Original paper

M. Fuzik, A. Prysyazhnyuk, Y. Shibata, A. Romanenko, Z. Fedorenko, L. Gulak, Y. Goroh, N. Gudzenko, N. Trotsyuk, O. Khukhrianska, V. Saenko, S. Yamashita

Thyroid cancer incidence in Ukraine: trends with reference to the Chernobyl accident

M. Fuzik, Y. Shibata, V. Saenko, S. Yamashita
Atomic Bomb Disease Institute, Nagasaki University Graduate School of Biomedical Sciences, 1-12-4 Sakamoto, Nagasaki 852-8523, Japan

M. Fuzik (✉), A. Prysyazhnyuk, A. Romanenko, N. Gudzenko, N. Trotsyuk, O. Khukhrianska
Research Centre for Radiation Medicine, National Academy of Medical Sciences of Ukraine, 53 Melnikov str., Kyiv 04050, Ukraine
E-mail: mfuzik@gmail.com

Z. Fedorenko, L. Gulak Y. Goroh
National Cancer Institute, Ministry of Health of Ukraine
33/43 Lomonosov str., Kiev 03022, Ukraine

Abstract For the first time, a comparative analysis of thyroid cancer incidence in Ukraine after the Chernobyl accident was done in a cohort that is almost as large as the general population. On the basis of thyroid doses from radioactive iodine in individuals aged 1-18 years at the time of accident, geographical regions of Ukraine with low and high average accumulated thyroid doses were established and designated “low-exposure” and “high-exposure” territories, respectively. A significant difference of thyroid cancer incidence rates as a function of time between the two territories was found. That is, the increase in the incidence was higher in high-exposure regions than in low-exposure regions. The incidence rates varied substantially among the different attained age groups, especially in the youngest one (up to 19 years old). The analysis which was adjusted for screening and technological effects also indicated that in the high-exposure regions thyroid cancer incidence rates at the age of diagnosis of 5-9, 10-14 and 15-19 years were significantly higher in those born in 1982-1986 compared to those born in 1987-1991, while in the low-exposure regions no significant difference was observed. The observed probable excess of radiation-induced thyroid cancer cases in adults exposed to radioactive iodine from the Chernobyl accident, especially in females, may be due to the high power of the present study. However, it should be noted that our investigation was not essentially free from ecological biases.

Introduction

Thyroid cancer is the most common malignancy of the endocrine system. However, it accounts only for a small fraction of all human cancers (Franceschi et al. 1993). In 1980ies, the annual incidence of thyroid cancer varied considerably in different European registries, ranging from 0.6 to 6.2 in males and from 1.0 to 8.3 in females per 100,000 individuals (Parkin et al. 1992).

Before the accident at the Chernobyl nuclear power plant in 1986, the thyroid cancer incidence rate in Ukraine increased slowly but steadily. After the accident this increase became steeper (Prysyazhnyuk et al. 2002): From 1989 to 2007, the thyroid cancer incidence rate increased from 0.9 to 1.6 in males and from 2.7 to 6.2 in females, per 100,000 individuals. The overall fraction of thyroid cancer among all human cancers increased about twofold for both genders: from 0.33% to 0.62% in males and from 1.59% to 3.28% in females (Gulak et al. 2004; Shchepotin et al. 2009).

The vulnerability of the thyroid to ionizing radiation has already been known before the accident; therefore it gained particular attention after the Chernobyl accident. For this reason, since 1989, thyroid cancer has been singled out as a separate entry in the official statistics on cancer incidence by the Ministry of Health of Ukraine, while before it was included into the category “others”. Furthermore, thyroid cancers diagnosed up to an age of 29 years were specified by 5-year age classes (Winkelmann et al. 1998) allowing to obtain more detailed information about cancer incidence in children and adolescents.

Due to radioiodine released to the environment after the Chernobyl accident, a large number of inhabitants of Ukraine, Russia and Belarus received radiation doses to the thyroid that were much higher than doses to other organs and tissues (UNSCEAR 2000). It is also remarkable that the Chernobyl accident became an issue not only in adjacent but also in remote countries and promoted research of its possible consequences in respective populations (e.g. Tirmarche and Catelinos 2002; Verger et al. 2003).

The increase in thyroid cancer is one of the most recognized health consequences of the Chernobyl accident in those territories of Ukraine, Belarus and Russia surrounding the Chernobyl nuclear power plant. In fact, the first radiation-induced thyroid cancer cases were registered four years after the Chernobyl accident (Prysyazhnyuk et al. 1991, 1995; Kazakov et al. 1992).

A number of studies estimated thyroid cancer risk of people exposed to Chernobyl radiation in childhood and adolescence (Sobolev et al. 1996; Demidchik et al. 2002; Ivanov et al. 2002, 2004; Kenigsberg et al. 2002; Likhtarov et al. 2006; Davis et al. 2004; Jacob et al. 2006; Kopecky et al., 2006). Although significantly increased radiation risk has been demonstrated in all of them, estimates vary quite widely.

As to adult population, three different affected groups have been commonly explored: recovery operation workers, evacuees, and residents of the most heavily contaminated territories. In all these groups an excess of thyroid cancer incidence was registered (compared with national levels), but it is disputable to which extent this is due to ionizing radiation, because of the potential influence of screening and introduction of modern ultrasound diagnostic equipment (Prysyazhnyuk et al. 2007; Ivanov et al. 2003, 2008).

Most of previous studies on thyroid cancer incidence were fragmentary and covered only particular groups of the population affected by the Chernobyl accident. The objective of the present study was to elucidate the trends of thyroid cancer incidence in the whole Ukrainian population.

Materials and methods

Information on thyroid cancer cases in Ukraine from 1989 through 2008 was collected from the Ukrainian cancer registry; from 1989 through 2007, gender- and 5-year-age-specific annual data for the population of each region in the country were obtained from official publications of the State Committee of Statistics.

All regions of Ukraine were classified into two groups based on ^{131}I thyroid doses that were reconstructed for the entire Ukrainian population aged 1-18 years at the time of the accident (Likhtarov et al. 2005). Assuming that the ranking of regions by the distribution of accumulated dose in those individuals aged 1-18 years was similar to that in older age groups in the same regions, we designated the regions “high-exposure” if thyroid dose exceeded 35 mGy (Fig. 1).

Although the average individual thyroid dose was 32 mGy in Kyiv city, we included it into the high-exposure regions, because a significant proportion of all recovery operation workers (over 23%) and evacuees from the city of Prypyat, and from the 30-km zone (over 15%) reside in Kyiv city. These high numbers are characteristic for the Kiev region only, while the fraction of recovery operation workers and evacuees in all other high-exposure regions is substantially lower. For instance, these two risk groups account for 4.6% and 2.6%, respectively, in Chernihiv region (Bobylyova, 1999). It should also be noted that according to our calculations that were done on the basis of the available data (UNSCEAR, 2000), the average thyroid dose of the evacuees is 328 mGy.

Thus, Cherkasy, Chernihiv, Kyiv, Rivne, Zhytomyr regions and Kyiv city were designated as high-exposure regions while all other locations were designated as low-exposure regions.

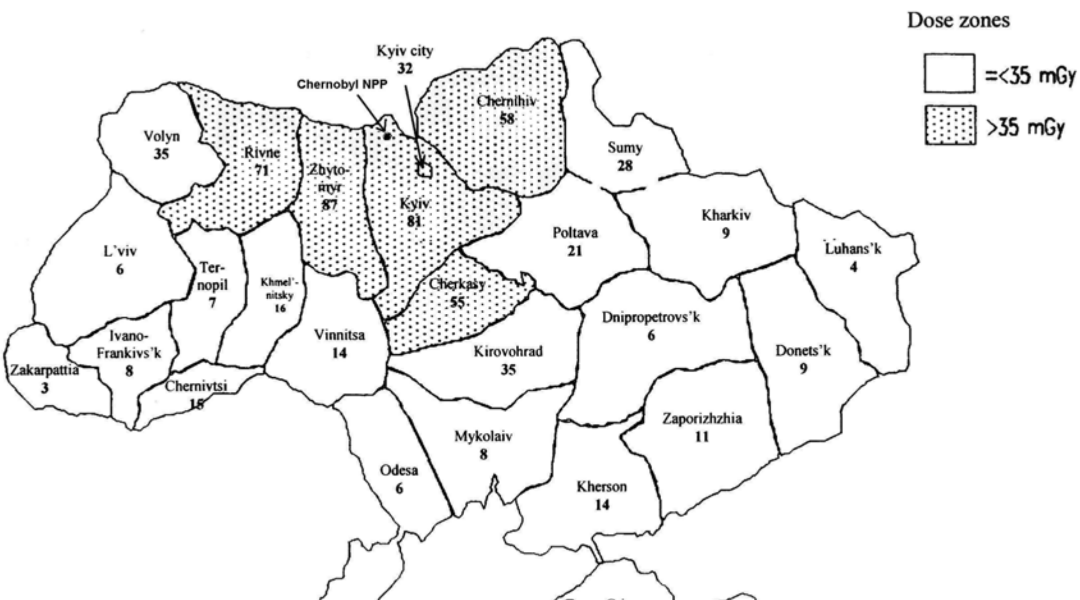

Fig 1 Average accumulated thyroid doses (bold numbers, given in mGy) in all regions of Ukraine, for individuals aged 1-18 years at the time of the Chernobyl accident (Likhtarov et al. 2005)

We calculated both the age-specific and age-adjusted thyroid cancer incidence rates for each year and for aggregated time periods, where age adjustment was done using the World Standard Population. For aggregated age groups (such as 0-19, 20-39, 40-59, 60+ years), truncated age-standardized incidence rates (TASR) were calculated. The reference period was limited to 1989 only because the first radiation-induced thyroid cancer cases were registered in 1990 (Prysyazhnyuk et al. 1991, 1995; Kazakov et al. 1992) and because we considered 1989 the last year of the latency period. The data for earlier years were not available, as already pointed out above.

The rate ratio (RR) was used to compare thyroid cancer incidence rates between high-exposure and low-exposure regions, and calculated 95% confidence intervals (95% CI) assuming Poisson distribution for the annual incidence of thyroid cancer (Rothman 1986). The lower and upper limits of the confidence interval for the ratios of two age-standardized rates (ASR_1 and ASR_2) are:

$$(ASR_1 / ASR_2)^{1 \pm (z_{\alpha/2} / X)},$$

where $z_{\alpha/2}$ denotes the 100(1-α/2) percentile of the standard normal distribution, and $z_{\alpha/2}$ = 1.96 for α = 0.05. For X, we used an approximation proposed by Smith (1987):

$$X = \frac{(ASR_1 - ASR_2)}{\sqrt{\{\mathrm{SE}(ASR_1)\}^2 + \{\mathrm{SE}(ASR_2)\}^2}},$$

where SE denotes the standard error.

Results

The thyroid cancer incidence rate and its dynamics in the two groups of regions were quite different. The level and average annual increase of thyroid cancer incidence were higher in the high-exposure regions than in the low-exposure regions, both for males and females (Fig. 2).

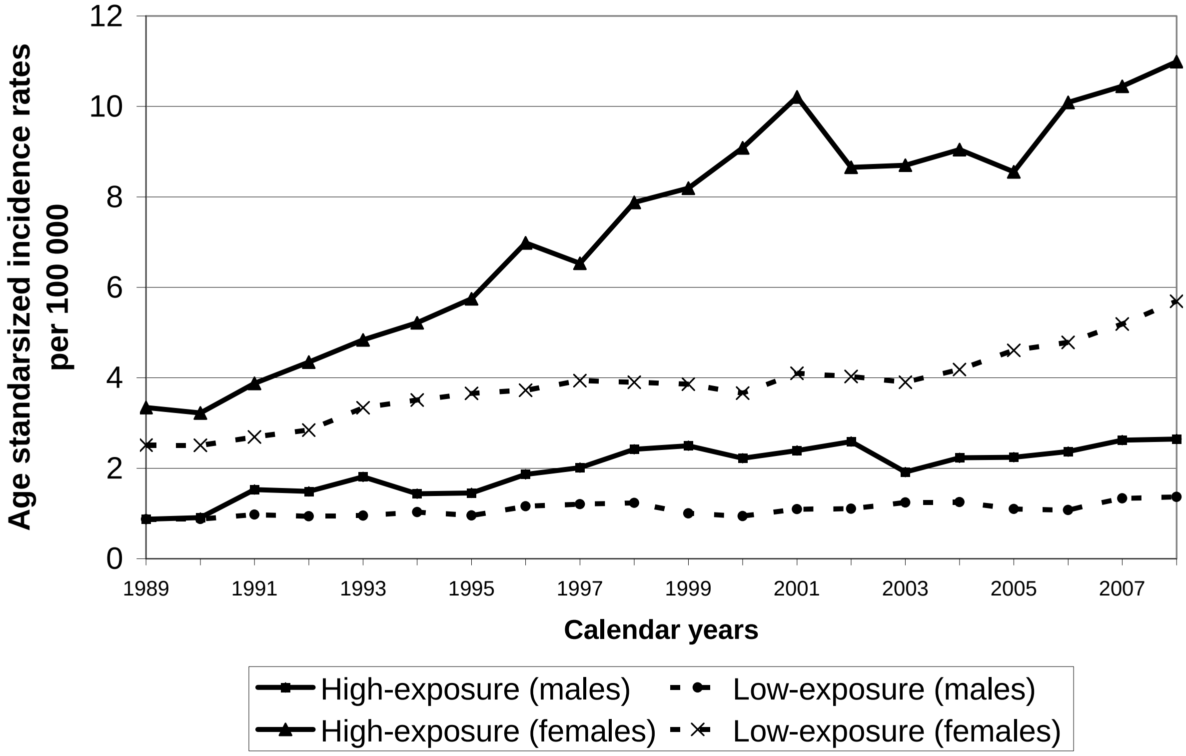

Figure 2 Trends in thyroid cancer incidence from 1989 through 2008 in Ukraine by gender and dose category

Throughout the period of the present study (1989-2008), age-adjusted thyroid cancer incidence rate in females of the high-exposure regions increased from 3.34 to 10.99 per 100,000, i.e. 3.3-fold, while in females of the low-exposure regions it increased from 2.51 to 5.69 per 100,000, i.e. 2.3-fold. In contrast, in males the thyroid cancer incidence rate was 0.87 per 100,000 at the beginning of the observation (1989) for both the high-exposure and low-exposure regions. In 2008 it increased to 2.64 in the high-exposure and 1.37 in the low-exposure regions, corresponding to factors 3.0 and 1.6, respectively. The slopes of the regression lines through the four trends in Fig. 2 are as follows: 0.079 (standard error (SE) = 0.011) for males of the high-exposure regions and 0.019 (SE = 0.004) for those of the low-exposure regions; 0.405 (SE = 0.029) for females of the high-exposure regions and 0.133 (SE = 0.011) for those of the low-exposure regions. This means that in the high-exposure regions, the thyroid cancer incidence rate increased faster compared to that in the low-exposure regions both for males and females, over the period of observation. The difference in the regression coefficients for deduced for the high- and low-exposure regions is statistically significant for both genders ($p < 0.01$).

Table 1 compares rate ratios of truncated age-standardized incidence rates (TASR) for thyroid cancer by age group and sex across the five-year intervals, for the high-exposure regions. Marked increases in RRs were noted for both males and females. The increases were most pronounced for those individuals aged 0-19 years at the time of diagnosis, being 13.99 and 5.55 in males and females, respectively, when the rates for the 1995-1999 period were compared with those of 1989. The RRs decreased steadily during the periods of 2000-2004 and 2005-2008 compared to the RR of 1995-1999, and the increase was already non-significant both for males and females diagnosed in 2005-2008. In all age groups except for 0-19 years at the time of diagnosis, the RR steadily increased both in males and females; this increase was statistically significant for nearly all periods. The exceptions were the period of 1990-1994 for males and females diagnosed at 40-59 years and 60+ years, and 1995-1999 for males diagnosed at 60+ years.

Table 1 Rate ratios by gender and age at diagnosis for thyroid cancer incidence rates per 100,000 among the residents of the high-exposure regions in Ukraine, 1989-2008; n: number of cases; CI: confidence interval

0-19 years at diagnosis

Year of diagnosis	Males				Females			
	n	TASR	RR	95% CI	n	TASR	RR	95% CI
1989	1	0.06	1		5	0.34	1	
1990-1994	56	0.71	11.58	5.02-26.71	99	1.29	3.78	2.18-6.55
1995-1999	71	0.86	13.99	6.47-30.26	150	1.89	5.55	3.47-8.87
2000-2004	60	0.71	11.48	5.08-25.97	110	1.36	4.00	2.35-6.81
2005-2008	6	0.10	1.54	0.24-9.81	41	0.09	1.77	0.82-3.79

20-39 years at diagnosis

Year of diagnosis	Males				Females			
	n	TASR	RR	95% CI	n	TASR	RR	95% CI
1989	8	0.52	1		56	3.46	1	
1990-1994	82	1.10	2.11	1.21-3.68	316	4.00	1.16	1.13-1.18
1995-1999	106	1.47	2.81	1.71-4.63	475	6.34	1.83	1.71-1.97
2000-2004	143	2.05	3.94	2.53-5.13	706	9.99	2.89	2.64-3.17
2005-2008	137	2.42	4.65	3.00-7.21	614	8.47	2.45	2.25-2.67

40-59 years at diagnosis								
Year of diagnosis	Males				Females			
	n	TASR	RR	95% CI	n	TASR	RR	95% CI
1989	20	1.69	1		103	7.85	1	
1990-1994	131	2.24	1.33	0.86-2.03	609	9.34	1.19	0.98-1.45
1995-1999	224	3.83	2.27	1.61-3.20	1061	15.75	2.01	1.71-2.35
2000-2004	235	4.07	2.41	1.73-3.37	1396	20.68	2.63	2.29-3.03
2005-2008	256	5.27	3.12	2.29-4.27	1338	18.58	2.27	2.05-2.74

60+ years at diagnosis								
Year of diagnosis	Males				Females			
	n	TASR	RR	95% CI	n	TASR	RR	95% CI
1989	18	3.14	1		66	5.33	1	
1990-1994	108	3.35	1.07	0.66-1.74	397	6.31	1.18	0.93-1.51
1995-1999	148	4.53	1.44	0.94-2.21	606	11.10	2.08	1.71-2.54
2000-2004	178	5.06	1.61	1.07-2.42	747	13.22	2.48	2.06-2.98
2005-2008	149	5.78	1.84	1.24-2.74	661	13.42	2.52	2.09-3.04

Table 2 Rate ratios by gender and age at diagnosis for thyroid cancer incidence rates per 100,000 among the residents of the low-exposure regions in Ukraine, 1989-2008; n: number of cases; CI: confidence interval

0-19 years at diagnosis								
Year of diagnosis	Males				Females			
	n	TASR	RR	95% CI	n	TASR	RR	95% CI
1989	8	0.13	1		12	0.19	1	
1990-1994	39	0.12	0.94	0.43-2.04	76	0.24	1.25	0.71-2.20
1995-1999	62	0.19	1.49	0.79-2.83	142	0.44	2.26	1.46-3.51
2000-2004	49	0.15	1.16	0.57-2.36	110	0.35	1.82	1.13-2.95
2005-2008	27	0.12	0.94	0.42-2.09	88	0.41	2.12	1.31-3.44
20-39 years at diagnosis								
Year of diagnosis	Males				Females			
	n	TASR	RR	95% CI	n	TASR	RR	95% CI
1989	32	0.52	1		145	2.22	1	
1990-1994	177	0.55	1.07	0.74-1.55	920	2.88	1.30	1.26-1.34
1995-1999	203	0.65	1.27	0.90-1.79	1136	3.64	1.64	1.57-1.72
2000-2004	208	0.74	1.43	1.03-1.99	1041	3.66	1.65	1.58-1.73
2005-2008	217	0.97	1.88	1.38-2.56	1051	4.69	2.12	2.00-2.25

40-59 years at diagnosis

Year of diagnosis	Males				Females			
	n	TASR	RR	95% CI	n	TASR	RR	95% CI
1989	69	1.40	1		290	5.28	1	
1990-1994	482	1.93	1.37	1.10-1.72	1733	6.32	1.20	1.06-1.35
1995-1999	497	2.11	1.50	1.20-1.87	2292	8.44	1.60	1.44-1.77
2000-2004	520	2.28	1.63	1.32-2.01	2550	9.45	1.79	1.62-1.97
2005-2008	457	2.32	1.65	1.33-2.05	2781	11.98	2.27	2.07-2.49

60+ years at diagnosis

Year of diagnosis	Males				Females			
	n	TASR	RR	95% CI	n	TASR	RR	95% CI
1989	83	3.46	1		304	6.41	1	
1990-1994	402	3.10	0.90	0.70-1.14	1667	6.68	1.04	0.92-1.18
1995-1999	509	3.72	1.07	0.86-1.35	1864	7.72	1.20	1.07-1.35
2000-2004	494	3.44	0.99	0.79-1.25	1823	7.46	1.16	1.04-1.31
2005-2008	401	3.74	1.08	0.86-1.36	1701	9.68	1.51	1.36-1.68

In the low-exposure regions, an increase in thyroid cancer incidence in males was noted only among those diagnosed at 20-39 years in 2000-2004 and 2005-2008, and among those diagnosed at 40-59 years in any time period. In females, the RR was significantly greater than unity for all periods and all diagnostic ages, except those diagnosed at 0-19 and 60+ years in 1990-1994 (Table 2).

Table 3 compares ratios between TASRs for thyroid cancer in the high-exposure and low-exposure regions by age group and sex across time periods: 1989, 1990-1994, 1995-1999, 2000-2004 and 2005-2008. While the ratios of incidence rates for 1989 were generally comparable for the high- and low-exposure regions, the RRs in the three age groups (except 0-19 years) increased for all of the later time periods. In those diagnosed at 0-19 years it, however, passed its peak in 1990-1994 and sharply decreased in 2005-2008.

Table 3 Rate ratios (RR) by gender and age at diagnosis for thyroid cancer incidence rates per 100,000 between residents of the high-exposure and low-exposure regions in Ukraine, 1989-2008; CI: confidence interval

Age at diagnosis	Year of diagnosis									
	1989		1990-1994		1995-1999		2000-2004		2005-2008	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
0-19										
Males	0.48	0.09-2.52	5.95	3.56-10.55	4.53	2.85-7.21	4.78	2.86-7.98	0.80	0.35-1.83
Females	1.77	0.52-6.02	5.34	3.53-8.10	4.33	3.17-5.93	3.88	2.73-5.52	1.47	0.98-2.21
20-39										
Males	1.01	0.47-2.20	1.99	1.45-2.73	2.24	1.67-3.00	2.79	2.13-3.67	2.50	1.91-3.27
Females	1.56	1.10-2.21	1.39	1.21-1.60	1.74	1.54-1.97	2.73	2.42-3.08	1.80	1.61-2.02
40-59										
Males	1.20	0.71-2.03	1.16	0.95-1.42	1.82	1.51-2.19	1.78	1.49-2.13	2.27	1.88-2.74
Females	1.49	1.15-1.91	1.48	1.33-1.64	1.87	1.71-2.03	2.19	2.02-2.37	1.55	1.44-1.67
60+										
Males	0.90	0.55-1.49	1.08	0.87-1.34	1.22	1.00-1.48	1.47	1.22-1.78	1.54	1.25-1.91
Females	0.83	0.65-1.07	0.94	0.85-1.05	1.44	1.30-1.59	1.77	1.60-1.96	1.39	1.26-1.53

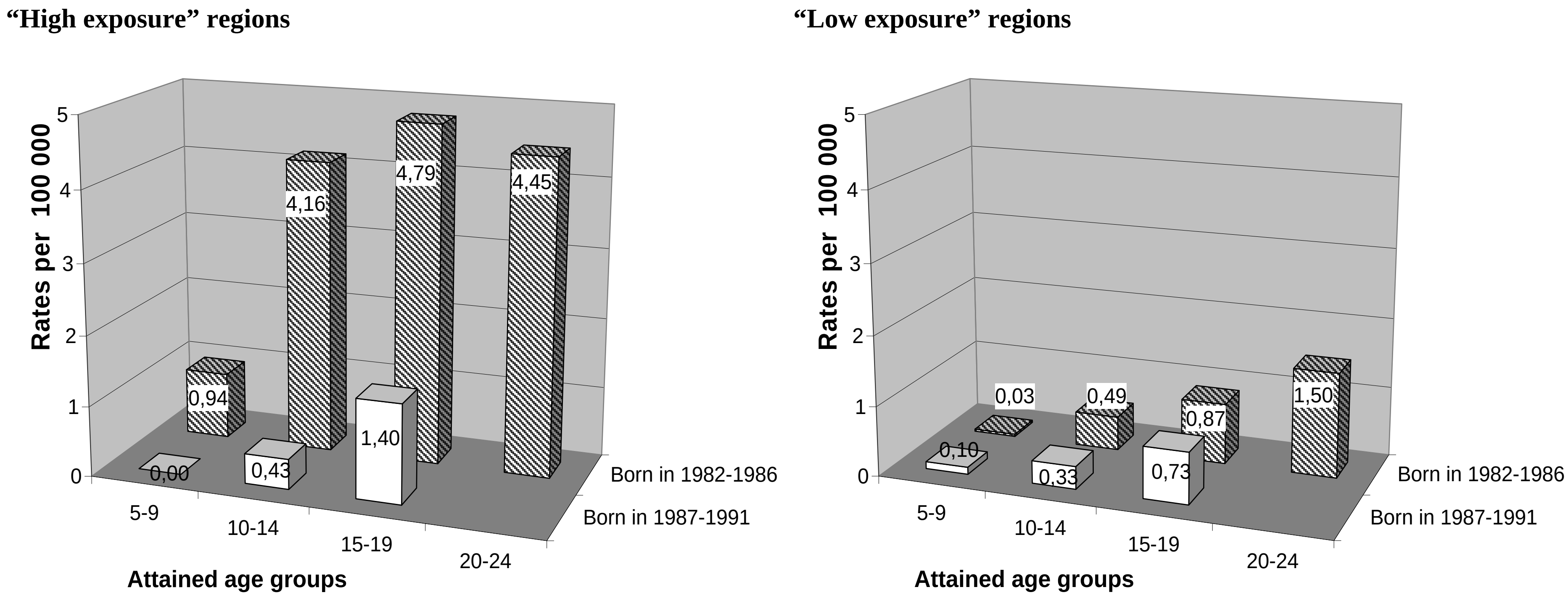

Fig 3 Thyroid cancer incidence rate per 100,000 by birth year and age at diagnosis in the high-exposure regions (left panel) and low-exposure regions (right panel)

Figure 3 presents thyroid cancer incidence at the age of diagnosis of 5-9, 10-14, 15-19 and 20-24 years for those individuals of the high- and low-exposure regions born in 1982-1986 and 1987-1991. In the high-exposure regions, thyroid cancer incidence rates at the age of diagnosis of 5-9, 10-14 and 15-19 years were significantly higher in those born in 1982-1986 compared to those born in 1987-1991, while in the low-exposure regions no such difference was observed.

Since the level of soil ^{131}I contamination is known to have been essentially zero in 1987 (Shibata et al. 2001), it is possible to use the maximal values (to avoid an overestimation of the screening effect) of the thyroid cancer incidence rate in the rest three groups of individuals presented in this figure (conditionally, low-exposed): residents of the high-exposure regions born in 1987-1991 and in those of the low-exposure regions at each age of diagnosis for estimating the rate in individuals not affected by radioactive iodine. At ages of 5-9, 10-14, 15-19 and 20-24 years, these were 0.10 (low-exposure, born in 1987-1991, 0.49 (low-exposure, born in 1982-1986), 1.40 (high-exposure, born in 1987-1991) and 1.50 (low-exposure, born in 1982-1986) per 100,000, respectively. Subtraction of these values from the corresponding rates in the high-exposure regions for individuals born in 1982-1986 yields the estimates of radiation-induced thyroid cancer incidence per 100,000: 0.84 (0.94-0.10) for those diagnosed at 5-9 years, 3.67 (4.16-3.49) for those at 10-14 years, 3.39 (4.79-1.40) for those at 15-19 years and 2.95 (4.45-1.50) for those at 20-24 years. Thus, the proportion of radiation-induced thyroid cancer cases can be estimated as 89.2% in those diagnosed at 5-9 years; 88.3% at 10-14 years; 70.8% at 15-19 years and 66.4% at 20-24 years.

Table 4 Rate ratios (95% confidence intervals) for age-specific thyroid cancer incidence rates in females of the high- and low-exposure regions in Ukraine by age at the time of the Chernobyl accident and year of diagnosis

Age at the time of the Chernobyl accident (years)	Year of diagnosis							
	1991		1996		2001		2006	
0-4	12.33	(0.54, 280.40)	10.83	(3.48, 33.71)	5.60	(2.29, 13.74)	2.62	(1.40, 4.92)
5-9	28.63	(2.16, 380.15)	2.41	(1.02, 5.70)	3.42	(1.75, 6.67)	2.28	(1.36, 3.85)
10-14	2.82	(0.82, 9.77)	2.12	(0.87, 5.16)	3.64	(2.15, 6.17)	2.46	(1.54, 3.95)
15-19	1.30	(0.44, 3.84)	1.38	(0.73, 2.63)	2.29	(1.35, 3.88)	2.37	(1.53, 3.68)
20-24	1.00	(0.44, 2.29)	1.74	(1.04, 2.92)	2.64	(1.72, 4.06)	2.13	(1.47, 3.09)
25-29	1.98	(1.09, 3.60)	1.67	(1.08, 2.60)	2.68	(1.82, 3.95)	2.46	(1.79, 3.38)
30-34	1.97	(1.17, 3.33)	2.06	(1.37, 3.11)	2.41	(1.74, 3.34)	2.27	(1.69, 3.06)
35-39	0.95	(0.58, 1.56)	1.82	(1.25, 2.65)	2.02	(1.48, 2.76)	1.73	(1.30, 2.30)
40-44	1.70	(0.97, 2.98)	1.71	(1.14, 2.57)	2.44	(1.59, 3.77)	1.63	(1.10, 2.42)
45-49	1.66	(1.09, 2.54)	1.80	(1.26, 2.59)	2.31	(1.65, 3.24)	1.95	(1.38, 2.78)
50-54	1.32	(0.77, 2.27)	2.59	(1.61, 4.15)	2.04	(1.26, 3.30)	1.28	(0.75, 2.19)
55-59	0.83	(0.53, 1.31)	0.93	(0.61, 1.41)	1.57	(1.01, 2.44)	0.99	(0.62, 1.57)

Table 4 summarizes trends for four years of 1991, 1996, 2001 and 2006 in terms of RR for age-specific thyroid cancer incidence rates in females of the high- and low-exposure regions by age at the time of the Chernobyl accident. Although some irregularities exist, the data indicate that except for those exposed at 0-4, 5-9, 15-19 yr and 50-54 years, the RR reached a maximum in 2001. In females exposed at 0-4 years, the RR steadily decreased since 1991. The trends in males, however, were not as clear as in females except for those exposed at 0-4 years (Table 5).

Table 5 Rate ratios (95% confidence intervals) for age-specific thyroid cancer incidence rates in males of the high- and low-exposure regions in Ukraine by age at the time of the Chernobyl accident and year of diagnosis

Age at the time of the Chernobyl accident (years)	Year of diagnosis							
	1991		1996		2001		2006	
0-4	NA	NA	5.91	(1.53, 22.86)	5.40	(1.78, 16.38)	4.91	(1.29, 18.77)
5-9	16.40	(0.87, 310.53)	2.93	(0.66, 12.98)	2.39	(0.60, 9.54)	4.38	(1.29, 14.85)
10-14	0.68	(0.10, 4.40)	3.08	(0.43, 21.80)	3.86	(1.05, 14.24)	1.80	(0.63, 5.12)
15-19	4.05	(0.46, 35.34)	0.37	(0.08, 1.61)	1.69	(0.44, 6.56)	1.31	(0.48, 3.54)
20-24	6.32	(1.06, 37.70)	0.79	(0.25, 2.48)	2.97	(1.13, 7.80)	4.09	(1.55, 10.79)
25-29	2.52	(0.70, 9.11)	2.37	(0.85, 6.60)	2.71	(1.17, 6.24)	1.24	(0.56, 2.74)
30-34	0.51	(0.16, 1.66)	2.89	(1.29, 6.45)	1.66	(0.71, 3.89)	2.48	(1.04, 5.90)
35-39	0.42	(0.14, 1.26)	2.20	(1.04, 4.65)	2.64	(1.26, 5.52)	2.43	(1.17, 5.06)
40-44	1.13	(0.36, 3.58)	1.08	(0.43, 2.73)	2.08	(0.82, 5.26)	1.88	(0.83, 4.25)
45-49	0.64	(0.30, 1.36)	1.80	(0.88, 3.67)	0.99	(0.51, 1.93)	1.75	(0.84, 3.65)
50-54	1.50	(0.70, 3.25)	0.45	(0.18, 1.11)	2.00	(0.81, 4.97)	2.36	(0.80, 6.94)
55-59	2.18	(0.85, 5.59)	0.84	(0.37, 1.91)	1.07	(0.35, 3.28)	1.79	(0.68, 4.76)

NA: not available.

Discussion

The present analysis revealed significant differences in trends of the thyroid cancer incidence rate in the two groups of regions investigated: the increase in this malignancy was higher in high- than in low-exposure regions; the incidence rate varied among the attained age groups. The steepest increase was registered in the young age groups (up to 19 years) of the high-exposure regions suggesting that the thyroid is particularly vulnerable to radiation in childhood and adolescence. The incidence rate in these groups substantially decreased in 2005-2008 probably because the majority of the members of these groups (and all since 2006) are individuals born in 1987 or later who were not exposed to ^{131}I from the Chernobyl accident.

In the groups of other ages at diagnosis, the age-specific incidence rate was characterized by a steady increase which was significantly higher in the high- than in the low-exposure regions. The least clear tendency was observed in the oldest age group of 60+ years in the low-exposure regions. This could be explained by the lower vulnerability of the thyroid to radiation in adults and by a possible increase in the period of latency with age.

The significant increase in thyroid cancer incidence observed in the low-exposure regions for all age groups at diagnosis was not as steep as in the high-exposure regions. This increase could be due to both an increase in background and screening effects.

The results of the present study evidently confirm the high vulnerably of young age groups to radiation carcinogenesis. Especially sensitive is the youngest age group born in 1982-1986 aged 0-4 years at the time of the Chernobyl accident. The observed dramatic increase in the thyroid cancer incidence rate in this age group is predominantly attributed to ionizing radiation. This conclusion is strongly suggested by the results obtained when the incidence in this age group was compared between the high- and low-exposure regions, where other confounding and modifying non-radiation factors (e.g. quality of registration, screening) were similar.

As for the incidence in adults, rate ratios in females significantly exceeded unity in 1996, 2001 and 2006 in those exposed at ages of 20-49 years, reaching the maximum in 2001 (Table 4), while in males this tendency was less clear (Table 5). One may conceive from these results that there is a probable excess in radiation-induced thyroid cancer cases in exposed people, especially in females, irrespectively of age at the accident. This conclusion seems quite important because even relatively recent papers report a lack of convincing evidence of radiation excess in thyroid cancer in exposed adults (Ivanov et al. 1999; Moysich et al. 2002; Hatch et al. 2005; Williams 2008; Ron 2007).

The present study also suggests that the latency period of radiation-induced thyroid cancer development may depend on age at exposure: the peak of rate ratio in youngest age groups at the time of the Chernobyl accident was in 1991, but in elder ages it shifted to later years (tables 4, 5). Previous investigations of this problem are very limited, but Dedov et al. (1993) pointed out the possibility of such a dependence in patients subjected to radiation therapy. Further studies are necessary to confirm these observations.

It should be noted that the character of the data presented and the analytical methods used are very similar to those by Mahoney et al. (2004) who explored the trends of thyroid cancer incidence and impact of the Chernobyl accident in Belarus. These authors concluded that radiation exposure led to an increase in thyroid cancer incidence rate not only in children and adolescents, but in adults as well. In particular, an excess of thyroid cancer was found in the age group of 35-54 years at diagnosis. Since their study was completed in 2001, this age group included persons who already were adults in 1986. However, calculations were performed only with regard to age at diagnosis, while age at exposure is also important for the evaluation of risk factors in radiation carcinogenesis. Presumably, the risk of radiation-induced thyroid cancer should be higher in those adults who were younger at exposure than in those who were elder. That is why age at exposure has also to be taken into account. In our work we considered both age at the time of diagnosis and age at the time of the Chernobyl accident. This approach allowed demonstration of an extraordinarily high vulnerability of the youngest group aged 0-4 years at exposure, and also investigation of radiation-related thyroid carcinogenesis in exposed adults.

The decrease in incidence rate ratios observed in 2006 in all groups of age at the time of accident may imply that the peak of excess of radiation-induced thyroid cancer is already passed. This statement, however, should be taken cautiously because similar annual data presented by Tronko et al. (2009) for persons aged 0-14 and 15-18 years at the time of the Chernobyl accident do not comply with our observations.

Conclusions

It should be stressed that for the first time, a comparative analysis of thyroid cancer incidence in Ukraine after the Chernobyl accident was performed in a cohort that is almost as large as the general population. The finding of a probable excess of radiation-induced thyroid cancer cases in adults, especially in females, may be due just to the adequately high study power. From the international literature it is well known that the excess thyroid cancer rates due to exposure to radioactive iodine tend to increase over time for more than 20 years, mainly for those exposed as young children. In the present ecological study it was difficult, however, to evaluate the potential contribution of an increased screening of the thyroid glands, which may partly have contributed to the observed increase of thyroid cancer cases, for example because of a more frequent use of ultrasound devices in medical diagnostics. However, we performed such evaluation of the screening effect in young age groups.

It should be acknowledged, that our investigation was not free from ecological biases and limitations. Precise estimation of radiation risks requires thoroughly designed cohort or case-control studies including detailed information about doses and confounding factors (both endogenous and exogenous) that might also affect the investigated thyroid cancer incidence, in addition to ionizing radiation.

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