or diseases of the digestive system).[46, 47] Thus, it is important to pay attention to both mental and somatic diseases of Chernobyl cleanup workers simultaneously.

CONCLUSIONS

No obvious excess morbidity consistent with biological effects of radiation was seen in the exposed cohort, with the possible exception of benign thyroid diseases. Increased alcohol-induced morbidity reflects alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported. The future challenge will be to study mental and physical co-morbidities in the Chernobyl cleanup workers cohort.

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Contributors KR and MR designed the study. KR performed the statistical analyses and drafted the manuscript. EB, TH, AA, AU and MR contributed to the interpretation of the results and revised critically the manuscript. MR supervised the whole process. All authors have seen and approved the final version of the manuscript.

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Competing interests None.

Ethics approval The study was approved by the Tallinn Medical Ethics Committee (no. 1939, February 11, 2010), and by the Estonian Data Protection Inspectorate (no. 2.2-3/10/120r, April 9, 2010).

Data sharing statement No additional data are available.

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Table 1 Characteristics of the Estonian cohort of Chernobyl cleanup workers (exposed cohort) and the unexposed comparison cohort

Characteristic	Exposed cohort		Unexposed cohort	
	No.	(%)	No.	(%)
Total	3680	(100)	7631	(100)
Vital status on December 31, 2012				
Living in Estonia	3132	(85.1)	6795	(89.0)
Dead	474	(12.9)	798	(10.5)
Emigrated	74	(2.0)	38	(0.5)
Age at start of follow-up (full years)				
35–44	1265	(34.4)	2645	(34.7)
45–54	1850	(50.3)	3738	(49.0)
55–64	536	(14.6)	1186	(15.5)
≥65	29	(0.8)	62	(0.8)
Person-years in an age group (2004–2012)				
35–44	4718.4	(15.4)	9416.1	(14.5)
45–54	15,513.5	(50.6)	32,825.3	(50.4)
55–64	9303.9	(30.3)	20,126.9	(30.9)
≥65	1138.6	(3.7)	2743.5	(4.2)
Total	30,674.4	(100)	65,111.8	(100)
Ethnicity				
Estonian	2036	(55.3)	4690	(61.5)
Non-Estonian	1643	(44.6)	2848	(37.3)
Unknown	1	(0.0)	93	(1.2)
Education				
Higher	322	(8.8)	1159	(15.2)
Secondary	2446	(66.5)	4017	(52.6)
Basic or less	824	(22.4)	1200	(15.7)
Unknown	88	(2.4)	1255	(16.4)
Time of arrival in the Chernobyl area				
1986, April–May	1154	(31.4)		
1986, June–December	1128	(30.7)		
1986, month unknown	13	(0.4)		
1987	820	(22.3)		
1988	417	(11.3)		
1989–1991	67	(1.8)		
Unknown	81	(2.2)		
Duration of stay in the Chernobyl area (days)				
<30	220	(6.0)		
30–89	1487	(40.4)		
90–149	1163	(31.6)		
150–209	648	(17.6)		
≥210	60	(1.6)		
Unknown	102	(2.8)		
Documented dose (cGy)				
<5.0	810	(22.0)		
5.0–9.9	1022	(27.8)		
10.0–14.9	555	(15.1)		
15.0–19.9	519	(14.1)		
20.0–24.9	195	(5.3)		
≥25.0	21	(0.6)		
Unknown	558	(15.2)		

Table 2 Number of morbidity cases* and age-adjusted morbidity rate ratios† (RR) with 95% confidence intervals (CI) in the Estonian cohort of Chernobyl cleanup workers (exposed cohort) in relation to the unexposed comparison cohort, 2004–2012

ICD-10	Diagnosis/ external cause of morbidity	No. of cases		RR (95% CI)
		Exposed cohort	Unexposed cohort	
A00–R99, V01–Z99	All diagnoses and external causes	41,370	86,441	1.02 (1.01–1.03‡
A00–R99, except C00–C97	All diseases, except cancer	31,757	66,799	1.01 (1.00–1.03)
A00–B99	Infectious diseases	1338	3022	0.94 (0.88–1.00)
A15–A16	Respiratory tuberculosis	41	73	1.19 (0.81–1.74)
D00–D48	In situ and benign neoplasms	517	1060	1.04 (0.94–1.16)
D50–D89	Diseases of the blood and blood-forming organs	97	195	1.07 (0.84–1.36)
E00–E90	Endocrine, nutritional and metabolic diseases	806	1754	0.98 (0.90–1.07)
E00–E07	Diseases of thyroid gland	167	211	1.69 (1.38–2.07)‡
F00–F99	Mental disorders	1380	2918	1.00 (0.94–1.07)
F10	Mental disorders due to alcohol	328	570	1.21 (1.06–1.39)‡
F32–F33	Depressive disorders	290	633	0.97 (0.84–1.11)
F41	Anxiety disorders	119	275	0.91 (0.74–1.13)
F43	Stress reactions	55	162	0.72 (0.53–0.97)‡
G00–G99	Diseases of the nervous system	1352	2550	1.13 (1.06–1.21)‡
G31.2	Degeneration of nervous system due to alcohol	48	68	1.51 (1.04–2.18)‡
G40	Epilepsy	148	223	1.40 (1.14–1.73)‡
G43–G44	Migraine and other headache	125	256	1.03 (0.83–1.28)
G50–G59	Nerve, nerve root and plexus disorders	447	829	1.15 (1.02–1.29)‡
F51, G47	Sleep disorders	267	529	1.08 (0.93–1.25)
H00–H59	Diseases of the eye	2004	4592	0.93 (0.89–0.98)‡
H25–H26, H28	Cataract	155	449	0.77 (0.64–0.92)‡
H40, H42	Glaucoma	109	247	0.96 (0.77–1.20)
H60–H95	Diseases of the ear	1228	2707	0.97 (0.91–1.04)
I00–I99	Diseases of the circulatory system	4432	9477	1.00 (0.97–1.04)
I10–I15	Hypertensive diseases	1936	4210	0.98 (0.93–1.04)
I20–I25	Ischemic heart disease	773	1537	1.09 (1.00–1.18)
I21	Acute myocardial infarction	104	214	1.05 (0.83–1.33)
I60–I69	Cerebrovascular diseases	291	606	1.05 (0.91–1.20)
J00–J99	Diseases of the respiratory system	4699	10,079	0.99 (0.95–1.02)
J30–J39	Diseases of upper respiratory tract	592	1431	0.87 (0.79–0.96)‡
J40–J47	Lower respiratory diseases	580	1130	1.10 (1.00–1.22)
K00–K93	Diseases of the digestive system	3179	6068	1.11 (1.07–1.16)‡
K20–K31	Diseases of oesophagus, stomach and duodenum	1415	2648	1.14 (1.06–1.21)‡
K25–K27	Peptic ulcer	464	857	1.15 (1.02–1.28)‡
K70–K77	Diseases of liver	194	357	1.16 (0.97–1.38)
K70	Alcoholic liver disease	68	117	1.23 (0.91–1.66)
K85–K86	Diseases of pancreas	128	213	1.27 (1.02–1.58)‡
K86.0	Alcohol-induced pancreatitis	25	41	1.27 (0.77–2.09)
L00–L99	Diseases of the skin	1793	3730	1.02 (0.97–1.08)
M00–M99	Diseases of the musculoskeletal system	6296	12,623	1.06 (1.03–1.09)‡
M15–M19	Arthrosis	925	1881	1.06 (0.98–1.14)
M54	Dorsalgia	1475	2817	1.11 (1.04–1.18)‡
N00–N99	Diseases of the genitourinary system	1518	3648	0.89 (0.84–0.95)‡
N20	Calculus of kidney and ureter	140	321	0.93 (0.76–1.14)
N40	Hyperplasia of prostate	418	1032	0.88 (0.79–0.99)‡
R00–R99	Findings, not elsewhere classified	1091	2297	1.01 (0.94–1.09)
V01–Y98	External causes of morbidity	5084	10,055	1.07 (1.03–1.11)‡
V01–V99	Transport accidents	171	423	0.85 (0.71–1.02)
W00–W19	Falls	2010	3817	1.11 (1.06–1.18)‡
W20–W49	Exposure to mechanical forces	1864	3799	1.03 (0.98–1.09)
X31	Excessive cold	26	32	1.74 (1.04–2.92)‡
X40–X49	Accidental poisoning	34	69	1.05 (0.69–1.58)
X60–X84	Intentional self-harm	53	76	1.47 (1.04–2.09)‡
Z00–Z99	Contact with health services	4135	8862	0.99 (0.96–1.03)
Z03	Medical observation for suspected disease	389	788	1.06 (0.94–1.19)
F10, G31.2, I42.6, K70,	Selected alcohol-induced diagnoses and	528	896	1.25 (1.12–1.39)‡

K86.0, X45, X65, Y15	external causes of morbidity

* The first occurrence of the three-digit ICD-10 code in the study period was considered.
† Adjusted for age at diagnosis.
‡ $p<0.05$

Table 3 Adjusted morbidity rate ratios* (RR) with 95% confidence intervals (CI) by exposure for selected diagnoses and external causes of morbidity in the Estonian cohort of Chernobyl cleanup workers (3506 persons), 2004–2012

ICD-10	Diagnosis/ external cause of morbidity	Year of arrival 1986†	Duration of stay ≥92 days†	Ethnicity Non-Estonian†	Education Basic or less†
D00–D48	In situ and benign neoplasms	1.15 (0.95–1.39)	0.77 (0.64–0.92)‡	1.09 (0.91–1.30)	0.76 (0.61–0.96)‡
E00–E07	Diseases of thyroid gland	0.94 (0.68–1.31)	1.00 (0.73–1.38)	0.85 (0.62–1.17)	0.82 (0.55–1.22)
F00–F99	Mental disorders	1.08 (0.96–1.21)	0.85 (0.76–0.95)‡	0.82 (0.74–0.92)‡	1.11 (0.97–1.27)
F32–F33, F43	Depressive disorders and stress reactions	1.27 (1.00–1.62)	0.72 (0.58–0.90)‡	0.53 (0.41–0.67)‡	0.88 (0.66–1.17)
G00–G99	Diseases of the nervous system	1.01 (0.90–1.13)	0.93 (0.83–1.04)	0.97 (0.87–1.09)	1.20 (1.05–1.37)‡
G43–G44	Migraine and other headache	1.69 (1.10–2.60)‡	0.79 (0.55–1.14)	1.48 (1.03–2.12)‡	0.97 (0.59–1.58)
H25–H26, H28	Cataract	1.07 (0.77–1.49)	1.05 (0.76–1.45)	1.29 (0.93–1.77)	0.93 (0.65–1.33)
H40, H42	Glaucoma	1.26 (0.83–1.89)	0.78 (0.52–1.15)	1.20 (0.81–1.78)	0.80 (0.51–1.27)
I10–I15	Hypertensive diseases	1.03 (0.94–1.14)	0.92 (0.84–1.01)	1.07 (0.98–1.17)	0.99 (0.88–1.11)
I20–I25	Ischemic heart disease	1.15 (0.99–1.34)	0.81 (0.70–0.94)‡	1.12 (0.97–1.30)	1.10 (0.93–1.30)
I21	Acute myocardial infarction	1.11 (0.74–1.68)	0.94 (0.63–1.39)	1.53 (1.03–2.26)‡	1.17 (0.74–1.83)
I60–I69	Cerebrovascular diseases	1.11 (0.86–1.42)	1.03 (0.81–1.42)	1.65 (1.30–2.11)‡	1.61 (1.25–2.08)‡
K70–K77	Diseases of liver	1.13 (0.82–1.54)	1.13 (0.84–1.51)	1.42 (1.07–1.90)‡	1.12 (0.79–1.58)
N20	Calculus of kidney and ureter	1.08 (0.74–1.57)	0.88 (0.62–1.26)	1.99 (1.39–2.85)‡	0.73 (0.45–1.19)
X60–X84	Intentional self-harm	1.27 (0.68–2.36)	0.77 (0.43–1.37)	1.43 (0.82–2.52)	2.73 (1.48–5.05)‡
F10, G31.2, I42.6, K70, K86.0, X45, X65, Y15	Selected alcohol-induced diagnoses and external causes of morbidity	0.92 (0.76–1.11)	0.98 (0.82–1.17)	1.37 (1.15–1.63)‡	1.76 (1.44–2.15)‡

* Models include age at diagnosis, year of arrival, duration of stay, ethnicity, and education.
† The reference categories for these variables are as follows: year of arrival 1987–1991; duration of stay <92 days; ethnicity Estonian; education higher/ secondary.
‡ $p<0.05$.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	7-8
		(*d*) If applicable, explain how loss to follow-up was addressed	no losses (Table 1)
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8, Table 1
		(b) Give reasons for non-participation at each stage	5-6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	8, Table 1
		(c) Summarise follow-up time (eg, average and total amount)	8, Table 1
Outcome data	15*	Report numbers of outcome events or summary measures over time	8, Table 2
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-10, Table 2-3
		(*b*) Report category boundaries when continuous variables were categorized	8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-10, Table 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations			10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			14-15
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Non-cancer morbidity among Estonian Chernobyl cleanup workers: a register-based cohort study

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Non-cancer morbidity among Estonian Chernobyl cleanup workers: a register-based cohort study

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ABSTRACT

Objective: To examine non-cancer morbidity in the Estonian Chernobyl cleanup workers cohort compared to the population sample with special attention to radiation-related diseases and mental health disorders.

Design: Register-based cohort study.

Setting: Estonia.

Participants: An exposed cohort of 3680 men (cleanup workers) and an unexposed cohort of 7631 men (population sample) were followed 2004–2012 through the Population Registry and Health Insurance Fund database.

Methods: Morbidity in the exposed cohort compared to the unexposed controls was estimated in terms of rate ratio (RR) with 95% confidence intervals (CI) using Poisson regression models.

Results: Elevated morbidity in the exposed cohort was found for diseases of the nervous system, digestive system, musculoskeletal system, ischemic heart disease, and for external causes. The most salient excess risk was observed for thyroid diseases (RR=1.69; 95% CI 1.38–2.07), intentional self-harm (RR=1.47; 95% CI 1.04–2.09), and selected alcohol-related diagnoses (RR=1.25; 95% CI 1.12–1.39). No increase in morbidity for stress reactions, depression, headaches or sleep disorders was detected.

Conclusions: No obvious excess morbidity consistent with biological effects of radiation was seen in the exposed cohort, with the possible exception of benign thyroid diseases. Increased alcohol-induced morbidity may reflect alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported. The future challenge will be to study mental and physical co-morbidities in the Chernobyl cleanup workers cohort.

ARTICLE SUMMARY

Article focus

- There is limited information about the impact of the Chernobyl accident on the non-cancer morbidity among the cleanup workers. Earlier studies of Estonian cleanup workers revealed an excess of suicide.
- This study provides insight into non-cancer morbidity in the cohort of Estonian cleanup workers with emphasis on radiation-related diseases and mental health disorders.

Key messages

- No obvious excess morbidity consistent with biological effects of radiation was found in the cleanup workers cohort, with the possible exception of benign thyroid diseases.
- Increased alcohol-induced morbidity in the cleanup workers cohort may reflect alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported.

Strengths and limitations of this study

- Morbidity information provided in this study was obtained from population-based registries via electronic record linkages using personal identification number as the key variable.
- Limitations of the study are as follows: relatively short follow-up; the probable presence of tentative and preliminary diagnoses in the health insurance database; questionable accuracy and precision of officially documented doses; probable overestimation of findings due to multiple comparisons.

INTRODUCTION

In the aftermath of the accident at the Chernobyl nuclear power station in April, 1986, about 530,000 men from throughout the former Soviet Union were commissioned to the area to clean up the environment.[1] Among them were nearly 5000 (mostly) military reservists from Estonia who worked in the contaminated area for three months on average; their mean received cumulative whole-body radiation dose was 0.1 Gy.[2]

Epidemiological evidence of non-cancer disease risk in the cohorts exposed to ionizing radiation is mainly based on mortality since administratively registered death records are available and easy to use for linkages. Most of these studies have focused on circulatory diseases, the major cause of death in developed countries. Excess mortality from all circulatory diseases, stroke and heart disease was observed in atomic-bomb survivors; however the association below dose of 0.5 Gy was not significant.[3] Follow-up of nuclear industry workers from 15 countries resulted with no significant findings for a dose-dependent rise in mortality from circulatory diseases.[4] Elevated risk of death for the broad categories of the respiratory and digestive systems has been found among atomic-bomb survivors,[5] but not in other environmentally exposed populations [6] or in nuclear industry workers.[4]

A few studies have reported morbidity outcomes. The most informative non-cancer disease incidence study in atomic-bomb survivors found significant radiation effects for thyroid diseases, liver disease, cataract, and calculus of the kidney and ureter.[7] The morbidity study of Mayak nuclear weapons facility workers demonstrated an increasing dose-related trend for cerebrovascular diseases [8] and ischemic heart disease,[9] but did not provide information on risk at doses below 0.2 Gy. A meta-analysis by Little et al. [10] combining morbidity and mortality studies of occupationally and environmentally exposed populations with mean dose below 0.5 Gy, demonstrated significantly increased dose-

dependent risk for ischemic heart disease, cerebrovascular diseases and other circulatory diseases.

Analyses of non-cancer morbidity in a cohort of Russian Chernobyl cleanup workers have shown dose-dependent excess (per 1 Gy) for endocrine and metabolic diseases, mental disorders, diseases of the nervous system, diseases of the digestive system, cerebrovascular diseases, hypertension, and ischemic heart disease.[11, 12] However, risk estimates at low doses still remain uncertain.[13]

Although the psychological aftermath of the Chernobyl accident has been acknowledged as the major long-term public health problem in the exposed populations,[1, 14] the mental health of cleanup workers has only been assessed in small-scale studies in Ukraine.[15–16] There is an urgent need to examine mental health along with somatic diseases when considering the health of cleanup workers.[16]

An updated analysis of mortality and cancer incidence in the Estonian Chernobyl cohort revealed higher incidence of alcohol-related cancers and excess of suicide.[2] Suicide risk has been persistently elevated since the beginning of follow-up.[17, 18] The current research provides the first overview of morbidity other than cancer in the Estonian cohort of Chernobyl cleanup workers with special attention to radiation-related diseases and mental health disorders.

METHODS

Sample and follow-up

The Estonian cohort of Chernobyl cleanup workers (exposed cohort) includes 4831 men recruited in 1986–1991 to the Chernobyl area by the Soviet authorities for decontamination, building and other related activities. The "Chernobyl area" here denotes the 30-km zone (an area of 30-km radius from the nuclear power station) and territories outside, where the

workers were engaged with different activities during their mission period. Detailed information on the assembly and description of the cohort is given elsewhere.[19] To examine morbidity in this cohort, we used data from the Estonian Health Insurance Fund (EHIF) database available since January 2004. Thus, for the morbidity analyses we identified all cohort members aged 35–69 years and living in Estonia on January 1, 2004. Altogether, of 4831 men in the initial cohort, 1129 were excluded because of loss in follow-up (21), death (602) and emigration (506). In addition, we did not include men aged under 35 (9) and over 69 years (13) to have more homogeneous age group. This left just 3680 cleanup workers in the study. An unexposed population-based comparison cohort was selected corresponding to the age distribution of the exposed cohort. A random sample stratified by 5-year age groups with the exposed to unexposed ratio of 1:2 and 5% extra men in each age group was extracted from the Estonian Population Registry (EPR). In the unexposed cohort, after excluding 87 men who had worked in the Chernobyl area (cleanup workers), there remained 7631 men.

The cohort of cleanup workers was linked to the EPR to update vital status (emigration or death with corresponding date), ethnicity and education. Each person in both cohorts was followed up from January 1, 2004 until death, emigration or December 31, 2012 (whichever date came first). From the EHIF database, we obtained dates and ICD-10 codes for each contact with a health provider. All linkages were performed using the unique personal identification number (assigned to all permanent residents of Estonia) as the key variable. EHIF manages the mandatory universal health insurance system that is based on solidarity and covers 95% of the Estonian population.[20] All employees and self-employed persons contribute 13% of their wages, some groups of the population are financed by the State (e.g. registered unemployed, Chernobyl veterans), and some groups are insured without contribution (e.g. children, students, pensioners). People without coverage from the above mentioned sources can pay the tax voluntarily.

Health care contacts were identified from the EHIF database for 2004–2012 using the first occurrence of the three-digit ICD-10 code. If the contact involved multiple diagnoses, the first occurrence of each of them was separately counted. All diseases (except cancer, ICD-10 C00–C97), external causes of morbidity, and examinations or counseling were considered. Four-digit codes were taken separately only for some alcohol-induced diseases. A combined category of alcohol-induced diagnoses included mental disorders due to alcohol (F10), degeneration of the nervous system due to alcohol (G31.2), alcoholic cardiomyopathy (I42.6), alcoholic liver disease (K70), alcohol-induced pancreatitis (K86.0), accidental poisoning by alcohol (X45), intentional self-poisoning by alcohol (X65), and poisoning by alcohol, undetermined intent (Y15). The accuracy of the diagnosis was the responsibility of the physician issuing the invoice to EHIF for ambulatory or hospital care.

Morbidity measures and statistical analysis

We estimated morbidity in the cleanup workers cohort by means of rate ratio (RR) with 95% confidence intervals (CI) using the Poisson regression models with the logarithm of the person-years at risk (summed by five-year age groups) as the offset.[21] At first, we performed analysis comparing the exposed cohort with the unexposed cohort (external analysis) to obtain an overview of morbidity rate ratios. Diagnoses were grouped into broad categories with selected specific diagnoses. Analyses were adjusted for age at diagnosis by five-year age groups.

Additionally, analysis was done between different subgroups within the exposed cohort (internal analysis) to assess possible effects of year of arrival in the Chernobyl area (1986; 1987–1991), duration of stay (<92; ≥92 days), and documented cumulative whole-body radiation dose (<5.0; 5.0–9.9; ≥10.0 cGy) on morbidity risk. As described elsewhere, [1, 22, 23] the cleanup workers were dominantly exposed to γ-radiation released mainly by ^{131}I,

^{134}Cs and ^{137}Cs. Received radiation doses were measured by individual or group dosimeters, or estimated by work area measurements. The readings were documented in the workers' military passports/ records. Considering, that documented doses were unreliable,[19] and not recorded for 15.2% of the cohort members, we used the year of arrival and duration of stay as proxy variables for radiation exposure.

Potential confounders – educational level (higher or secondary; basic or less) and ethnicity (Estonian; non-Estonian (mainly Russians)) – were included in the analysis as surrogates for health behavior. The prevalence of alcohol consumption at least once a week (28.5%) and current smoking (69.0%) among the cleanup workers was studied in a postal questionnaire survey conducted in 1992–1993,[19] but not included in current analyses due to small cohort size and lack of longitudinal data on these factors of health behavior. Thus, the selection of variables (potential confounders) was determined by the availability of them and a review of our previous studies.

Analyses within the exposed cohort focused on disease risks previously reported in atomic-bomb survivors and Chernobyl cleanup workers.[7, 11, 12] The first set of models included the year of arrival in the Chernobyl area, duration of stay, age at diagnosis, education and ethnicity. One hundred and seventy four subjects with missing information for any characteristic were excluded from the analysis. In the second set of models we included documented radiation dose; due to unrecorded values, an additional 452 subjects were excluded.

We used Visual FoxPro 6.0 (Microsoft Corporation, Redmond, WA, USA) for database management, and Stata 12 (StataCorp LP, College Station, TX, USA) for statistical modeling.

RESULTS

Description of the exposed and unexposed cohorts

We followed 3680 exposed and 7631 unexposed men from January 1, 2004 until December 31, 2012 (Table 1). The exposed and unexposed cohorts contributed 30,674 and 65,112 person-years, respectively. Mean age at the start of follow-up was 48 years in both cohorts. During the follow-up, 12.9% of the exposed cohort and 10.5% of the unexposed cohort died. The proportions of non-Estonians (mainly Russians) and less educated persons were higher in the exposed cohort, although educational level was unknown for the 16.4% of the subjects in the unexposed cohort. Two-thirds of the cleanup workers entered the Chernobyl area in 1986; the mean and median durations of the mission were 102 and 92 days, respectively (range: 1–833 days). The cohort was exposed to low-level whole-body radiation with the mean and median documented radiation doses of 9.9 and 8.9 cGy, respectively (range: 0.0–54.5 cGy).

Nearly all men had at least one record in the EHIF database (93.6% of the exposed and 95.3% of the unexposed cohort). On average, members of both cohorts had 12 different diagnoses (three-digit ICD-10 codes). Men in the exposed cohort had their first health services contact on average half a year earlier than their unexposed counterparts (52.1 vs. 52.6 years of age).

(Insert Table 1 here)

Morbidity in the exposed cohort in relation to the unexposed cohort (external analysis)

In the external analysis (Table 2), we observed a very small increase of borderline significance in all-disease risk among Chernobyl cleanup workers (RR=1.01; 95% CI 1.00–1.03). From the non-cancer late effects that might be related to the Chernobyl accident (UNSCEAR 2011), we found significantly elevated morbidity for diseases of thyroid gland (RR=1.69; 95% CI 1.38–2.07) and ischemic heart disease (RR=1.09; 95% CI 1.00–1.18). There was evidence of lower occurrence of cataract in the exposed cohort. Stress reactions, depression, severe headaches and sleep disorders were not diagnosed more frequently in the exposed cohort than in the reference cohort.

Increased morbidity was apparent for the broad categories of diseases of the nervous system, digestive system, musculoskeletal system, and alcohol-induced diagnoses. Morbidity from external causes in the exposed cohort exceeded that in the unexposed cohort (RR=1.07; 95% CI 1.03–1.11). Significantly higher morbidity was registered for falls, intentional self-harm and exposure to excessive cold. Cleanup workers did not undergo medical observations for suspected diseases (ICD-10 Z03) more frequently than unexposed men (RR=1.06; 95% CI 0.94–1.19). Additional adjustments for ethnicity and education (rate ratios not presented) did not materially alter these results.

(Insert Table 2 here)

Differences between subgroups in the exposed cohort (internal analysis)

Internal analysis revealed more depressive disorders and stress reactions (RR=1.27; 95% CI 1.00–1.62), and severe headaches (RR=1.69; 95% CI 1.10–2.60) among cleanup workers who entered the area shortly after the accident than in those arriving later (Table 3). Higher thyroid diseases morbidity was not related to year or month (April-May versus June-December, 1986) of arrival in the contaminated area. Longer mission did not increase the morbidity of any disease. Acute myocardial infarction, cerebrovascular diseases, diseases of liver, calculus of kidney and ureter, headaches, and alcohol-induced morbidity occurred more frequently among non-Estonians, while mental disorders were more frequent among Estonians. Less educated cleanup workers had higher risk for diseases of the nervous system, cerebrovascular diseases, intentional self-harm, and alcohol-induced morbidity, and lower risk for in situ and benign neoplasms.

Including education and ethnicity in the model did not alter markedly the crude point estimates of RR for year of arrival or duration of stay (rate ratios not presented). Higher documented radiation dose (5.0–9.9 or ≥10.0 vs. <5.0 cGy) was not associated with higher morbidity of thyroid diseases (RR=0.92; 95% CI 0.60–1.40; 0.92; 0.60–1.40, respectively), cataract (RR=1.26; 95% CI 0.80–1.98; 1.13; 0.70–1.83, respectively), or any of the other selected diseases.

(Insert Table 3 here)

DISCUSSION

The first non-cancer morbidity analysis of the Estonian cohort of Chernobyl cleanup workers revealed elevated morbidity for diseases of the nervous system, digestive system, musculoskeletal system, ischemic heart disease, and for external causes. The most salient excess risk was observed for thyroid diseases, and as expected, for intentional self-harm and selected alcohol-induced diagnoses.

Limitations

First, this study was limited to morbidity cases in 2004–2012. We had no information about morbidity prior to this time period. Thus, it was not possible to specify incident cases or assess early effects of exposure.

Second, among given diseases there could be tentative and preliminary diagnoses unconfirmed afterwards. We are aware of the possibility of diagnostic errors, upcoding and unbundling of codes associated with the use of a reimbursement-administrative database, originally created not for research purposes, but proved to be an important source for medical studies in Estonia.[24–26] A small number of cases might have been diagnosed by commercial health care providers and not reported to the EHIF. However, because of universal health insurance, these limitations would be expected to affect the exposed and unexposed cohorts in a similar fashion**.** This kind of non-differential misclassification of disease or of disease status probably either does not bias the rate ratio or biases it towards the null. The same may be said in a hypothetical situation when the validity of diagnoses in the EHIF will be almost perfect. In the last case as the most important, the number and heterogeneity of diagnostic entries would be reduced, and the accuracy of measurements improved.

Third, the documented radiation doses are not entirely accurate, and there could be incorrect readings in both directions as discussed elsewhere.[2, 19] Although no correlation was observed between individual doses from military passports (lists) and the biodosimetry estimates for the sub-cohort of cleanup workers, it is estimated that the cohort was exposed to low-dose radiation around 0.1 Gy on average.[22, 27] A similar dose level was reported for Latvian and Lithuanian Chernobyl cleanup workers.[28] Thus, we used year of arrival and duration of stay as proxy variables for radiation exposure.

Fourth, the small size of the cohort has reduced the power of analysis. In addition, because of multiple comparisons, it is possible that some statistically significant findings could be due to chance. Given these limitations, our conclusions are duly tempered.

Possible radiation effects?

Thyroid diseases have been under close surveillance after the Chernobyl accident since radioiodine (mainly ^{131}I with a half-life of eight days) released during the explosion is concentrated in the thyroid gland. Ron and Brenner [29] summarized the evidence of benign thyroid diseases after radiation exposure. They concluded that associations have been weak and elevated risk occurred mainly in subjects with high doses, exposed at young ages, and in women. Keeping in mind that the cohort of cleanup workers includes only adult men who were exposed to low doses, we cannot attribute the thyroid findings to radiation. This interpretation is supported by the lack of excess among the early entrants or subjects with the highest documented radiation doses**.** At the same time, we cannot exclude the possibility that a higher rate ratio among the cleanup workers is caused by close medical attention sought by them. During thyroid screening among the Estonian cleanup workers in 1995, no clear correlation was found between the prevalence of thyroid nodules and the year of arrival or recorded radiation dose.[30]

High radiation doses increase the risk of circulatory diseases, but less is known about the effect of low or moderate doses (<0.5 Gy). Difficulty in estimating dose-response at low dose levels is due to paucity of large cohorts with high-quality data on doses and confounders.[10, 31] As the Estonian cohort of cleanup workers is small and with low average radiation dose, we cannot attribute the small increase in ischemic heart disease morbidity seen in the cohort to biological effects of radiation exposure. This conclusion is also supported by the mortality analyses, where no excess deaths from circulatory diseases were found.[2]

An increased risk of cataract, observed in atomic-bomb survivors [7] and Ukrainian cleanup workers,[32] did not emerge in the Estonian cohort. An observed statistically significant deficit of cataract cases may be an occasional finding without any epidemiological relevance. Although cataract has been conventionally regarded as a late deterministic effect of radiation with a threshold dose of 0.5 Gy, recent studies have suggested a need to lower this dose limit and reconsider the threshold model.[31, 33] Nevertheless, it is unlikely that radiation-related cataracts will be detectable among the Estonian cleanup workers in the future, given the low dose level.

Mental and neurological disorders

Natural or man-made disasters can inflict psychological consequences to the affected populations. Radiation events evoke images of the bombings of Hiroshima and Nagasaki, and mental health effects such as post-traumatic stress, depression, anxiety, and somatization can be long-lasting.[34] After the Chernobyl accident, the mental health of the local population

and cleanup workers was considered to be the main public health concern.[1, 14] Cleanup workers were exposed not only to radiation, but also to the lack of protective gear and to the poor living conditions, sometimes doing meaningless jobs, and drinking large amounts of alcohol (mainly home-distilled).[19, 35] Misleading or no information about the possible long-term health effects generated rumors and misapprehensions, and radiation fears were exaggerated.[36, 37] The situation bred profound mistrust of all authorities. One of the most difficult lessons from Chernobyl has been to gain the public's trust and to deliver scientific information about the radiation risks, as there exists an insuperable gap between the experts' and public's perceptions about radiation.[38–40]

To date, the persistently elevated suicide risk in the Estonian cohort has been the definitive indication of psychological impairment as a result of working as a Chernobyl cleanup worker.[2] However, the current morbidity analyses showed a mixed pattern of mental and neurological disorders. Based on the results from a study of Ukrainian cleanup workers,[15] we expected higher rates of depression, anxiety, post-traumatic stress disorder, and headaches. Yet, there was no overall increase of mental disorders as a group (RR=1.00), or of physician-diagnosed depression or anxiety. During the follow-up period, the cleanup workers used health care services significantly less frequently for stress reactions than the unexposed cohort. No excess of severe headaches or sleep disorders was found among cleanup workers. However, depression and stress reactions, and severe headaches were more frequent in the early entrants. Elevated morbidity due to intentional self-harm is also an indicator of psychological distress. This finding is consistent with the increased suicide rate in the cohort,[2] which is strongly related to alcohol dependence among middle-aged men in Estonia.[41]

Smoking and heavy alcohol consumption are more prevalent in less educated men in Estonia.[42, 43] Although population-based health (behavior) prevalence studies do not

report differences in smoking and drinking habits between Estonians and non-Estonians,[42, 43] mortality is higher in non-Estonians,[44] particularly alcohol-related mortality.[45]

Excess morbidity emerged for alcohol-induced diseases – mental disorders due to alcohol and degeneration of nervous system due to alcohol. Morbidity from alcohol-induced diagnoses as a group was 25% higher among cleanup workers than in the unexposed cohort. Considering common alcohol abuse among men in Estonia (especially with lower educational level),[43] it is not surprising that cleanup workers used alcohol to cope with stressful situation, and still do. Higher morbidity due to excessive cold is most likely attributable to homelessness and suggests that periods of homelessness were more common in cleanup workers than in men in the comparison cohort. Results of our study demonstrate that the men with Estonian ethnicity and/ or higher educational level coped better with Chernobyl consequences including alcohol abuse.

Although Ukrainian cleanup workers had more mental disorders than controls, no excess of alcoholism was observed.[15] This illustrates how analysis of similar cohorts with different design and risk measures can produce entirely opposite results. Very likely, mental disorders other than alcoholism were under-diagnosed in the Estonian cohort, and the prevalence of alcohol problems was underestimated in the Ukrainian cohort. It is common that people do not seek professional help for mental health problems.[34] Untreated mental disorders can manifest as unexplained physical complaints such as headache or back pain, or they are risk factors for somatic diseases (e.g. thyroid diseases or diseases of the digestive system).[46, 47] Thus, it is important to pay attention to both mental and somatic diseases of Chernobyl cleanup workers simultaneously.

CONCLUSIONS

No obvious excess morbidity consistent with biological effects of radiation was seen in the exposed cohort, with the possible exception of benign thyroid diseases. Increased alcohol-induced morbidity reflects alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported. The future challenge will be to study mental and physical co-morbidities in the Chernobyl cleanup workers cohort.

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Contributors KR and MR designed the study. KR performed the statistical analyses and drafted the manuscript. EB, TH, AA, AU and MR contributed to the interpretation of the results and revised critically the manuscript. MR supervised the whole process. All authors have seen and approved the final version of the manuscript.

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Competing interests None.

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Table 1 Characteristics of the Estonian cohort of Chernobyl cleanup workers (exposed cohort) and the unexposed comparison cohort

Characteristic	Exposed cohort		Unexposed cohort	
	No.	(%)	No.	(%)
Total	3680	(100)	7631	(100)
Vital status on December 31, 2012				
Living in Estonia	3132	(85.1)	6795	(89.0)
Dead	474	(12.9)	798	(10.5)
Emigrated	74	(2.0)	38	(0.5)
Age at start of follow-up (full years)				
35–44	1265	(34.4)	2645	(34.7)
45–54	1850	(50.3)	3738	(49.0)
55–64	536	(14.6)	1186	(15.5)
≥65	29	(0.8)	62	(0.8)
Person-years in an age group (2004–2012)				
35–44	4718.4	(15.4)	9416.1	(14.5)
45–54	15,513.5	(50.6)	32,825.3	(50.4)
55–64	9303.9	(30.3)	20,126.9	(30.9)
≥65	1138.6	(3.7)	2743.5	(4.2)
Total	30,674.4	(100)	65,111.8	(100)
Ethnicity				
Estonian	2036	(55.3)	4690	(61.5)
Non-Estonian	1643	(44.6)	2848	(37.3)
Unknown	1	(0.0)	93	(1.2)
Education				
Higher	322	(8.8)	1159	(15.2)
Secondary	2446	(66.5)	4017	(52.6)
Basic or less	824	(22.4)	1200	(15.7)
Unknown	88	(2.4)	1255	(16.4)
Time of arrival in the Chernobyl area				
1986, April–May	1154	(31.4)		
1986, June–December	1128	(30.7)		
1986, month unknown	13	(0.4)		
1987	820	(22.3)		
1988	417	(11.3)		
1989–1991	67	(1.8)		
Unknown	81	(2.2)		
Duration of stay in the Chernobyl area (days)				
<30	220	(6.0)		
30–89	1487	(40.4)		
90–149	1163	(31.6)		
150–209	648	(17.6)		
≥210	60	(1.6)		
Unknown	102	(2.8)		
Documented dose (cGy)				
<5.0	810	(22.0)		
5.0–9.9	1022	(27.8)		
10.0–14.9	555	(15.1)		
15.0–19.9	519	(14.1)		
20.0–24.9	195	(5.3)		
≥25.0	21	(0.6)		
Unknown	558	(15.2)		

Table 2 Number of morbidity cases* and age-adjusted morbidity rate ratios† (RR) with 95% confidence intervals (CI) in the Estonian cohort of Chernobyl cleanup workers (exposed cohort) in relation to the unexposed comparison cohort, 2004–2012

ICD-10	Diagnosis/ external cause of morbidity	No. of cases		RR (95% CI)
		Exposed cohort	Unexposed cohort	
A00–R99, V01–Z99	All diagnoses and external causes	41,370	86,441	1.02 (1.01–1.03‡
A00–R99, except C00–C97	All diseases, except cancer	31,757	66,799	1.01 (1.00–1.03)
A00–B99	Infectious diseases	1338	3022	0.94 (0.88–1.00)
A15–A16	Respiratory tuberculosis	41	73	1.19 (0.81–1.74)
D00–D48	In situ and benign neoplasms	517	1060	1.04 (0.94–1.16)
D50–D89	Diseases of the blood and blood-forming organs	97	195	1.07 (0.84–1.36)
E00–E90	Endocrine, nutritional and metabolic diseases	806	1754	0.98 (0.90–1.07)
E00–E07	Diseases of thyroid gland	167	211	1.69 (1.38–2.07)‡
F00–F99	Mental disorders	1380	2918	1.00 (0.94–1.07)
F10	Mental disorders due to alcohol	328	570	1.21 (1.06–1.39)‡
F32–F33	Depressive disorders	290	633	0.97 (0.84–1.11)
F41	Anxiety disorders	119	275	0.91 (0.74–1.13)
F43	Stress reactions	55	162	0.72 (0.53–0.97)‡
G00–G99	Diseases of the nervous system	1352	2550	1.13 (1.06–1.21)‡
G31.2	Degeneration of nervous system due to alcohol	48	68	1.51 (1.04–2.18)‡
G40	Epilepsy	148	223	1.40 (1.14–1.73)‡
G43–G44	Migraine and other headache	125	256	1.03 (0.83–1.28)
G50–G59	Nerve, nerve root and plexus disorders	447	829	1.15 (1.02–1.29)‡
F51, G47	Sleep disorders	267	529	1.08 (0.93–1.25)
H00–H59	Diseases of the eye	2004	4592	0.93 (0.89–0.98)‡
H25–H26, H28	Cataract	155	449	0.77 (0.64–0.92)‡
H40, H42	Glaucoma	109	247	0.96 (0.77–1.20)
H60–H95	Diseases of the ear	1228	2707	0.97 (0.91–1.04)
I00–I99	Diseases of the circulatory system	4432	9477	1.00 (0.97–1.04)
I10–I15	Hypertensive diseases	1936	4210	0.98 (0.93–1.04)
I20–I25	Ischemic heart disease	773	1537	1.09 (1.00–1.18)
I21	Acute myocardial infarction	104	214	1.05 (0.83–1.33)
I60–I69	Cerebrovascular diseases	291	606	1.05 (0.91–1.20)
J00–J99	Diseases of the respiratory system	4699	10,079	0.99 (0.95–1.02)
J30–J39	Diseases of upper respiratory tract	592	1431	0.87 (0.79–0.96)‡
J40–J47	Lower respiratory diseases	580	1130	1.10 (1.00–1.22)
K00–K93	Diseases of the digestive system	3179	6068	1.11 (1.07–1.16)‡
K20–K31	Diseases of oesophagus, stomach and duodenum	1415	2648	1.14 (1.06–1.21)‡
K25–K27	Peptic ulcer	464	857	1.15 (1.02–1.28)‡
K70–K77	Diseases of liver	194	357	1.16 (0.97–1.38)
K70	Alcoholic liver disease	68	117	1.23 (0.91–1.66)
K85–K86	Diseases of pancreas	128	213	1.27 (1.02–1.58)‡
K86.0	Alcohol-induced pancreatitis	25	41	1.27 (0.77–2.09)
L00–L99	Diseases of the skin	1793	3730	1.02 (0.97–1.08)
M00–M99	Diseases of the musculoskeletal system	6296	12,623	1.06 (1.03–1.09)‡
M15–M19	Arthrosis	925	1881	1.06 (0.98–1.14)
M54	Dorsalgia	1475	2817	1.11 (1.04–1.18)‡
N00–N99	Diseases of the genitourinary system	1518	3648	0.89 (0.84–0.95)‡
N20	Calculus of kidney and ureter	140	321	0.93 (0.76–1.14)
N40	Hyperplasia of prostate	418	1032	0.88 (0.79–0.99)‡
R00–R99	Findings, not elsewhere classified	1091	2297	1.01 (0.94–1.09)
V01–Y98	External causes of morbidity	5084	10,055	1.07 (1.03–1.11)‡
V01–V99	Transport accidents	171	423	0.85 (0.71–1.02)
W00–W19	Falls	2010	3817	1.11 (1.06–1.18)‡
W20–W49	Exposure to mechanical forces	1864	3799	1.03 (0.98–1.09)
X31	Excessive cold	26	32	1.74 (1.04–2.92)‡
X40–X49	Accidental poisoning	34	69	1.05 (0.69–1.58)
X60–X84	Intentional self-harm	53	76	1.47 (1.04–2.09)‡
Z00–Z99	Contact with health services	4135	8862	0.99 (0.96–1.03)
Z03	Medical observation for suspected disease	389	788	1.06 (0.94–1.19)
F10, G31.2, I42.6, K70,	Selected alcohol-induced diagnoses and	528	896	1.25 (1.12–1.39)‡

K86.0, X45, X65, Y15	external causes of morbidity

* The first occurrence of the three-digit ICD-10 code in the study period was considered.
† Adjusted for age at diagnosis.
‡ p<0.05

Table 3 Adjusted morbidity rate ratios* (RR) with 95% confidence intervals (CI) by exposure for selected diagnoses and external causes of morbidity in the Estonian cohort of Chernobyl cleanup workers (3506 persons), 2004–2012

ICD-10	Diagnosis/ external cause of morbidity	Year of arrival 1986†	Duration of stay ≥92 days†	Ethnicity Non-Estonian†	Education Basic or less†
D00–D48	In situ and benign neoplasms	1.15 (0.95–1.39)	0.77 (0.64–0.92)‡	1.09 (0.91–1.30)	0.76 (0.61–0.96)‡
E00–E07	Diseases of thyroid gland	0.94 (0.68–1.31)	1.00 (0.73–1.38)	0.85 (0.62–1.17)	0.82 (0.55–1.22)
F00–F99	Mental disorders	1.08 (0.96–1.21)	0.85 (0.76–0.95)‡	0.82 (0.74–0.92)‡	1.11 (0.97–1.27)
F32–F33, F43	Depressive disorders and stress reactions	1.27 (1.00–1.62)	0.72 (0.58–0.90)‡	0.53 (0.41–0.67)‡	0.88 (0.66–1.17)
G00–G99	Diseases of the nervous system	1.01 (0.90–1.13)	0.93 (0.83–1.04)	0.97 (0.87–1.09)	1.20 (1.05–1.37)‡
G43–G44	Migraine and other headache	1.69 (1.10–2.60)‡	0.79 (0.55–1.14)	1.48 (1.03–2.12)‡	0.97 (0.59–1.58)
H25–H26, H28	Cataract	1.07 (0.77–1.49)	1.05 (0.76–1.45)	1.29 (0.93–1.77)	0.93 (0.65–1.33)
H40, H42	Glaucoma	1.26 (0.83–1.89)	0.78 (0.52–1.15)	1.20 (0.81–1.78)	0.80 (0.51–1.27)
I10–I15	Hypertensive diseases	1.03 (0.94–1.14)	0.92 (0.84–1.01)	1.07 (0.98–1.17)	0.99 (0.88–1.11)
I20–I25	Ischemic heart disease	1.15 (0.99–1.34)	0.81 (0.70–0.94)‡	1.12 (0.97–1.30)	1.10 (0.93–1.30)
I21	Acute myocardial infarction	1.11 (0.74–1.68)	0.94 (0.63–1.39)	1.53 (1.03–2.26)‡	1.17 (0.74–1.83)
I60–I69	Cerebrovascular diseases	1.11 (0.86–1.42)	1.03 (0.81–1.42)	1.65 (1.30–2.11)‡	1.61 (1.25–2.08)‡
K70–K77	Diseases of liver	1.13 (0.82–1.54)	1.13 (0.84–1.51)	1.42 (1.07–1.90)‡	1.12 (0.79–1.58)
N20	Calculus of kidney and ureter	1.08 (0.74–1.57)	0.88 (0.62–1.26)	1.99 (1.39–2.85)‡	0.73 (0.45–1.19)
X60–X84	Intentional self-harm	1.27 (0.68–2.36)	0.77 (0.43–1.37)	1.43 (0.82–2.52)	2.73 (1.48–5.05)‡
F10, G31.2, I42.6, K70, K86.0, X45, X65, Y15	Selected alcohol-induced diagnoses and external causes of morbidity	0.92 (0.76–1.11)	0.98 (0.82–1.17)	1.37 (1.15–1.63)‡	1.76 (1.44–2.15)‡

* Models include age at diagnosis, year of arrival, duration of stay, ethnicity, and education.
† The reference categories for these variables are as follows: year of arrival 1987–1991; duration of stay <92 days; ethnicity Estonian; education higher/ secondary.
‡ p<0.05.

Non-cancer morbidity among Estonian Chernobyl cleanup workers: a register-based cohort study

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ABSTRACT

Objective: To examine non-cancer morbidity in the Estonian Chernobyl cleanup workers cohort compared to the population sample with special attention to radiation-related diseases and mental health disorders.

Design: Register-based cohort study.

Setting: Estonia.

Participants: An exposed cohort of 3680 men (cleanup workers) and an unexposed cohort of 7631 men (population sample) were followed 2004–2012 through the Population Registry and Health Insurance Fund database.

Methods: Morbidity in the exposed cohort compared to the unexposed controls was estimated in terms of rate ratio (RR) with 95% confidence intervals (CI) using Poisson regression models.

Results: Elevated morbidity in the exposed cohort was found for diseases of the nervous system, digestive system, musculoskeletal system, ischemic heart disease, and for external causes. The most salient excess risk was observed for thyroid diseases (RR=1.69; 95% CI 1.38–2.07), intentional self-harm (RR=1.47; 95% CI 1.04–2.09), and selected alcohol-related diagnoses (RR=1.25; 95% CI 1.12–1.39). No increase in morbidity for stress reactions, depression, headaches or sleep disorders was detected.

Conclusions: No obvious excess morbidity consistent with biological effects of radiation was seen in the exposed cohort, with the possible exception of benign thyroid diseases. Increased alcohol-induced morbidity may reflect alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported. The future challenge will be to study mental and physical co-morbidities in the Chernobyl cleanup workers cohort.

ARTICLE SUMMARY

Article focus

- There is limited information about the impact of the Chernobyl accident on the non-cancer morbidity among the cleanup workers. Earlier studies of Estonian cleanup workers revealed an excess of suicide.
- This study provides insight into non-cancer morbidity in the cohort of Estonian cleanup workers with emphasis on radiation-related diseases and mental health disorders.

Key messages

- No obvious excess morbidity consistent with biological effects of radiation was found in the cleanup workers cohort, with the possible exception of benign thyroid diseases.
- Increased alcohol-induced morbidity in the cleanup workers cohort may reflect alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported.

Strengths and limitations of this study

- Morbidity information provided in this study was obtained from population-based registries via electronic record linkages using personal identification number as the key variable.
- Limitations of the study are as follows: relatively short follow-up; the probable presence of tentative and preliminary diagnoses in the health insurance database; questionable accuracy and precision of officially documented doses; probable overestimation of findings due to multiple comparisons.

INTRODUCTION

In the aftermath of the accident at the Chernobyl nuclear power station in April, 1986, about 530,000 men from throughout the former Soviet Union were commissioned to the area to clean up the environment.[1] Among them were nearly 5000 (mostly) military reservists from Estonia who worked in the contaminated area for three months on average; their mean received cumulative whole-body radiation dose was 0.1 Gy.[2]

Epidemiological evidence of non-cancer disease risk in the cohorts exposed to ionizing radiation is mainly based on mortality since administratively registered death records are available and easy to use for linkages. Most of these studies have focused on circulatory diseases, the major cause of death in developed countries. Excess mortality from all circulatory diseases, stroke and heart disease was observed in atomic-bomb survivors; however the association below dose of 0.5 Gy was not significant.[3] Follow-up of nuclear industry workers from 15 countries resulted with no significant findings for a dose-dependent rise in mortality from circulatory diseases.[4] Elevated risk of death for the broad categories of the respiratory and digestive systems has been found among atomic-bomb survivors,[5] but not in other environmentally exposed populations [6] or in nuclear industry workers.[4]

A few studies have reported morbidity outcomes. The most informative non-cancer disease incidence study in atomic-bomb survivors found significant radiation effects for thyroid diseases, liver disease, cataract, and calculus of the kidney and ureter.[7] The morbidity study of Mayak nuclear weapons facility workers demonstrated an increasing dose-related trend for cerebrovascular diseases [8] and ischemic heart disease,[9] but did not provide information on risk at doses below 0.2 Gy. A meta-analysis by Little et al. [10] combining morbidity and mortality studies of occupationally and environmentally exposed populations with mean dose below 0.5 Gy, demonstrated significantly increased dose-

dependent risk for ischemic heart disease, cerebrovascular diseases and other circulatory diseases.

Analyses of non-cancer morbidity in a cohort of Russian Chernobyl cleanup workers have shown dose-dependent excess (per 1 Gy) for endocrine and metabolic diseases, mental disorders, diseases of the nervous system, diseases of the digestive system, cerebrovascular diseases, hypertension, and ischemic heart disease.[11, 12] However, risk estimates at low doses still remain uncertain.[13]

Although the psychological aftermath of the Chernobyl accident has been acknowledged as the major long-term public health problem in the exposed populations,[1, 14] the mental health of cleanup workers has only been assessed in small-scale studies in Ukraine.[15–16] There is an urgent need to examine mental health along with somatic diseases when considering the health of cleanup workers.[16]

An updated analysis of mortality and cancer incidence in the Estonian Chernobyl cohort revealed higher incidence of alcohol-related cancers and excess of suicide.[2] Suicide risk has been persistently elevated since the beginning of follow-up.[17, 18] The current research provides the first overview of morbidity other than cancer in the Estonian cohort of Chernobyl cleanup workers with special attention to radiation-related diseases and mental health disorders.

METHODS

Sample and follow-up

The Estonian cohort of Chernobyl cleanup workers (exposed cohort) includes 4831 men recruited in 1986–1991 to the Chernobyl area by the Soviet authorities for decontamination, building and other related activities. The “Chernobyl area” here denotes the 30-km zone (an area of 30-km radius from the nuclear power station) and territories outside, where the workers were engaged with different activities during their mission period. Detailed information on the assembly and description of the cohort is given elsewhere.[19] To examine morbidity in this cohort, we used data from the Estonian Health Insurance Fund (EHIF) database available since January 2004. Thus, for the morbidity analyses we identified all cohort members aged 35–69 years and living in Estonia on January 1, 2004. Altogether, of 4831 men in the initial cohort, 1129 were excluded because of loss in follow-up (21), death (602) and emigration (506). In addition, we did not include men aged under 35 (9) and over 69 years (13) to have more homogeneous age group. This left just 3680 cleanup workers in the study. An unexposed population-based comparison cohort was selected corresponding to the age distribution of the exposed cohort. A random sample stratified by 5-year age groups with the exposed to unexposed ratio of 1:2 and 5% extra men in each age group was extracted from the Estonian Population Registry (EPR). In the unexposed cohort, after excluding 87 men who had worked in the Chernobyl area (cleanup workers), there remained 7631 men.

The cohort of cleanup workers was linked to the EPR to update vital status (emigration or death with corresponding date), ethnicity and education. Each person in both cohorts was followed up from January 1, 2004 until death, emigration or December 31, 2012 (whichever date came first). From the EHIF database, we obtained dates and ICD-10 codes for each contact with a health provider. All linkages were performed using the unique personal identification number (assigned to all permanent residents of Estonia) as the key variable. EHIF manages the mandatory universal health insurance system that is based on solidarity and covers 95% of the Estonian population.[20] All employees and self-employed persons contribute 13% of their wages, some groups of the population are financed by the State (e.g. registered unemployed, Chernobyl veterans), and some groups are insured without contribution (e.g. children, students, pensioners). People without coverage from the above mentioned sources can pay the tax voluntarily.

Health care contacts were identified from the EHIF database for 2004–2012 using the first occurrence of the three-digit ICD-10 code. If the contact involved multiple diagnoses, the first occurrence of each of them was separately counted. All diseases (except cancer, ICD-10 C00–C97), external causes of morbidity, and examinations or counseling were considered. Four-digit codes were taken separately only for some alcohol-induced diseases. A combined category of alcohol-induced diagnoses included mental disorders due to alcohol (F10), degeneration of the nervous system due to alcohol (G31.2), alcoholic cardiomyopathy (I42.6), alcoholic liver disease (K70), alcohol-induced pancreatitis (K86.0), accidental poisoning by alcohol (X45), intentional self-poisoning by alcohol (X65), and poisoning by alcohol, undetermined intent (Y15). The accuracy of the diagnosis was the responsibility of the physician issuing the invoice to EHIF for ambulatory or hospital care.

Morbidity measures and statistical analysis

We estimated morbidity in the cleanup workers cohort by means of rate ratio (RR) with 95% confidence intervals (CI) using the Poisson regression models with the logarithm of the person-years at risk (summed by five-year age groups) as the offset.[21] At first, we performed analysis comparing the exposed cohort with the unexposed cohort (external analysis) to obtain an overview of morbidity rate ratios. Diagnoses were grouped into broad categories with selected specific diagnoses. Analyses were adjusted for age at diagnosis by five-year age groups.

Additionally, analysis was done between different subgroups within the exposed cohort (internal analysis) to assess possible effects of year of arrival in the Chernobyl area (1986; 1987–1991), duration of stay (<92; ≥92 days), and documented cumulative whole-body radiation dose (<5.0; 5.0–9.9; ≥10.0 cGy)~~, education (higher or secondary; basic or less), and ethnicity (Estonian; non-Estonian (mainly Russians))~~ on morbidity risk. As described elsewhere, [1, 22, 23] the cleanup workers were dominantly exposed to γ-radiation released mainly by ^{131}I, ^{134}Cs and ^{137}Cs. Received radiation doses were measured by individual or group dosimeters, or estimated by work area measurements. The readings were documented in the workers' military passports/ records. Considering, that documented doses were unreliable,[19] and not recorded for 15.2% of the cohort members, we used the year of arrival and duration of stay as proxy variables for radiation exposure.

Potential confounders – educational level (higher or secondary; basic or less) and ethnicity (Estonian; non-Estonian (mainly Russians)) – were included in the analysis as surrogates for health behavior. The prevalence of alcohol consumption at least once a week (28.5%) and current smoking (69.0%) among the cleanup workers was studied in a postal questionnaire survey conducted in 1992–1993,[19] but not included in current analyses due to small cohort size and lack of longitudinal data on these factors of health behavior. Thus, the selection of variables (potential confounders) was determined by the availability of them and a review of our previous studies.

Analyses within the exposed cohort focused on disease risks previously reported in atomic-bomb survivors and Chernobyl cleanup workers.[7, 11, 12] The first set of models included the year of arrival in the Chernobyl area, duration of stay, age at diagnosis, education and ethnicity. One hundred and seventy four subjects with missing information for any characteristic were excluded from the analysis. In the second set of models we included documented radiation dose; due to unrecorded values, an additional 452 subjects were excluded.

We used Visual FoxPro 6.0 (Microsoft Corporation, Redmond, WA, USA) for database management, and Stata 12 (StataCorp LP, College Station, TX, USA) for statistical modeling.

RESULTS

Description of the exposed and unexposed cohorts

We followed 3680 exposed and 7631 unexposed men from January 1, 2004 until December 31, 2012 (Table 1). The exposed and unexposed cohorts contributed 30,674 and 65,112 person-years, respectively. Mean age at the start of follow-up was 48 years in both cohorts. During the follow-up, 12.9% of the exposed cohort and 10.5% of the unexposed cohort died. The proportions of non-Estonians (mainly Russians) and less educated persons were higher in the exposed cohort, although educational level was unknown for the 16.4% of the subjects in the unexposed cohort. Two-thirds of the cleanup workers entered the Chernobyl area in 1986; the mean and median durations of the mission were 102 and 92 days, respectively (range: 1–833 days). The cohort was exposed to low-level whole-body radiation with the mean and median documented radiation doses of 9.9 and 8.9 cGy, respectively (range: 0.0–54.5 cGy).

Nearly all men had at least one record in the EHIF database (93.6% of the exposed and 95.3% of the unexposed cohort). On average, members of both cohorts had 12 different diagnoses (three-digit ICD-10 codes). Men in the exposed cohort had their first health services contact on average half a year earlier than their unexposed counterparts (52.1 vs. 52.6 years of age).

(Insert Table 1 here)

Morbidity in the exposed cohort in relation to the unexposed cohort (external analysis)

In the external analysis (Table 2), we observed a very small increase of borderline significance in all-disease risk among Chernobyl cleanup workers (RR=1.01; 95% CI 1.00–1.03). From the non-cancer late effects that might be related to the Chernobyl accident (UNSCEAR 2011), we found significantly elevated morbidity for diseases of thyroid gland (RR=1.69; 95% CI 1.38–2.07) and ischemic heart disease (RR=1.09; 95% CI 1.00–1.18). There was evidence of lower occurrence of cataract in the exposed cohort. Stress reactions, depression, severe headaches and sleep disorders were not diagnosed more frequently in the exposed cohort than in the reference cohort.

Increased morbidity was apparent for the broad categories of diseases of the nervous system, digestive system, musculoskeletal system, and alcohol-induced diagnoses. Morbidity from external causes in the exposed cohort exceeded that in the unexposed cohort (RR=1.07; 95% CI 1.03–1.11). Significantly higher morbidity was registered for falls, intentional self-harm and exposure to excessive cold. Cleanup workers did not undergo medical observations for suspected diseases (ICD-10 Z03) more frequently than unexposed men (RR=1.06; 95% CI 0.94–1.19). Additional adjustments for ethnicity and education (rate ratios not presented) did not materially alter these results.

(Insert Table 2 here)

Differences between subgroups in the exposed cohort (internal analysis)

Internal analysis revealed more depressive disorders and stress reactions (RR=1.27; 95% CI 1.00–1.62), and severe headaches (RR=1.69; 95% CI 1.10–2.60) among cleanup workers who entered the area shortly after the accident than in those arriving later (Table 3). Higher thyroid diseases morbidity was not related to year or month (April-May versus June-December, 1986) of arrival in the contaminated area. Longer mission did not increase the morbidity of any disease. Acute myocardial infarction, cerebrovascular diseases, diseases of liver, calculus of kidney and ureter, headaches, and alcohol-induced morbidity occurred more frequently among non-Estonians, while mental disorders were more frequent among Estonians. Less educated cleanup workers had higher risk for diseases of the nervous system, cerebrovascular diseases, intentional self-harm, and alcohol-induced morbidity, and lower risk for in situ and benign neoplasms.

Including education and ethnicity in the model did not alter markedly the crude point estimates of RR for year of arrival or duration of stay (rate ratios not presented). Higher documented radiation dose (5.0–9.9 or ≥10.0 vs. <5.0 cGy) was not associated with higher morbidity of thyroid diseases (RR=0.92; 95% CI 0.60–1.40; 0.92; 0.60–1.40, respectively), cataract (RR=1.26; 95% CI 0.80–1.98; 1.13; 0.70–1.83, respectively), or any of the other selected diseases.

(Insert Table 3 here)

DISCUSSION

The first non-cancer morbidity analysis of the Estonian cohort of Chernobyl cleanup workers revealed elevated morbidity for diseases of the nervous system, digestive system, musculoskeletal system, ischemic heart disease, and for external causes. The most salient excess risk was observed for thyroid diseases, and as expected, for intentional self-harm and selected alcohol-induced diagnoses.

Limitations

First, this study was limited to morbidity cases in 2004–2012. We had no information about morbidity prior to this time period. Thus, it was not possible to specify incident cases or assess early effects of exposure.

Second, among given diseases there could be tentative and preliminary diagnoses unconfirmed afterwards. We are aware of the possibility of diagnostic errors, upcoding and unbundling of codes associated with the use of a reimbursement-administrative database, originally created not for research purposes, but proved to be an important source for medical studies in Estonia.[24–26] A small number of cases might have been diagnosed by commercial health care providers and not reported to the EHIF. However, because of universal health insurance, these limitations would be expected to affect the exposed and unexposed cohorts in a similar fashion**.** This kind of non-differential misclassification of disease or of disease status probably either does not bias the rate ratio or biases it towards the null. The same may be said in a hypothetical situation when the validity of diagnoses in the EHIF will be almost perfect. In the last case as the most important, the number and heterogeneity of diagnostic entries would be reduced, and the accuracy of measurements improved.

Third, the documented radiation doses are not entirely accurate, and there could be incorrect readings in both directions as discussed elsewhere.[2, 19] Although no correlation was observed between individual doses from military passports (lists) and the biodosimetry estimates for the sub-cohort of cleanup workers, it is estimated that the cohort was exposed to low-dose radiation around 0.1 Gy on average.[22, 27] A similar dose level was reported for Latvian and Lithuanian Chernobyl cleanup workers.[28] Thus, we used year of arrival and duration of stay as proxy variables for radiation exposure. ~~Given these limitations, our conclusions are duly tempered.~~

Fourth, the small size of the cohort has reduced the power of analysis. In addition, because of multiple comparisons, it is possible that some statistically significant findings could be due to chance. Given these limitations, our conclusions are duly tempered.

Possible radiation effects?

Thyroid diseases have been under close surveillance after the Chernobyl accident since radioiodine (mainly ^{131}I with a half-life of eight days) released during the explosion is concentrated in the thyroid gland. Ron and Brenner [29] summarized the evidence of benign thyroid diseases after radiation exposure. They concluded that associations have been weak and elevated risk occurred mainly in subjects with high doses, exposed at young ages, and in women. Keeping in mind that the cohort of cleanup workers includes only adult men who were exposed to low doses, we cannot attribute the thyroid findings to radiation. This interpretation is supported by the lack of excess among the early entrants or subjects with the highest documented radiation doses. At the same time, we cannot exclude the possibility that a higher rate ratio among the cleanup workers is caused by close medical attention sought by them. During thyroid screening among the Estonian cleanup workers in 1995, no clear correlation was found between the prevalence of thyroid nodules and the year of arrival or recorded radiation dose.[30] ~~Moreover, these whole-body external doses have little relevance to thyroid diseases because they are not thyroid doses.~~

High radiation doses increase the risk of circulatory diseases, but less is known about the effect of low or moderate doses (<0.5 Gy). Difficulty in estimating dose-response at low dose levels is due to paucity of large cohorts with high-quality data on doses and confounders.[10, 31] As the Estonian cohort of cleanup workers is small and with low average radiation dose, we cannot attribute the small increase in ischemic heart disease morbidity seen in the cohort to biological effects of radiation exposure. This conclusion is also supported by the mortality analyses, where no excess deaths from circulatory diseases were found.[2]

An increased risk of cataract, observed in atomic-bomb survivors [7] and Ukrainian cleanup workers,[32] did not emerge in the Estonian cohort. An observed statistically significant deficit of cataract cases may be an occasional finding without any epidemiological relevance. Although cataract has been conventionally regarded as a late deterministic effect of radiation with a threshold dose of 0.5 Gy, recent studies have suggested a need to lower this dose limit and reconsider the threshold model.[31, 33] Nevertheless, it is unlikely that radiation-related cataracts will be detectable among the Estonian cleanup workers in the future, given the low dose level.

Mental and neurological disorders

Natural or man-made disasters can inflict psychological consequences to the affected populations. Radiation events evoke images of the bombings of Hiroshima and Nagasaki, and mental health effects such as post-traumatic stress, depression, anxiety, and somatization can be long-lasting.[34] After the Chernobyl accident, the mental health of the local population and cleanup workers was considered to be the main public health concern.[1, 14] Cleanup workers were exposed not only to radiation, but also to the lack of protective gear and to the poor living conditions, sometimes doing meaningless jobs, and drinking large amounts of alcohol (mainly home-distilled).[19, 35] Misleading or no information about the possible long-term health effects generated rumors and misapprehensions, and radiation fears were exaggerated.[36, 37] The situation bred profound mistrust of all authorities. One of the most difficult lessons from Chernobyl has been to gain the public's trust and to deliver scientific information about the radiation risks, as there exists an insuperable gap between the experts' and public's perceptions about radiation.[38–40]

To date, the persistently elevated suicide risk in the Estonian cohort has been the definitive indication of psychological impairment as a result of working as a Chernobyl cleanup worker.[2] However, the current morbidity analyses showed a mixed pattern of mental and neurological disorders. Based on the results from a study of Ukrainian cleanup workers,[15] we expected higher rates of depression, anxiety, post-traumatic stress disorder, and headaches. Yet, there was no overall increase of mental disorders as a group (RR=1.00), or of physician-diagnosed depression or anxiety. During the follow-up period, the cleanup workers used health care services significantly less frequently for stress reactions than the unexposed cohort. No excess of severe headaches or sleep disorders was found among cleanup workers. However, depression and stress reactions, and severe headaches were more frequent in the early entrants. Elevated morbidity due to intentional self-harm is also an indicator of psychological distress. This finding is consistent with the increased suicide rate in the cohort,[2] which is strongly related to alcohol dependence among middle-aged men in Estonia.[41]

Smoking and heavy alcohol consumption are more prevalent in less educated men in Estonia.[42, 43] Although population-based health (behavior) prevalence studies do not report differences in smoking and drinking habits between Estonians and non-Estonians,[42, 43] mortality is higher in non-Estonians,[44] particularly alcohol-related mortality.[45]

Excess morbidity emerged for alcohol-induced diseases – mental disorders due to alcohol and degeneration of nervous system due to alcohol. Morbidity from alcohol-induced diagnoses as a group was 25% higher among cleanup workers than in the unexposed cohort. Considering common alcohol abuse among men in Estonia (especially with lower educational level),[43] it is not surprising that cleanup workers used alcohol to cope with stressful situation, and still do. Higher morbidity due to excessive cold is most likely attributable to homelessness and suggests that periods of homelessness were more common in cleanup workers than in men in the comparison cohort. Results of our study demonstrate that the men with Estonian ethnicity and/ or higher educational level coped better with Chernobyl consequences including alcohol abuse.

Although Ukrainian cleanup workers had more mental disorders than controls, no excess of alcoholism was observed.[15] This illustrates how analysis of similar cohorts with different design and risk measures can produce entirely opposite results. Very likely, mental disorders other than alcoholism were under-diagnosed in the Estonian cohort, and the prevalence of alcohol problems was underestimated in the Ukrainian cohort. It is common that people do not seek professional help for mental health problems.[34] Untreated mental disorders can manifest as unexplained physical complaints such as headache or back pain, or they are risk factors for somatic diseases (e.g. thyroid diseases or diseases of the digestive system).[46, 47] Thus, it is important to pay attention to both mental and somatic diseases of Chernobyl cleanup workers simultaneously.

CONCLUSIONS

No obvious excess morbidity consistent with biological effects of radiation was seen in the exposed cohort, with the possible exception of benign thyroid diseases. Increased alcohol-induced morbidity reflects alcohol abuse, and could underlie some of the higher morbidity rates. Mental disorders in the exposed cohort were probably underreported. The future challenge will be to study mental and physical co-morbidities in the Chernobyl cleanup workers cohort.

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Competing interests None.

Ethics approval The study was approved by the Tallinn Medical Ethics Committee (no. 1939, February 11, 2010), and by the Estonian Data Protection Inspectorate (no. 2.2-3/10/120r, April 9, 2010).

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Table 1 Characteristics of the Estonian cohort of Chernobyl cleanup workers (exposed cohort) and the unexposed comparison cohort

Characteristic	Exposed cohort		Unexposed cohort	
	No.	(%)	No.	(%)
Total	3680	(100)	7631	(100)
Vital status on December 31, 2012				
Living in Estonia	3132	(85.1)	6795	(89.0)
Dead	474	(12.9)	798	(10.5)
Emigrated	74	(2.0)	38	(0.5)
Age at start of follow-up (full years)				
35–44	1265	(34.4)	2645	(34.7)
45–54	1850	(50.3)	3738	(49.0)
55–64	536	(14.6)	1186	(15.5)
≥65	29	(0.8)	62	(0.8)
Person-years in an age group (2004–2012)				
35–44	4718.4	(15.4)	9416.1	(14.5)
45–54	15,513.5	(50.6)	32,825.3	(50.4)
55–64	9303.9	(30.3)	20,126.9	(30.9)
≥65	1138.6	(3.7)	2743.5	(4.2)
Total	30,674.4	(100)	65,111.8	(100)
Ethnicity				
Estonian	2036	(55.3)	4690	(61.5)
Non-Estonian	1643	(44.6)	2848	(37.3)
Unknown	1	(0.0)	93	(1.2)
Education				
Higher	322	(8.8)	1159	(15.2)
Secondary	2446	(66.5)	4017	(52.6)
Basic or less	824	(22.4)	1200	(15.7)
Unknown	88	(2.4)	1255	(16.4)
Time of arrival in the Chernobyl area				
1986, April–May	1154	(31.4)		
1986, June–December	1128	(30.7)		
1986, month unknown	13	(0.4)		
1987	820	(22.3)		
1988	417	(11.3)		
1989–1991	67	(1.8)		
Unknown	81	(2.2)		
Duration of stay in the Chernobyl area (days)				
<30	220	(6.0)		
30–89	1487	(40.4)		
90–149	1163	(31.6)		
150–209	648	(17.6)		
≥210	60	(1.6)		
Unknown	102	(2.8)		
Documented dose (cGy)				
<5.0	810	(22.0)		
5.0–9.9	1022	(27.8)		
10.0–14.9	555	(15.1)		
15.0–19.9	519	(14.1)		
20.0–24.9	195	(5.3)		
≥25.0	21	(0.6)		
Unknown	558	(15.2)		

Table 2 Number of morbidity cases* and age-adjusted morbidity rate ratios† (RR) with 95% confidence intervals (CI) in the Estonian cohort of Chernobyl cleanup workers (exposed cohort) in relation to the unexposed comparison cohort, 2004–2012

ICD-10	Diagnosis/ external cause of morbidity	No. of cases		RR (95% CI)
		Exposed cohort	Unexposed cohort	
A00–R99, V01–Z99	All diagnoses and external causes	41,370	86,441	1.02 (1.01–1.03‡
A00–R99, except C00–C97	All diseases, except cancer	31,757	66,799	1.01 (1.00–1.03)
A00–B99	Infectious diseases	1338	3022	0.94 (0.88–1.00)
A15–A16	Respiratory tuberculosis	41	73	1.19 (0.81–1.74)
D00–D48	In situ and benign neoplasms	517	1060	1.04 (0.94–1.16)
D50–D89	Diseases of the blood and blood-forming organs	97	195	1.07 (0.84–1.36)
E00–E90	Endocrine, nutritional and metabolic diseases	806	1754	0.98 (0.90–1.07)
E00–E07	Diseases of thyroid gland	167	211	1.69 (1.38–2.07)‡
F00–F99	Mental disorders	1380	2918	1.00 (0.94–1.07)
F10	Mental disorders due to alcohol	328	570	1.21 (1.06–1.39)‡
F32–F33	Depressive disorders	290	633	0.97 (0.84–1.11)
F41	Anxiety disorders	119	275	0.91 (0.74–1.13)
F43	Stress reactions	55	162	0.72 (0.53–0.97)‡
G00–G99	Diseases of the nervous system	1352	2550	1.13 (1.06–1.21)‡
G31.2	Degeneration of nervous system due to alcohol	48	68	1.51 (1.04–2.18)‡
G40	Epilepsy	148	223	1.40 (1.14–1.73)‡
G43–G44	Migraine and other headache	125	256	1.03 (0.83–1.28)
G50–G59	Nerve, nerve root and plexus disorders	447	829	1.15 (1.02–1.29)‡
F51, G47	Sleep disorders	267	529	1.08 (0.93–1.25)
H00–H59	Diseases of the eye	2004	4592	0.93 (0.89–0.98)‡
H25–H26, H28	Cataract	155	449	0.77 (0.64–0.92)‡
H40, H42	Glaucoma	109	247	0.96 (0.77–1.20)
H60–H95	Diseases of the ear	1228	2707	0.97 (0.91–1.04)
I00–I99	Diseases of the circulatory system	4432	9477	1.00 (0.97–1.04)
I10–I15	Hypertensive diseases	1936	4210	0.98 (0.93–1.04)
I20–I25	Ischemic heart disease	773	1537	1.09 (1.00–1.18)
I21	Acute myocardial infarction	104	214	1.05 (0.83–1.33)
I60–I69	Cerebrovascular diseases	291	606	1.05 (0.91–1.20)
J00–J99	Diseases of the respiratory system	4699	10,079	0.99 (0.95–1.02)
J30–J39	Diseases of upper respiratory tract	592	1431	0.87 (0.79–0.96)‡
J40–J47	Lower respiratory diseases	580	1130	1.10 (1.00–1.22)
K00–K93	Diseases of the digestive system	3179	6068	1.11 (1.07–1.16)‡
K20–K31	Diseases of oesophagus, stomach and duodenum	1415	2648	1.14 (1.06–1.21)‡
K25–K27	Peptic ulcer	464	857	1.15 (1.02–1.28)‡
K70–K77	Diseases of liver	194	357	1.16 (0.97–1.38)
K70	Alcoholic liver disease	68	117	1.23 (0.91–1.66)
K85–K86	Diseases of pancreas	128	213	1.27 (1.02–1.58)‡
K86.0	Alcohol-induced pancreatitis	25	41	1.27 (0.77–2.09)
L00–L99	Diseases of the skin	1793	3730	1.02 (0.97–1.08)
M00–M99	Diseases of the musculoskeletal system	6296	12,623	1.06 (1.03–1.09)‡
M15–M19	Arthrosis	925	1881	1.06 (0.98–1.14)
M54	Dorsalgia	1475	2817	1.11 (1.04–1.18)‡
N00–N99	Diseases of the genitourinary system	1518	3648	0.89 (0.84–0.95)‡
N20	Calculus of kidney and ureter	140	321	0.93 (0.76–1.14)
N40	Hyperplasia of prostate	418	1032	0.88 (0.79–0.99)‡
R00–R99	Findings, not elsewhere classified	1091	2297	1.01 (0.94–1.09)
V01–Y98	External causes of morbidity	5084	10,055	1.07 (1.03–1.11)‡
V01–V99	Transport accidents	171	423	0.85 (0.71–1.02)
W00–W19	Falls	2010	3817	1.11 (1.06–1.18)‡
W20–W49	Exposure to mechanical forces	1864	3799	1.03 (0.98–1.09)
X31	Excessive cold	26	32	1.74 (1.04–2.92)‡
X40–X49	Accidental poisoning	34	69	1.05 (0.69–1.58)
X60–X84	Intentional self-harm	53	76	1.47 (1.04–2.09)‡
Z00–Z99	Contact with health services	4135	8862	0.99 (0.96–1.03)
Z03	Medical observation for suspected disease	389	788	1.06 (0.94–1.19)
F10, G31.2, I42.6, K70,	Selected alcohol-induced diagnoses and	528	896	1.25 (1.12–1.39)‡

K86.0, X45, X65, Y15	external causes of morbidity

* The first occurrence of the three-digit ICD-10 code in the study period was considered.
† Adjusted for age at diagnosis.
‡ $p<0.05$

Table 3 Adjusted morbidity rate ratios* (RR) with 95% confidence intervals (CI) by exposure for selected diagnoses and external causes of morbidity in the Estonian cohort of Chernobyl cleanup workers (3506 persons), 2004–2012

ICD-10	Diagnosis/ external cause of morbidity	Year of arrival 1986†	Duration of stay ≥92 days†	Ethnicity Non-Estonian†	Education Basic or less†
D00–D48	In situ and benign neoplasms	1.15 (0.95–1.39)	0.77 (0.64–0.92)‡	1.09 (0.91–1.30)	0.76 (0.61–0.96)‡
E00–E07	Diseases of thyroid gland	0.94 (0.68–1.31)	1.00 (0.73–1.38)	0.85 (0.62–1.17)	0.82 (0.55–1.22)
F00–F99	Mental disorders	1.08 (0.96–1.21)	0.85 (0.76–0.95)‡	0.82 (0.74–0.92)‡	1.11 (0.97–1.27)
F32–F33, F43	Depressive disorders and stress reactions	1.27 (1.00–1.62)	0.72 (0.58–0.90)‡	0.53 (0.41–0.67)‡	0.88 (0.66–1.17)
G00–G99	Diseases of the nervous system	1.01 (0.90–1.13)	0.93 (0.83–1.04)	0.97 (0.87–1.09)	1.20 (1.05–1.37)‡
G43–G44	Migraine and other headache	1.69 (1.10–2.60)‡	0.79 (0.55–1.14)	1.48 (1.03–2.12)‡	0.97 (0.59–1.58)
H25–H26, H28	Cataract	1.07 (0.77–1.49)	1.05 (0.76–1.45)	1.29 (0.93–1.77)	0.93 (0.65–1.33)
H40, H42	Glaucoma	1.26 (0.83–1.89)	0.78 (0.52–1.15)	1.20 (0.81–1.78)	0.80 (0.51–1.27)
I10–I15	Hypertensive diseases	1.03 (0.94–1.14)	0.92 (0.84–1.01)	1.07 (0.98–1.17)	0.99 (0.88–1.11)
I20–I25	Ischemic heart disease	1.15 (0.99–1.34)	0.81 (0.70–0.94)‡	1.12 (0.97–1.30)	1.10 (0.93–1.30)
I21	Acute myocardial infarction	1.11 (0.74–1.68)	0.94 (0.63–1.39)	1.53 (1.03–2.26)‡	1.17 (0.74–1.83)
I60–I69	Cerebrovascular diseases	1.11 (0.86–1.42)	1.03 (0.81–1.42)	1.65 (1.30–2.11)‡	1.61 (1.25–2.08)‡
K70–K77	Diseases of liver	1.13 (0.82–1.54)	1.13 (0.84–1.51)	1.42 (1.07–1.90)‡	1.12 (0.79–1.58)
N20	Calculus of kidney and ureter	1.08 (0.74–1.57)	0.88 (0.62–1.26)	1.99 (1.39–2.85)‡	0.73 (0.45–1.19)
X60–X84	Intentional self-harm	1.27 (0.68–2.36)	0.77 (0.43–1.37)	1.43 (0.82–2.52)	2.73 (1.48–5.05)‡
F10, G31.2, I42.6, K70, K86.0, X45, X65, Y15	Selected alcohol-induced diagnoses and external causes of morbidity	0.92 (0.76–1.11)	0.98 (0.82–1.17)	1.37 (1.15–1.63)‡	1.76 (1.44–2.15)‡

* Models include age at diagnosis, year of arrival, duration of stay, ethnicity, and education.
† The reference categories for these variables are as follows: year of arrival 1987–1991; duration of stay <92 days; ethnicity Estonian; education higher/ secondary.
‡ p<0.05.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	7-8
		(*d*) If applicable, explain how loss to follow-up was addressed	no losses (Table 1)
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8, Table 1
		(b) Give reasons for non-participation at each stage	5-6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	8, Table 1
		(c) Summarise follow-up time (eg, average and total amount)	8, Table 1
Outcome data	15*	Report numbers of outcome events or summary measures over time	8, Table 2
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-10, Table 2-3
		(*b*) Report category boundaries when continuous variables were categorized	8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-10, Table 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations			10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			14-15
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.