Radiat Environ Biophys (1997) 36: 9–16

ORIGINAL PAPER

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Leukaemia and thyroid cancer in emergency workers of the Chernobyl accident:

Estimation of radiation risks (1986–1995)

Received: 10 July 1996 / Accepted in revised form: 17 December 1996

Abstract This work focuses on the direct epidemiological assessment of the risks of radiation-induced leukaemia and thyroid cancer in emergency workers (EW) after the Chernobyl accident. The Russian National Medical Dosimetric Registry (RNMDR) contains data for 168 000 EW as of January 1, 1996. The analysis relates to 48 leukaemias and 47 thyroid cancers, diagnosed and verified. Radiation risks are estimated by comparing the EW data with national data for a male population of the same age distribution. For leukaemia, an excess relative risk per Gy (ERR/Gy) of 4.30 (95% CI: 0.83, 7.75) is obtained, while the excess absolute risk per 10^4 person-years (PY) Gy (EAR/10^4 PY Gy) is found to be 1.31 (95% CI: 0.23, 2.39); for thyroid cancer an ERR/Gy of 5.31 (95% CI: 0.04, 10.58) is obtained, and an EAR/10^4 PY Gy of 1.15 (95% CI: 0.08, 2.22).

Introduction

Few, if any, estimates of radiation risk for low doses of ionizing radiation (0.2–0.3 Gy) exist that are based on direct epidemiological studies. The prediction of the radiation induction of malignant tumours in this range of low doses is normally based on the extrapolation of observed risk coefficients from relatively high doses (>1 Gy) to low doses. It is, therefore, of particular interest to determine risk coefficients directly at low doses and to provide, thus, for this range of doses an additional test of the presently recommended risk coefficients and prediction models.

In this sense, the data accumulated since the Chernobyl accident are of singular value. Indeed, during the first 10 years of follow-up, large volumes of epidemiological data have been collected, characterizing the health status of hundreds of thousands of persons who received low doses. At the same time, there are few studies concerned with the estimation of the radiation risks due to Chernobyl, and, in fact, the question arises as to whether it is feasible to assess radiation risks in direct epidemiological studies of the effects of the Chernobyl accident.

In our earlier work we derived estimates of the excess relative risk (ERR) for incidence and mortality of malignant tumours in emergency workers, and for thyroid cancer incidence in children of the contaminated territory of the Bryansk region [1, 2]. The risk coefficients thus obtained were in good agreement with currently recommended values.

The increase of leukaemia and thyroid cancer incidence rates is one of the first manifestations of late radiation effects. Among radiation-induced malignant tumours, leukaemia and thyroid cancer have the shortest latency periods (about 2–3 years for leukaemia, and 4–5 years for thyroid cancer [3, 4]). The time since the accident exceeds these latency periods.

This study deals with the epidemiological analysis of thyroid cancer and leukaemia incidence among emergency workers. Estimates of radiation risks based on observations up to the end of 1993 are presented first, and they are then compared with current prediction models. The cohort of emergency workers has been described in several of our earlier studies [5–7]. It is, therefore, sufficient to dwell briefly on the cohort followed in the framework of the Russian National Medical Dosimetric Registry (RNMDR).

Materials and methods

As of January 1, 1996, the RNMDR database comprised medical and dosimetric information on 168 000 emergency workers. Among these, 77 700 persons were involved in remediation work in 1986, 58 700 in 1987, and 31 600 within the period 1988–1990. More than 200 000 emergency workers from Russia participated in remediation activities inside the 30-km zone of the Chernobyl nuclear power

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Table 1 Dose distribution for emergency workers (EW) by years of arrival in zone

Year of arrival	Number of persons	Dose (mGy)					
		0–49	50–99	100–149	150–199	200–249	>250
1986	46 575	18.2%	10.2%	10.1%	20.7%	36.3%	4.5%
1987	48 077	24.0%	51.9%	9.7%	8.1%	5.8%	0.6%
1988–1990	24 764	87.3%	9.7%	1.3%	0.7%	0.6%	0.4%
1986–1990	119 416	34.5%	25.9%	8.1%	11.8%	17.5%	2.2%

Table 2 Age distribution for EW with an established external dose by years of arrival in zone

Year of arrival	Age to 1st January 1996 (years)								
	<30	30–34	35–39	40–44	45–49	50–54	55–59	60–64	> 65
1986	4.7%	13.8%	17.9%	22.0%	26.9%	8.6%	4.8%	0.9%	0.4%
1987	1.8%	7.9%	19.5%	36.6%	27.6%	4.9%	1.2%	0.3%	0.1%
1988–1990	1.6%	2.8%	29.1%	42.2%	20.7%	2.6%	0.7%	0.2%	0.1%
1986–1990	2.9%	9.3%	20.8%	31.7%	25.9%	5.9%	2.6%	0.5%	0.3%

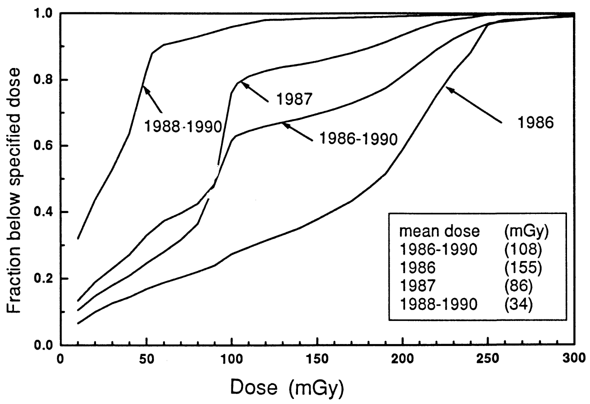

Fig. 1 Fraction of emergency workers up to specified assigned dose. The distributions are given for emergency workers employed in different periods

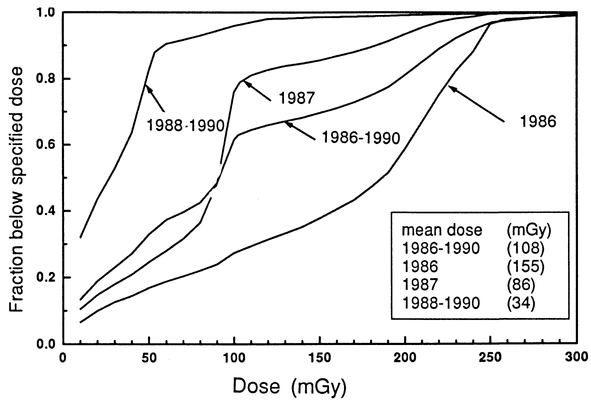

Fig. 2 Fraction of emergency workers up to specified age at the time of their entry into the 30 km-zone

plant between 1986 and 1990. Thus, 10 years after the disaster previously unaccounted emergency workers continue to be entered in RNMDR. At present, the RNMDR follows a strict procedure, in line with the Decree of the Russian Government: on the national level the registry is maintained at the Medical Radiological Research Centre in Obninsk, while 20 regional centres of the registry are responsible for the collection of data from the annual check-ups all around Russia and for providing these data to the national level.

With regard to dosimetric information on the cohort of the emergency workers, the registry includes only the officially assigned doses of external irradiation. The accuracy of these official values for emergency workers remains a complicated issue. The uncertainty of the individual doses can be substantial.

Of 168 000 emergency workers registered in the RNMDR up to now, 119 000 (71%) have been assigned individual doses of external exposure. As can be seen in Table 1, the highest radiation exposures for emergency workers occurred in 1986: 4.5% of the 46 575 persons have been officially assigned to doses in excess of 250 mGy. Figure 1 gives the same information in terms of the fraction of workers up to specified doses.

For the prediction of late stochastic radiation effects, it is necessary to account for the age distribution of the exposed (Table 2). The mean age of the emergency workers during their period of duty in the 30-km zone was 33.4 years, which means that their mean life expectancy after exposure exceeds 25 years. By January 1, 1996, most of the emergency workers were between 35 and 45 years of age. Figure 2 shows the fraction of emergency workers below specified ages at the time of their entry into the 30-km zone.

The primary aim of this study is the determination of the risk of radiation-induced leukaemia and thyroid cancer in the cohort of emergency workers. Standard methods of epidemiology are employed. The resulting risk coefficients are compared with the currently recommended values.

Results

Leukaemia incidence

The present analysis refers to 48 cases of leukaemia in emergency workers verified by the Medical Radiological

Table 3 Distribution of leukaemia cases among EW by date of entry into the Chernobyl zone

Date of entry (year)	Number of cases
1986	25 (52.1%)
1987	16 (33.3%)
1988	5 (10.4%)
1989	1 (2.1%)
1990	1 (2.1%)
Total	48 (100%)

Table 4 Distribution of leukaemia cases among EW by duration of stay in the Chernobyl zone

Duration of stay (months)	Number of cases
< 1	9 (18.8%)
1 – < 2	12 (25.0%)
2 – < 3	12 (25.0%)
3 – < 6	10 (20.8%)
6 – < 12	2 (4.2%)
12+	3 (6.2%)
Total	48 (100%)

Table 5 Distribution of leukaemia cases among EW by external irradiation dose

Dose (mGy)	Number of cases
< 50	12 (25.0%)
50–99	8 (16.7%)
100–149	6 (12.5%)
150–199	3 (6.2%)
200–249	7 (14.6%)
250+	1 (2.1%)
No data	11 (22.9%)
Total	48 (100%)

Table 6 Distribution of leukaemia cases among EW by date of diagnosis

Date of diagnosis (year)	Number of cases
1986	1
1987	5
1988	5
1989	3
1990	6
1991	11
1992	9
1993	8
Total	48

Table 7 Standardized incidence ratio (SIR) of leukaemia among EW

Observation period (years)	Observed number of cases	Expected number of cases	SIR	95% confidence interval
1986–1989	14	12.3	113	62 190
1990–1993	34	19.2	177	122 247

Scientific Center of the Russian Academy of Medical Sciences (RAMS) and local health care establishments, as of January 1, 1994. The verification of leukaemia is a complicated and lengthy procedure, and therefore, this study contains the analysis of incidence beginning in 1986, but extending only to the end of 1993. By January 1, 1994, the RNMDR database contained medical and dosimetric information for 142 000 emergency workers, among which the 48 leukaemias were reported in the period specified.

The medical documents, as the main information base of RNMDR, are completed for each emergency worker once a year. All reported diseases are classified by ICD 9 and are listed in these documents. For cases of cancer, the following additional information is given: time of diagnosis, histological verification, TNM classification, therapy outcome, etc. Only after a thorough examination of this information the oncological diagnosis is registered in the RNMDR database.

Tables 3–6 show the distribution of the identified leukaemias according to several characteristics. The analysis accounts for all leukaemia types (ICD-9, 204.0–208.9). Chronic lymphocytic leukaemia is not commonly considered a disease inducible by radiation. Nevertheless, all leukaemia types are included in the present study, their number in 1986–1993 being too small to warrant a subdivision into different types. The *anticipated* number of leukaemias of all types, i.e. the expected spontaneous number plus the cases that would be inferred from the dosimetric information and current risk estimates, was calculated by a multiplicative model with coefficients derived from the Japanese cohort of atomic bomb survivors [8]. The term *anticipated* is used here to avoid confusion with *expected*, which in most epidemiological studies refers to the spontaneous cases, i.e. the baseline incidence only.

Table 3 shows that 41 leukaemias (85.4% of the total number of cases) were observed in emergency workers from 1986 to 1987. The RNMDR database contains 116 000 emergency workers from 1986 and 1987, which amounts to 81.7% of the entire database of 142 000 emergency workers. Accordingly, an internal analysis based on the data of Table 3 does not permit unequivocal conclusions about risk factors. The incidence in the exposed cohort is, therefore, compared with the leukaemia incidence for the male population of Russia, standardized to the age distribution (see Fig. 2) of emergency workers. This provided the expected number of spontaneous cases. In the study we use the indicator standardized incidence ratio (SIR), the ratio of observed cases and expected spontaneous cases, as commonly employed in epidemiological studies.

Figure 3 compares the distributions of the emergency workers according to assigned specified dose with the corresponding distributions of the leukaemia cases. One would expect somewhat higher doses for the cases, but such a difference is suggested only for the workers of 1986.

Table 7 summarizes the SIR values for leukaemia in emergency workers for two time intervals: 1986–1989 and 1990–1993. In both cases the SIR is more than 100%, which means that the incidence among emergency work-

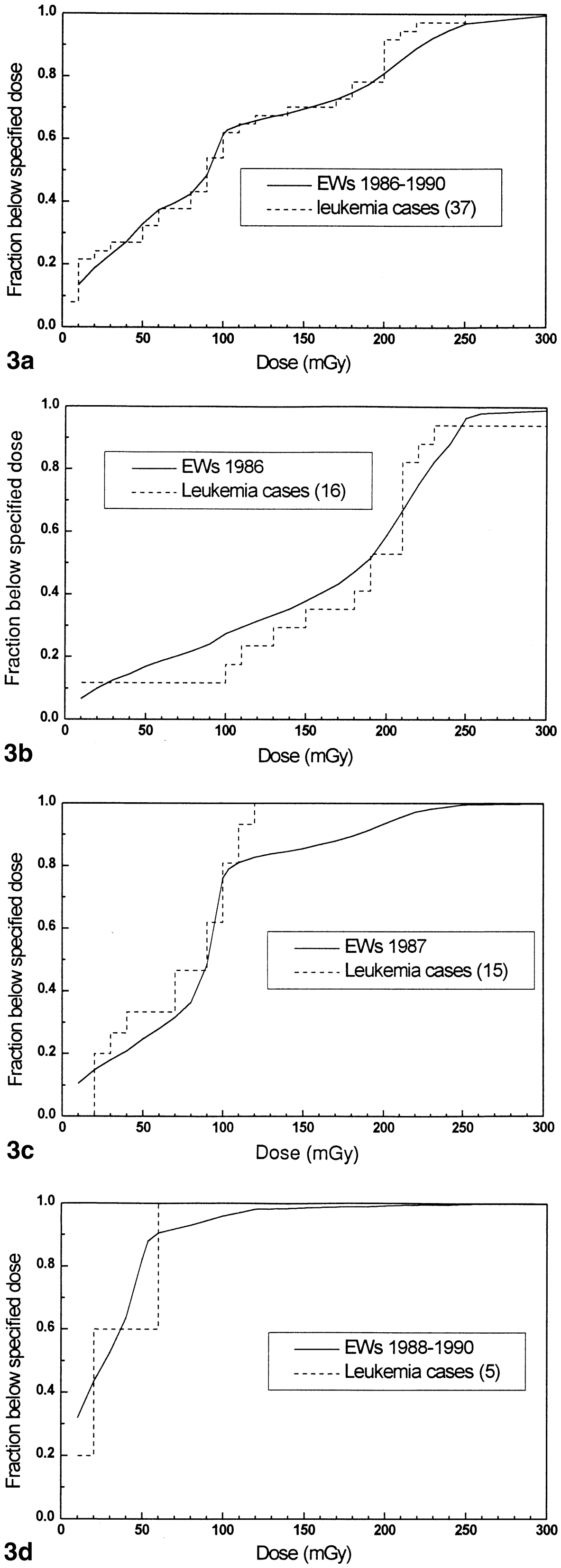

Fig. 3a–d Fraction of emergency workers (*solid line*) and fraction of leukaemia cases (*hatched line*) with assigned doses up to specified values for period of diagnosis 1986–1993. Date of entry into 30 km-zone: **a** 1986–1990; **b** 1986; **c** 1987; **d** 1988–1990

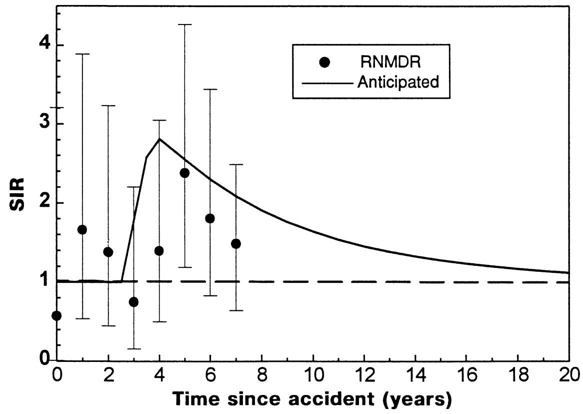

Fig. 4 Anticipated (*solid line*) and observed (*dots*) SIR of leukaemia in emergency workers cohort. *Bars* give the 95% confidence intervals

ers is higher than the mentioned average. However, at the 95% confidence level, the difference is statistically significant only for the cases diagnosed in the period 1990–1993. The absence of a significant increase of leukaemia cases in the years 1986–1989 is in line with the latency period of 2–3 years for the induction of radiogenic leukaemia assumed in the risk models.

In the calculations of the number of anticipated cancer incidences, we used the time and dose dependence from the model derived for leukaemia (all types) in the Japanese cohort of atomic bomb survivors [8], taking into account the age and dose distribution of the cohort of emergency workers and the age-specific spontaneous leukaemia incidence rates for the Russian Federation.

Figure 4 shows data of the Chernobyl Registry on leukaemia incidence in emergency workers and the corresponding anticipated rates. There are several major conclusions. First, within the limits of the statistical errors, the prediction and the observed data are in good agreement. Secondly, in line with the prediction, it appears from the registry data that the peak of radiogenic leukaemia occurred 4–5 years after the accident, the attributable risk (AR) being 45%-60% (AR = 1–1/SIR). This suggests that one of every two leukaemias diagnosed in emergency workers today could be radiation-induced. Although the proportion of radiogenic leukaemias in emergency workers is expected to decrease steadily with time, the continuation of studies in this area is one of the priority tasks of RNMDR.

The four panels of Fig. 5 give additional information on the distribution of the leukaemias according to age at diagnosis and on the number of person-years at risk. Cumulative observed numbers of cases are plotted together with the 95% confidence limits according to Poisson statistics. These curves are compared to the cumulative numbers of the expected cases according to the age-specific leukaemia rates in the entire male Russian population. In each of the three cohorts of emergency workers, the observed numbers exceed – in accordance with the statements made above –

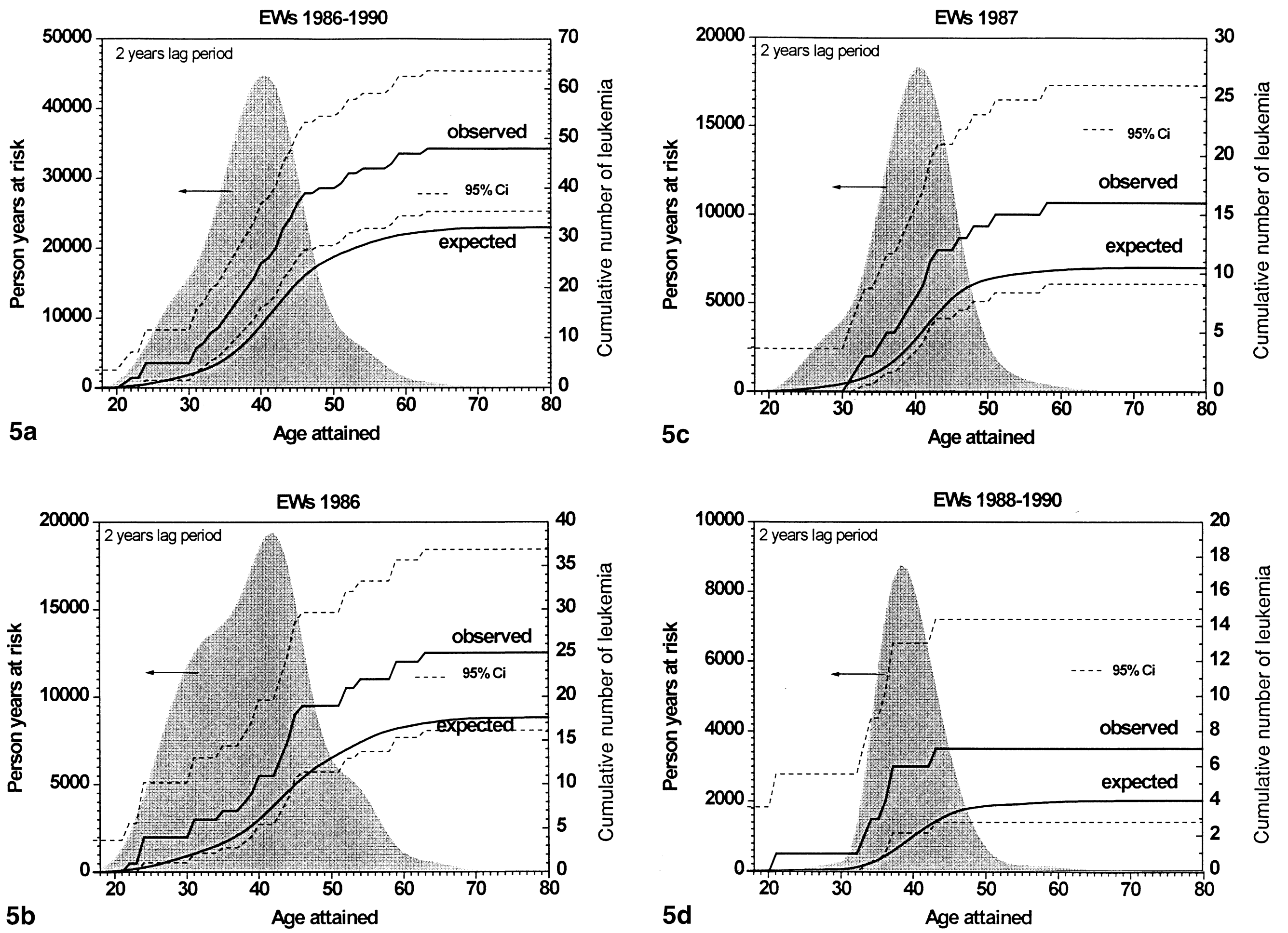

Fig. 5a–d Cumulative expected and observed leukaemia cases up to specified attained age at diagnosis and the number of person-years (*shaded area*) at risk at the specified attained age. Date of entry into 30 km-zone: **a** 1986–1990; **b** 1986; **c** 1987; **d** 1988–1990

the expected numbers. However, the difference is significant only when the cohorts are combined.

Thyroid cancer incidence

By January 1, 1995, the RNMDR included 47 thyroid cancers in emergency workers. These were diagnosed at different times since exposure, ranging from 1 to 8 years.The histological tumour types were: follicular cancer (42.8%), papillary cancer (33.3%) and some types of carcinoma (14.3%). Table 8 presents the main epidemiological data. Overall, 28 thyroid cancers were detected in 1986, 15 in 1987, and 4 in 1988–1990. The table also gives SIR for the observation period of 1986–1990, which corresponds to the assumed latency period for thyroid cancer, and for the post-latency period of 1991–1994. During 1986–1990 the SIRs do not differ significantly from 100% for all groups of emergency workers of 1986, 1987 and 1988–1990. In the post-latency period, however, the SIR exceeds by far the value 100% (except for the 1988–1990 emergency workers), which reflects increased incidence, as compared with the control values. The control group was taken to be the male population of Russia, standardized according to age. As can be seen from Table 8, the emergency workers of 1986 (SIR = 670%) and 1987 (SIR = 590%) are the groups with enhanced risks. Among the 1986 emergency workers, the highest risk is observed in those who worked in the 30-km zone in April-July.

To examine the hypothesis of the influence of an additional, internal exposure of the emergency workers of April to May 1986 due to radioiodine, we determined the cumulated SIRs by months (Fig. 6). It is seen that the risk of thyroid cancer is highest for the emergency workers involved in the recovery operations in June 1986. The risks for those working in April-May and July appear to be almost the same. Therefore, at this point, no definitive conclusion can be drawn about the potential role of radioiodine. On the other hand, although the external radiation doses in April to December 1986 were approximately the same (see Table 8), the risk of thyroid cancer decreases towards the end of 1986.

As a next step, the observed numbers of thyroid cancers are compared with the numbers anticipated on the basis of the assigned external doses. Figure 7 shows the observed incidence rates for emergency workers and the anticipated

Table 8 Main medico-dosimetric characteristics of EW used in thyroid cancer incidence

Date of entry	1986					1986	1987	1986–1987	1988–1990
	April–May	June	July	August–September	October–December	April–December	January–December	April 1986–Dec. 1987	January–December
Population	19600	9800	11000	20200	17100	77700	58700	136400	31600
Mean age (years)	32	32	34	34	35	33	33	33	34
Mean dose (Gy)	0.16	0.19	0.16	0.17	0.17	0.17	0.10	0.14	0.04
Number of thyroid cancers	8	6	4	6	4	28	15	43	4
Expected number of thyroid cancers	1.32	0.74	0.82	1.60	1.31	5.80	3.64	9.44	1.71
SIR (latent) (95% CI)	371 (119, 865)			150 (16, 542)		260 (100, 540)	260 (80, 600)	260 (134, 452)	180 (80, 730)
SIR (post-latent) (95% CI)	844 (449, 1440)			508 (218, 1002)		670 (420, 1030)	590 (280, 1080)	645 (438, 915)	330 (40, 1180)

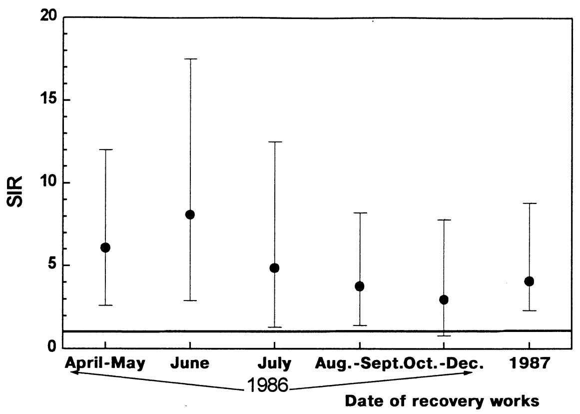

Fig. 6 SIR for thyroid cancer among emergency workers and 95% confidence intervals as a function of the time period of their work in the 30 km-zone

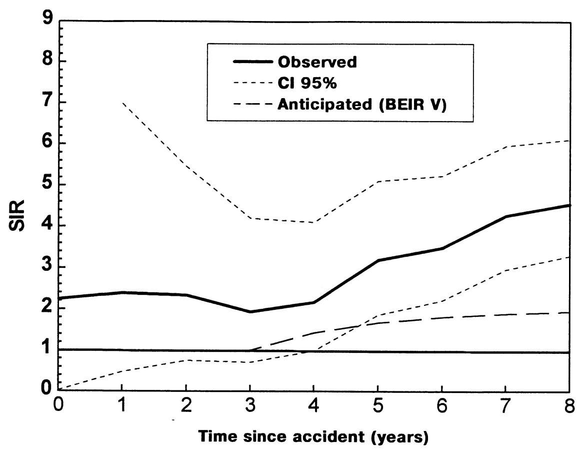

Fig. 8 Observed and anticipated SIR values for thyroid cancer among emergency workers of the period 1986–1987

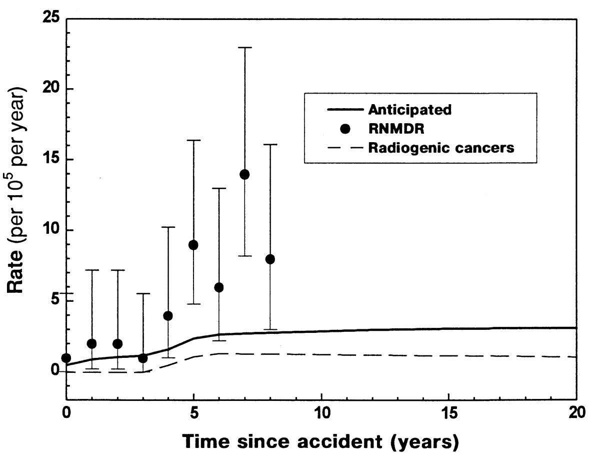

Fig. 7 Anticipated (*solid line*) and observed (*dots*) thyroid cancer incidence rates among emergency workers as a function of time since the accident

incidence rate, i.e. the radiogenic plus spontaneous cancer incidences. The spontaneous incidence is calculated on the basis of the age-specific incidence rates for the Russian Federation [9]. As pointed out above, there is a considerable discrepancy between the observed and the anticipated values in the period of more than 4 years after the disaster.

Figure 8 presents the change of the SIR values in the 8 calendar years of the follow-up period for emergency workers of 1986 and 1987. The SIR values remain practically constant at 2.2–2.6 for the time period that corresponds to the latency period of 4 years. If during this period no induction of radiogenic cancers is assumed to occur, then the excess of the observed SIR over 1 (100%) accounts for the screening effect (improved medical examination). The plot also gives an estimate of the anticipated contribution of radiogenic cancers to the SIR under the assumption that the thyroid dose is due merely to external exposure. It is seen that the calculation model and the cur-

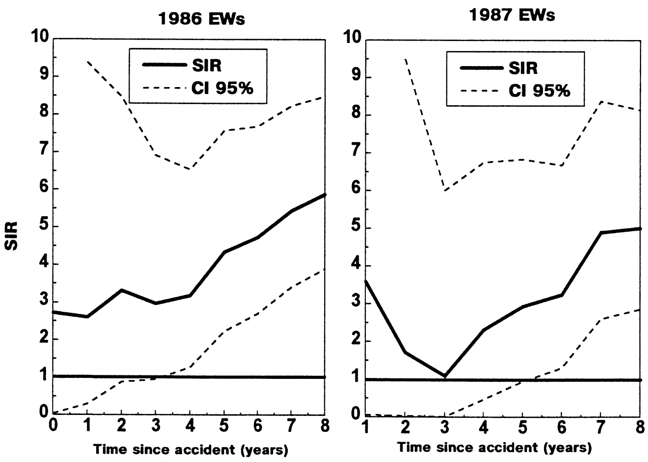

Fig. 9 Observed SIR values of thyroid cancer among emergency workers, separately for 1986 and 1987

rent risk coefficients [3, 4] account for only half of the observed excess of the SIR in the post-latency period. If radioiodine exposures can be disregarded, the observations imply that either the current risk estimates are too low, or that the external radiation doses are underestimated. In fact, both factors could apply.

Figure 9 shows SIR values for the emergency workers of 1986 and 1987 separately, depending on time since exposure. It is notable that there are – 4 years after the disaster – significant excess SIR values for the emergency workers of 1986, while for the emergency workers of 1987, the excess is seen 5 years after the accident. This reaffirms the existence of a latency period of about 4 years for the induction of radiogenic thyroid cancers in both cases (see also Fig. 8).

Estimation of radiation risks

As was stated above, the main aim of this study is not only epidemiological analysis in terms of SIR, but also the derivation of risk coefficients for leukaemia and thyroid incidence in emergency workers. Several risk coefficients are considered: excess relative risk per Gy (ERR/Gy), excess absolute risk per 10^4 person-years Gy (EAR/10^4 PY Gy) and attributable fraction of risk (AR%) at 1 Gy.

In the estimation of coefficients of radiation risk, it is assumed that the observed increases in leukaemia and thyroid cancer incidence are, indeed, due to radiation exposure. To ascertain this relation in an epidemiological investigation, an internal, dose-related analysis would be necessary. Our calculations suggest that such an analysis will require continued follow-up for the next 10–15 years; this would then provide about $2 \cdot 10^6$ person-years (PY) of observation of the cohort instead of the $1 \cdot 10^6$ PY achieved up to now.

The current follow-up of the emergency workers' cohort is too short to provide a sufficient number of cases of such rare diseases as leukaemia and thyroid cancer. An external analysis using national rates instead of an internal control group has, therefore, been employed for the risk estimation.

The EAR per Gy was estimated from the expression:

$$EAR = (O - E \cdot c)/(N_{PY} \cdot D) \quad (1)$$

O: observed number of cases;
E: expected number of cases according to national rates;
c: coefficient allowing for the screening effect;
N_{PY}: number of person-years under observation;
D: dose due to external irradiation in Gy.

The ERR per Gy was calculated in terms of the equation:

$$ERR = EAR \cdot N_{PY}/(E \cdot c) \quad (2)$$

The attributable risk at 1 Gy was obtained from the ratio:

$$AR = ERR/(1 + ERR) \cdot 100\% \quad (3)$$

The confidence intervals were calculated using the method of linearization of the function of random variables [10].

Risk coefficients are estimated merely for the cohort of the 1986–1987 emergency workers, as only for this cohort the follow-up has exceeded the latency periods for leukaemia and thyroid cancer.

It is essential to introduce the parameter c here to account for the effect of in-depth screening in the emergency workers. In line with the regulations of the Russian Ministry of Health, the emergency workers undergo an extensive annual medical examination. As pointed out, this can lead – in comparison with the entire male Russian population (the control group) – to an increased number of diagnosed cancers, which needs to be taken into account.

For leukaemia incidence the coefficient c is set equal to unity, because, as seen from Table 7 (1986–1989), the SIR = 113% during the latency period, which indicates no significant deviation from the national rates.

For thyroid cancer incidence c = 2.6. This corresponds to an increased value SIR = 260% during the latency period (1986 –1990), which is statistically significant and reflects the effect of in-depth screening (Table 8). This screening effect is well documented in the literature. For example, the in-depth screening coefficient for the cohort of atomic bomb survivors (Life Span Study, LSS) is 2.4 for women and 3.5 for men [11].

Tables 9 and 10 present radiation risk estimates for the cohort of emergency workers and their comparison with literature data from other studies. As can be seen, there is good agreement between the risk values obtained by us and published coefficients. Further epidemiological follow-up will be required to derive basic dependencies of the risk on dose, age at exposure and time since exposure.

Table 9 Radiation risk of leukaemia incidence among EW (1986–1993 observation period)

Data source	EAR/10^4 PY Gy (95% CI)	ERR/Gy	AR (at 1 Gy)%
EWs	1.31 (0.23, 2.39)	4.30 (0.83, 7.75)	81
LSS cohort	2.38	7.8	88

Table 10 Radiation risk of thyroid cancer incidence among EW (1986–1994 observation period)

Data source	$EAR/10^4$ PY Gy (95% CI)	ERR/Gy	AR (at 1 Gy)%
EWs	1.15 (0.08, 2.22)	5.31 (0.04, 10.58)	84
BEIR V	1.25	5.8	85

In an earlier large-scale epidemiological study the risk of thyroid incidence in children exposed to external radiation was studied, and the risk coefficients were estimated to be: ERR/Gy = 7.7; $EAR/10^4$ PY Gy = 4.4; AR = 88% [11]. On the other hand, there are few studies in the literature that deal with the estimation of the risk of thyroid cancer after exposure to radioiodine [12].

Discussion and conclusion

The results of this radoepidemiological study on leukaemia and thyroid cancer incidence among emergency workers after the Chernobyl accident are important in two aspects. First, they provide objective evidence of the medical consequences of the Chernobyl disaster. Indeed, dozens and hundreds of Chernobyl studies have been published recently with conflicting and often undocumented results. In some of these works, the consequences of the disaster are globally overestimated, which results in a further spreading of the “Chernobyl syndrome” of undocumented assertions. Others, in contrast, are biased to play down both the direct stochastic radiation effects and the indirect effects related to psychoemotional aspects. For an objective assessment it is necessary to document the data and the analysis, as has been attempted in this report.

The second issue of importance is the application of the Chernobyl experience to determine radiation risk coefficients based on the analysis of medical consequences of the disaster. There is an unique possibility of epidemiological analysis of the first 10 years since the accident. As a result of many years of follow-up of the Japanese cohort of atomic bomb survivors, epidemiological data based on several million person-years of observation is available. The current models and radiation risk coefficients are mostly based on these studies. On the other hand, the emergency workers alone have a collective dose due to the reactor accident that is similar to that of the atomic-bomb survivors, and the extent of epidemiological data on the Chernobyl accident is already comparable to the Japanese data (10 years after the disaster). It is, therefore, an essential task to re-examine models and radiation risk coefficients in the light of the Chernobyl epidemiology. The results will be particularly important, because they relate to low doses (<0.5 Gy) and low dose rates and can thus provide information that was previously not obtainable. This is, in fact, the main goal pursued in this study. At this point the results are preliminary, since they are based on a comparison with national rates. But they will be extended and improved in future studies to make more complete use of the information provided.

Acknowledgements The work on the Russian National Medical Dosimetric Registry is supported by a grant from the Government of Russia under the Federal Program on Population Protection from the Effects of the Chernobyl Disaster. We are grateful to the regional centres of RNMDR for collection and provision of primary medico-dosimetric data. We express our appreciation to Prof. A. M. Kellerer, Drs. E. Cardis, D. Preston and K. Mabuchi for discussion of epidemiological issues regarding the cohort of emergency workers.

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