Chapter 3

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Epidemiology of thyroid cancer in Ukraine after Chernobyl

Thyroid malignancies are relatively rare worldwide, yet their incidence has increased over the last few decades [1,2]. Epidemiology of thyroid cancer in the population of Ukraine exposed to radiation as a result of accident at the Chernobyl Nuclear Power Plant in April, 1986 is of a particular interest. Although the relationship between the Chernobyl radiation and increasing incidence of thyroid cancer among exposed children and adolescents in Belarus, Russia, and Ukraine is established in a number of studies and is the main proven health consequence of the accident [3,4], a continued monitoring and analysis of temporal trends of this disease have important medical and scientific impacts [5-7].

The purpose of this Chapter is to overview data on thyroid cancer incidence for the period from 1986 to 2010 in specific groups of population of Ukraine exposed in childhood or adolescence and also prenatally (*in utero*). In addition, the group of subjects born after the accident is included in the study because it provides important information on thyroid cancer incidence in the population of Ukraine which had not experienced Chernobyl fallouts.

A tool for recording and storage of data on the incidence of any cancer are population-based registries [8-11]; information can be used for subsequent analysis of morbidity and mortality in certain age groups and geographical areas. Domestic sources of data on thyroid cancer incidence in Ukraine are the site-specific Clinico-morphological Registry (CMR) of the State Institution "VP Komisarenko Institute of Endocrinology and Metabolism of the National Academy of Medical Sciences of Ukraine" (IEM) [12], and a classic cancer registry, which keeps records on all types of cancer, The National Cancer Registry of Ukraine (NCR) of the National Cancer Institute of the Ukraine Ministry of Public Health [13,14].

Specialized Clinico-morphological and National Cancer Registries of Ukraine

In the first half of the 1980-ies there were no personalized records of thyroid cancer cases in Ukraine [15]. Statistical summary of thyroid cancer could be derived from the archives of hospitals or from the reports of regional endocrinology services. After the Chernobyl accident in 1986, the Ministry of Public Health of USSR recommended to establish personalized registries of affected population and to improve recording system of patients with thyroid diseases which were anticipated to be one of the possible health effects of the Chernobyl accident [16,17]. In Ukraine, the collection of data on thyroid cancer incidence was coordinated by the Institute of Endocrinology and Metabolism (IEM) with participation of regional endocrinology services.

In 1992, a personalized Clinico-morphological Registry was established at the IEM for the first time in Ukraine, into which all cases of thyroid cancer in patients whose age at the time of accident did not exceed 18 years (i.e., born in 1968 and later) were entered. Creation of the Registry was promoted by the initiative of the Ukraine Ministry of Public Health in the Order No. 12 dated January 20, 1992 "On the improvement of endocrinological care to children and adults with thyroid diseases" in which the need for an increased attention to thyroid disorders after the Chernobyl accident and compulsory referral of children and adolescents with such diseases for surgical treatment to the Clinic of the IEM was formally stated. In addition, regional and municipal endocrinology and oncology clinics were imposed to collect and report complete information about thyroid cancer cases in corresponding age group to IEM, and to provide histological slides of tumors for additional expertise of the quality of pathomorphological diagnosis. Thus, IEM managed to collect the necessary data for comprehensive registry functioning.

In the post-Chernobyl period, the CMR has been continuously providing statistics on the number of cases and incidence of thyroid cancer among children and adolescents to the Ministry of Public Health and Academy of Medical Sciences of Ukraine, and also served as a source of data for a number of analytical studies on thyroid cancer incidence and assessment of radiation risks of thyroid cancer in the younger age groups of Ukraine [3,5,6,12].

Statistical records of thyroid cancer as of a separate entity in the structure of oncological services of Ukraine were started in 1989 [14,18]. At the same time, the Institute of Oncology of the Academy of Medical Sciences of Ukraine launched an automated National Cancer Registry (NCR) that covered all regions of Ukraine. NCR was based on a network of specialized cancer institutions and a State system of cancer registration. Practical realization and implementation of the information system in oncology at the regional level began in the mid-'90-s receiving governmental support according to the Order of the Ukraine Ministry of Public Health "On the establishment of a National Cancer Registry of Ukraine" dated December 30, 1996 [14]. In 2001, the creation of the system was completed by including all regions of Ukraine in the Registry [13,14].

A close cooperation between the CMR and NCR began in 2005. Today, the CMR is in some way a part of NCR [19-21]. Note however, that cross-check of the registries reveals some discordances. The CMR is a specialized Clinico-morphological Registry that includes particular age group (at high risk for developing thyroid cancer) and only operated cases with pathologically confirmed diagnosis. In contrast, besides the CMR records, National Cancer Registry also includes cases that had not been operated with only preoperative cytological conclusion about the possibility of thyroid cancer available. Moreover, the calculation of cases at the regional level in the CMR is based on the patient's place of residence at the time of Chernobyl accident, while the NCR system is based on the patient's place of residence at surgery. In other words, these differences should always be taken into account when comparing the two data Registries or analyzing the incidence according to data of one or another registry.

Pathological verification of diagnosis is essential for the case to be included in the CMR. The detailed pathological report including tumor type, subtype, invasive properties and tumor size is mandatory for cases operated at the Department of Surgery of Endocrine Glands of the IEM, and for the material (paraffin blocks, histological specimens) from patients operated elsewhere in Ukraine yet receiving radioactive iodine therapy at the Department of Clinical Radiology of the IEM (see Chapter 4).

Sources of information for the CMR are currently the reports of regional endocrinology services, data of regional oncological institutions (via the NCR of Ukraine), and clinical medical information system (MIS) of the IEM (www.therdep.com.ua). The principles of inclusion and recording of personal data coming from different sources correspond to the classical rules and procedures of cancer registries [22-24]. Automated procedures and control of completeness and quality of personal data play an important role [25].

Software realization of Clinico-morphological Registry

Entering and storage of Registry data is implemented using MS SQL Server software. This

- ensures data integrity;
- allows the use of a standard relational model for designing data structures and typical SQL for queries;
- provides a reliable import/export of data from most databases;
- allows performing application tasks using typical software tools (MS Access, Delphi, C + +, *. net , etc.).

The upgraded structure of registry databases provides some additional features:

- supports both Ukrainian and Russian versions of patient's surname and first name;
- implements a mechanism of saving changes or multiple patient's attributes' values (e.g. name, location, diagnosis);
- formalizes the place of residence according to the standard administrative territorial codifier "KOATO".

In addition, links have been established with databases with the geographical component at the regional, district and settlement level (MapInfo format), which extend the capabilities of data analysis and allow building various thematic maps. Today, the logical structure of the Registry includes three functional components: CaseRegist, CaseManager, and CaseReport.

- CaseRegist is a module of primary registration of data reported by the regional endocrinologists and IEM patients.
- CaseManager is a module of analysis, linkage, and verification of the Registry information. With this component, a comparative analysis of information from multiple sources is conducted including the search for and removal of duplicate records. A verified analytical version of the Registry record is generated that remains active for the year. A list of problematic cases to be verified by an expert morphologist and/or refined through queries to regional services could be created. The module also stores archives of the versions of analytical tables of the Registry from previous years; information about changes or refining of certain attributes of patients to be included in the next version of the Registry is accumulated.

- CaseReport component contains the current version of analytical tables of the Registry and a set of typical queries to generate standard numerical tables, charts and graphs that describe the available data for particular time and can be used for the preparation of reports, presentations, and publications.

The demographic component of the Clinico-morphological Registry

The demographic component of the Registry is based on a series of periodic publications of the State Statistics Committee of Ukraine; publications of regional statistics departments may be also involved detailing certain parameters for a specific region.

Census data represent the most reliable and detailed source of information on Ukrainian population. Our study period (from 1986 to 2010) includes two censuses: Ukrainian SSR census of 1989 and the All-Ukrainian census of 2001 [26, 27].

Primary sources of demographic data also include publications on the distribution of population by age and sex [28-33], the number of current and permanent population of Ukraine at the regional level, and annual demographic data records.

General statistical collections and the official website of the State Statistics Committee (www.ukrstat.gov.ua) [34] may also be used as sources of current demographic information.

The demographic component of the Registry includes data on the population of Ukraine for the period 1986 to 2010, and the following age groups are selected for monitoring:

- children under 14 years old (born before 1987);
- children under 14 years old (born in 1987 or later);
- adolescents aged 15 to 18 years (born before 1987);
- adolescents aged 15 to 18 years (born in 1987 or later);
- adults aged over 19 years (born before 1987, beginning from 1968);
- adults aged over 19 years (born in 1987 or later);
- *in utero* cohort (born from April 27 to December 31, 1986).

Population in the Registry (i.e., population size for which cases are registered) is growing from year to year: while for the first year of study (1986) it was slightly less than 14 million people, in 2010 it includes over 26 million subjects.

The demographic base of the Registry by attained age and ratio between exposed and unexposed subjects varies from year to year. The proportion of children and adolescents is monotonically decreasing (only that of born after Chernobyl remain practically unchanged), while the proportion of adults in the Registry is increasing (including those born both before and after Chernobyl).

The demographic base of the Registry allows assessing:

- annual dynamics of the age group from 0 to 14 years (born before and after Chernobyl separately);
- annual dynamics of the age group from 15 to 18 years (born before and after Chernobyl separately);
- annual dynamics of the age group over 19 years who were aged from 0 to 18 years at the time of the accident or born after Chernobyl;
- annual dynamics in the *in utero* cohort.

Since the size of groups in each region and in the whole of Ukraine is known, it is possible to make arbitrary combinations of regions and to compare the indices for the regions with the Ukraine as a whole.

To calculate the incidence, the most adequate determination of the number of person-years in a given cohort for a particular year is to use the average population size. It should be taken into account that we are not dealing with an exact number but with estimates characterized by some uncertainty. Some worsening of the quality of demographic estimates by the end of the study period (1986-2010) could be expected due to postponement of the next census of Ukraine to 2014 or later. A very informative overview of the problems of quality of demographic data, uncertainties in population parameters, and possible problems of their interpretation was recently published [35].

Methodology of descriptive analysis of the incidence

Current analysis of thyroid cancer incidence in younger age groups of the population of Ukraine represents methodologically, in general, a continuation of a series of previous publications [36-41]. By age at the time of accident and conditions of exposure, the study subjects are divided into the following three groups:

- exposed as children, aged 0-14 years at the time of accident (0-14 AE);
- exposed as adolescents, aged 15-18 years at the time of accident (15-18 AE);
- exposed *in utero*, born in May-December 1986 (EIU).

The first group (0-14 AE) is the largest and includes about 11.2 million subjects; the second group (15-18 AE) about 2.2 million persons, and the size of the cohort exposed prenatally is estimated to be about 0.52 million. It should be noted that, according to the conditions of CMR establishment, registered population includes those born beginning from December 1, 1968, i.e. actually the second group includes the subjects aged from 15 to <18.32 years at exposure (the population aged 18.32-18.99 belongs to the age cohort born in 1967).

Subdivision of population into these three groups, besides general medical considerations, has dosimetric rationale as well. Radiation doses to the thyroid have strong age dependency [42-46]. Under similar radioecological conditions, the maximal radiation dose is received by the population of younger age. For regional estimates of mean radiation dose [43], the relative exposure dose (normalized to the dose in adults) for children aged one year is 4.5-6; for children aged 5 years – 3-4; for children aged 10 years – 1.7-2; and for children aged 14 – about 1.5.

Similar age relationships are also inherent to risk coefficients (ERRD, EARD) of developing radiogenic cancer per exposure unit [4,47]. These patterns, taken together, indicate the highest expected radiogenic effects in the younger age groups of 0-4 years old and 5-9 years old compared with those aged 10 years and older.

Effects of thyroid exposure *in utero* are markedly different from those of postnatal irradiation, and information on risks is very limited [4,48,49].

The group born from 1987 was also used in later analyses as a control because it was not exposed to Chernobyl fallout and therefore does not include Chernobyl radiogenic cancers.

For the analysis by age at diagnosis, cases are subdivided into those diagnosed in children (aged 0-14 years at diagnosis), adolescents (aged 15-18 years at diagnosis), and adults (aged ≥19 years at diagnosis). Such subdivision is traditional for oncoepidemiology that recons childhood cancers a particular category [50,51]. A relatively new trend is to consider the group of adolescents and young adults (AYA) as patients requiring specific, tailored diagnostic procedures and streamlined procedures for cancer treatment [51-53].

Current analysis used a partition of 28 regions of Ukraine into two groups according to the level of thyroid exposure in children and adolescents [44,45, Chapter 2]:

- 6 most contaminated regions (Zhytomyr, Kyiv, Rivne, Chernihiv, Cherkasy regions and Kyiv City; average thyroid exposure dose in the group 0-18 years old at the time of the accident >35 mGy);
- 21 regions with relatively lower levels of contamination (average thyroid exposure dose in the group 0-18 years old <35 mGy).

Childhood and adolescent population of the 6 most contaminated regions accounted for 19-20% of the total population of corresponding age of Ukraine (Tables 3.1 and 3.2). It should be stressed that Zhytomyr, Kyiv, and Chernihiv regions are located at a distance up to 200 km from Chernobyl Nuclear Power Plant; the residents of northern areas of these regions received the highest thyroid doses [3,54].

Table 3.1
Thyroid cancer cases in selected groups of Ukrainian population in 1986-2010
(by periods of diagnosis)

	Population [a] million	1986-1989	1990-1994	1995-1999	2000-2004	2005-2010	1986-2010
0-14 years at exposure	11.1	59	383	827	1221	2554	**5044**
6 regions	2.2	15	191	384	574	1019	**2183**
21 regions	8.9	44	192	443	647	1535	**2861**
15-18 years at exposure	2.2	45	162	291	411	733	**1642**
6 regions	0.4	9	41	89	156	269	**564**
21 regions	1.8	36	121	202	255	464	**1078**
Subjects exposed *in utero*	0.5	0	3	5	26	78	**112**
6 regions	0.1	0	1	2	9	32	**44**
21 regions	0.4	0	2	3	17	46	**68**
Subjects born in 1987 and later	12.0 [b]	0	0	11	103	392	**506**
6 regions	2.5 [b]	0	0	3	32	123	**158**
21 regions	9.5 [b]	0	0	8	71	269	**348**
Total cases		**104**	**548**	**1134**	**1761**	**3757**	**7304**

[a] - exposed population on 1 January 1987; [b] - estimation of unexposed population on 1 January 2011

Table 3.2
Thyroid cancer cases in selected groups of Ukrainian population in 1986-2010 (by age at surgery)

	Population [a] million	Aged 0-14 years at surgery	Aged 15-18 years at surgery	Aged 19+ years at surgery	Total
0-14 years at exposure	11.1	453	496	4095	**5044**
6 regions	2.2	275	244	1664	**2183**
21 regions	8.9	178	252	2431	**2861**
15-18 years at exposure	2.2	-	31	1611	**1642**
6 regions	0.4	-	5	559	**564**
21 regions	1.8	-	26	1052	**1078**
Subjects exposed *in utero*	0.5	13	27	72	**112**
6 regions	0.1	5	11	28	**44**
21 regions	0.4	8	16	44	**68**
Subjects born in 1987 and later	12.0 [b]	177	183	146	**506**
6 regions	2.5 [b]	57	58	43	**158**
21 regions	9.5 [b]	120	125	103	**348**
Total cases		**643**	**737**	**5924**	**7304**

[a] - exposed population on 1 January 1987; [b] - estimation of unexposed population on 1 January 2011

In this work, the period of study is 1986-2010. The annual dynamics of cases and disease incidence are shown in Tables 3.3 and 3.4, respectively. In the analysis of time trends, the two-year intervals are used. Also, periods under comparison are subdivided into five intervals: 1986-1989 – the period shorter than the minimal duration of latency of radiation-induced thyroid cancer [4,47] when only sporadic thyroid cancers were diagnosed, and four subsequent intervals (1990-1994, 1995-1999, 2000-2004, 2005-2010) when both sporadic and radiogenic thyroid cancers are diagnosed in the population.

Analysis of thyroid cancer incidence in 1986-2010 according to the data of Clinico-morphological Registry

Tables 3.1 and 3.2 summarize data on thyroid cancer in the defined groups, and show population size in the 6 and 21 regions. Table 3.1 shows the number of cases for the five study periods. Table 3.2 shows the distribution of cases by age at diagnosis, depicting cancers diagnosed in childhood, adolescence, and adulthood.

Thus, the current analysis involves 6,798 cases in the exposed population, including

5,044 exposed as children, 1,642 cases in irradiated adolescents, and 112 cases of prenatal exposure. In subjects born after Chernobyl, i.e. in the unexposed population, 506 cases were diagnosed.

Detailed data on the number of cases, overall incidence for the whole of Ukraine, and for the 6 contaminated regions and 21 control regions are presented in Tables 3.3-3.7.

Data analysis for the groups by age at exposure takes into account that in every calendar year we are dealing with a virtual cohort with fixed characteristics of exposure that lived certain period after exposure. Thus, for a selected population group, over time, from year to year, the parameters of attained age change (increase) (minimum, maximum, median), as well as does the time after exposure. Attained age significantly affects the sporadic and radiogenic risks; time elapsed after exposure can also be an important parameter for calculating radiogenic risk. The attained age and time after exposure uniquely determine the age at exposure.

Detailed data on thyroid cancer cases and trends in the incidence among those exposed as children are shown in Table 3.3 and Figure 3.1. During the study period (1986-2010) in this group, the age varied from 0 to 14 years old in 1986 and from 24 to 38 years old in 2010. Table 3.3 shows the cases for the whole of Ukraine, as well as for 6 and 21 regions. Population size of this group was estimated to be 11.1 million persons at the beginning of 1987. This group showed the maximal number of cases (5,044) with about 43% of these (2,183 cases) registered in the 6 most contaminated regions. A significant increase in the incidence was observed in the first postlatent period (1990-1994) and continued until the end of the study (2010). Ascending trends are common to all four groups represented in Fig. 3.1 (males in 6 regions, females in 6 regions, males in 21 regions, females in 21 regions), although the growth rate and incidences are different for each group. For the low-dose regions, the increasing incidence is largely determined by the attained age; in the high-dose regions, there is an additional influence of radiogenic component and of the factor of intensive screening. The maximal incidence is expectedly observed in females from 6 contaminated areas (about 15 cases per 100,000 person-years). Incidence rates in the most contaminated areas are significantly higher than those in low-contaminated regions, although their ratio tends to be lower.

Rates in individuals exposed in adolescence are presented in Table 3.4 and Figure 3.2. The population size of this group was 2.2 million. In 2010, the age of this group reached 39-42 years old. The cumulative number of cases is 1,642, of which 564 (34%) were diagnosed in 6 regions with maximal thyroid doses. The main trends of incidence for males and females, in general, are similar to those in exposed during childhood. Due to differences in median attained age (about 9 years), the absolute values of the incidence for all four categories (males in 6 regions, females in 6 regions, males in 21 regions, and females in 21 regions) are somewhat higher than the corresponding values in exposed at childhood age. The incidence in females from 6 most contaminated regions reached 16-18 cases per 100,000 person-years at the end of the study period.

Figure 3.3 demonstrates incidence trends for those exposed at the age from 0 to 18 years old for different periods of study. Areas with the highest incidence (Kyiv, Chernihiv, Zhytomyr, and Kyiv-City) are located around the Chernobyl Nuclear Power Plant. Of note, there was a pronounced increase in the incidence in this group in low-contaminated regions during the last time period (2005-2010). Figure 3.4 presents ranked values of cumulative incidence [55] for those exposed at the age 0-18 years in postlatent period (1990-2010). High-dose regions, except for Rivne, demonstrate a value above the average for Ukraine. Also, an increased incidence was noted in Kherson and Vinnitsa regions. It should be mentioned that a number of studies [56-59] found Polisya (Rivne, Volyn, Zhytomyr regions) to be an area with low incidence of sporadic thyroid cancer. The contribution of radiogenic cancers led to the increase in incidence in this region, but the values were found to be slightly below the average for Ukraine (Rivne region) or below the extreme values for Kyiv and Chernihiv regions (Zhytomyr region). The increased incidence in the industrial regions of Ukraine (Kherson, Dnipropetrovsk, and Zaporizhya regions) was mostly observed in 2000-2010, and does not seem to be associated with radiation factor.

An estimate of the proportion of cases due to radiation among the total number of cases in the study population is of particular interest. Since thyroid cancers induced by radiation do not have definite markers and cannot be isolated from the whole group, the estimate can only be obtained within a particular statistical model describing the dynamics of the disease depending on exposure doses (risk assessment model). So, the proportion of radiogenic cancers for the Ukrainian population aged from 0 to 18 years at the time of accident and for the study period 1990-1997 was estimated to be 30% [56]. A comparative analysis at the level of regions of the country for the period of 1990-2001 [59] resulted in an estimate of the proportion of thyroid cancers attributable to Chernobyl radiation of 30% for the whole population of Ukraine and about 50% for the residents of the 3 most contaminated areas (Kyiv, Zhytomyr, and Chernihiv regions). Similar analysis performed in the individual cohort study for the residents (at the time of accident) of the 8 radiation-contaminated areas adjacent to the Chernobyl Nuclear Power Plant, yielded an estimate of excess cancer cases diagnosed during 1998-2000 of about 80% [60], and for the cases operated in 2001-2007 from 50 to 60% [61].

For individuals exposed *in utero*, data are presented in Tables 3.1, 3.2, and Figure 3.5. The population size of this group was estimated to be 0.52 million people. The number of diagnosed cases is 112. For the purpose of easier interpretation of data, Figure 3.5 also shows incidence trends for the cohort exposed at the age of 0-4 years old, and for the cohort of unexposed subjects born in 1987-1989 which could be considered a rough estimate of sporadic thyroid cancer incidence. The *in utero* group displayed an extremely low incidence for the period 1990-1999. During 2000-2010, however, the incidence increased sharply and reached values characteristic to the exposed subjects aged 0 to 4 years. If the increase in incidence in the *in utero* group was of radiogenic nature, it should be noted that the period of latency was substantially longer. Excess incidence for the *in utero* group was largely observed in the 6 contaminated regions where 44 cases were diagnosed (39%). Recently started, a study of radiation effects from *in utero* exposure is now actively carried out [48,49] in the framework of prospective observations. Since the number of cases of thyroid cancer registered in these studies so far is very low (<10), it would be promising to analyze the risks for this group in well-designed analytical ecologic or case-control studies using cases from the 6 contaminated areas.

Table 3.3

Thyroid cancer cases and incidence per 100,000 childhood population in 1986 (0-14 years old at exposure)

	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Cases (F)	4	7	8	22	29	31	64	59	82	92	108	108	143	170	145	214	213	180	228	241	308	331	386	407	446
Cases (M)	4	3	4	7	17	16	27	31	27	33	43	33	41	56	39	55	51	52	44	60	65	69	74	72	95
Cases (Both)	8	10	12	29	46	47	91	90	109	125	151	141	184	226	184	269	264	232	272	301	373	400	460	479	541
Incidence	0.1	0.1	0.1	0.3	0.4	0.4	0.8	0.8	1.0	1.1	1.4	1.3	1.7	2.0	1.7	2.4	2.4	2.1	2.5	2.7	3.4	3.6	4.1	4.3	4.9
6 regions, Cases (Both)	3	0	3	9	18	24	49	45	55	61	72	58	85	108	98	131	129	103	113	121	157	165	173	198	205
21 regions, Cases (Both)	5	10	9	20	28	23	42	45	54	64	79	83	99	118	86	138	135	129	159	180	216	235	287	281	336
6 regions, Incidence	0.1	0.0	0.1	0.4	0.9	1.1	2.3	2.1	2.6	2.9	3.4	2.8	4.0	5.1	4.7	6.2	6.1	4.9	5.4	5.8	7.5	7.9	8.2	9.4	9.8
21 regions, Incidence	0.1	0.1	0.1	0.2	0.3	0.3	0.5	0.5	0.6	0.7	0.9	0.9	1.1	1.3	1.0	1.5	1.5	1.4	1.8	2.0	2.4	2.6	3.2	3.1	3.7

Table 3.4

Thyroid cancer cases and incidence per 100,000 adolescent population in 1986 (15-18 years old at exposure)

	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Cases (F)	8	9	8	6	18	17	23	37	36	54	37	48	59	54	57	70	64	72	79	95	86	95	114	111	106
Cases (M)	3	5	2	4	2	5	8	7	9	6	8	8	9	8	11	14	24	13	7	13	18	21	19	23	32
Cases (Both)	11	14	10	10	20	22	31	44	45	60	45	56	68	62	68	84	88	85	86	108	104	116	133	134	138
Incidence	0.5	0.6	0.4	0.4	0.9	1.0	1.4	2.0	2.0	2.7	2.0	2.5	3.0	2.8	3.0	3.8	3.9	3.8	3.9	4.8	4.7	5.2	6.0	6.0	6.2
6 regions. Cases (Both)	1	5	0	3	5	8	7	10	11	20	13	15	26	15	26	31	34	35	30	40	45	46	50	44	44
21 regions, Cases (Both)	10	9	10	7	15	14	24	34	34	40	32	41	42	47	42	53	54	50	56	68	59	70	83	90	94
6 regions, Incidence	0.2	1.1	0.0	0.7	1.1	1.8	1.6	2.3	2.5	4.5	2.9	3.4	5.9	3.4	5.9	7.0	7.7	7.9	6.8	9.1	10.2	10.4	11.3	10.0	10.0
21 regions, Incidence	0.6	0.5	0.6	0.4	0.8	0.8	1.3	1.9	1.9	2.2	1.8	2.3	2.3	2.6	2.3	3.0	3.0	2.8	3.1	3.8	3.3	3.9	4.6	5.0	5.2

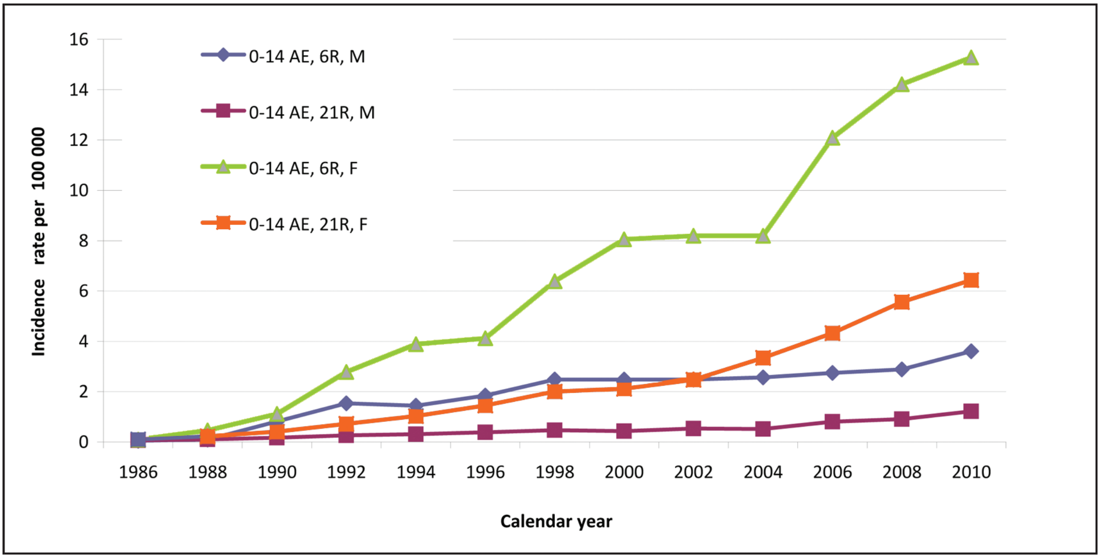

Figure 3.1. Time trends of thyroid cancer incidence in 6 and 21 regions of Ukraine for cohort aged 0-14 years at exposure. AE – age at exposure; 6R – 6 northern regions; 21R – other 21 regions; F – female; M – male.

Importantly, the interpretation of the number of cases and incidence in the groups defined by age at diagnosis (at surgery) should take into account that the composition of such groups changes from year to year as the cohorts become older. Both the size of the population and the proportion of exposed and unexposed subjects in the group are changing.

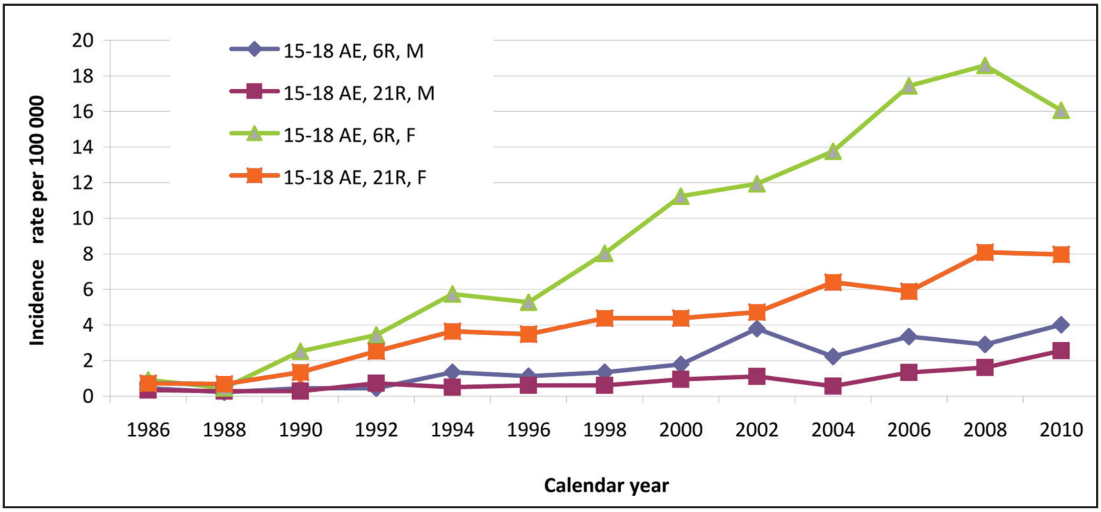

Figure 3.2. Time trends of thyroid cancer incidence in 6 and 21 regions of Ukraine for cohort aged 15-18 years at exposure. AE – age at exposure; 6R – 6 northern regions; 21R – other 21 regions; F – female; M – male.

Table 3.5
Thyroid cancer cases and incidence per 100,000 childhood population (0-14 years old at surgery: born before 1987, and in 1987 and later)

	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Born before 1987																									
Cases (F)	4	7	7	7	17	15	35	28	30	35	35	29	31	15	10	0	-	-	-	-	-	-	-	-	-
Cases (M)	4	2	3	4	13	8	19	20	20	14	20	7	11	8	6	2	-	-	-	-	-	-	-	-	-
Cases (Both)	8	9	10	11	30	23	54	48	50	49	55	36	42	23	16	2	-	-	-	-	-	-	-	-	-
Incidence	0.1	0.1	0.1	0.1	0.4	0.3	0.8	0.8	1.0	1.1	1.4	1.2	1.8	1.5	2.1	0.7	-	-	-	-	-	-	-	-	-
6 regions, cases (Both)	3	0	3	4	12	15	37	31	31	34	37	25	26	14	7	1									
21 regions, cases (Both)	5	9	7	7	18	8	17	17	19	15	18	11	16	9	9	1									
6 regions, incidence	0.1	0.0	0.2	0.2	0.7	1.0	2.8	2.6	3.0	3.8	4.9	4.1	5.7	4.6	4.6	2.0	-	-	-	-	-	-	-	-	-
21 regions, Incidence	0.1	0.1	0.1	0.1	0.3	0.1	0.3	0.3	0.4	0.4	0.6	0.4	0.9	0.7	1.5	0.5	-	-	-	-	-	-	-	-	-
Born in 1987 and in subsequent years																									
Cases (F)	-	-	-	-	-	-	-	-	-	1	0	1	1	2	10	8	19	7	6	18	7	14	8	11	18
Cases (M)	-	-	-	-	-	-	-	-	-	0	2	0	1	3	3	7	6	2	3	3	1	3	2	5	5
Cases (Both)	-	-	-	-	-	-	-	-	-	1	2	1	2	5	13	15	25	9	9	21	8	17	10	16	23
Incidence	-	-	-	-	-	-	-	-	-	0.02	0.03	0.02	0.03	0.1	0.2	0.2	0.3	0.1	0.1	0.3	0.1	0.3	0.2	0.2	0.4
6 regions, cases (Both)	-	-	-	-	-	-	-	-	-	-	-	1	-	2	2	6	11	3	2	4	3	5	2	7	9
21 regions, cases (Both)	-	-	-	-	-	-	-	-	-	1	2	-	2	3	11	9	14	6	7	17	5	12	8	9	14
6 regions, Incidence	-	-	-	-	-	-	-	-	-	-	-	0.08	-	0.1	0.1	0.4	0.7	0.2	0.1	0.3	0.2	0.4	0.2	0.5	0.7
21 regions, Incidence	-	-	-	-	-	-	-	-	-	0.02	0.04	-	0.04	0.1	0.2	0.1	0.2	0.1	0.1	0.3	0.1	0.2	0.2	0.2	0.3

Table 3.6
Thyroid cancer cases and incidence per 100,000 adolescent population (15-18 years old at surgery: born before 1987, and in 1987 and later)

	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Born before 1987																									
Cases (F)	1	4	0	5	6	7	7	9	19	8	15	12	18	29	30	32	29	20	5	4	-	-	-	-	-
Cases (M)	10	9	8	15	9	13	17	13	11	20	23	11	24	31	10	21	19	14	13	3	-	-	-	-	-
Cases (Both)	11	13	8	20	15	20	24	22	30	28	38	23	42	60	40	53	48	34	18	7	-	-	-	-	-
Incidence	0.4	0.5	0.3	0.7	0.5	0.7	0.8	0.8	1.0	1.0	1.3	0.8	1.4	2.0	1.3	1.7	2.1	2.2	2.3	2.8	-	-	-	-	-
6 regions, cases (Both)	1	4	0	5	6	7	7	9	19	8	15	12	18	29	30	32	29	20	5	4	-	-	-	-	-
21 regions, cases (Both)	10	9	8	15	9	13	17	13	11	20	23	11	24	31	10	21	19	14	13	3	-	-	-	-	-
6 regions, incidence	0.2	0.7	0.0	0.9	1.0	1.2	1.2	1.6	3.3	1.4	2.6	2.1	3.1	4.8	4.9	5.2	6.29	6.5	3.3	8.2	-	-	-	-	-
21 regions, incidence	0.5	0.4	0.3	0.6	0.4	0.6	0.7	0.6	0.5	0.9	1.0	0.5	1.0	1.3	0.4	0.9	0.8	1.1	2.1	1.4	-	-	-	-	-
Born in 1987 and in subsequent years																									
Cases (F)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	4	3	9	9	7	5	13	7
Cases (M)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3	7	14	22	19	14	16	15	15
Cases (Both)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4	11	17	31	28	21	21	28	22
Incidence	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5	0.7	1.0	1.4	1.1	0.8	0.9	1.3	1.1
6 regions, cases (Both)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	4	3	9	9	7	5	13	7
21 regions. cases (Both)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3	7	14	22	19	14	16	15	15
6 regions, incidence	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.7	1.3	0.7	1.7	1.7	1.4	1.0	2.9	1.6
21 regions, incidence	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5	0.6	0.8	1.1	0.9	0.7	0.8	0.8	0.9

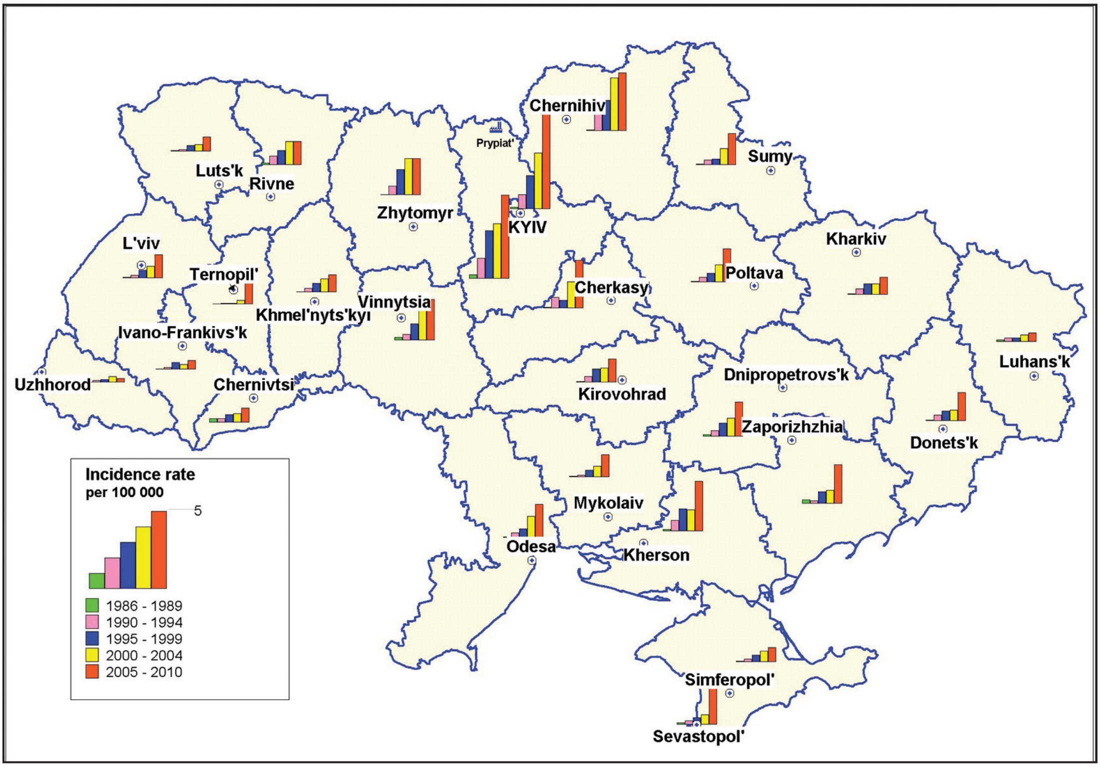

Figure 3.3. Region (oblast) specific time trends of thyroid cancer incidence in the cohort aged 0-18 years at exposure, both sexes.

Table 3.5 and Figure 3.6 demonstrate the statistics of cases and incidence trends for the age group 0-14 years at diagnosis. The incidence in this group was approximately 0.1 case per 100,000 person-years of childhood population during the period of latency (1986-1989), and then displayed a sharp increase already noticeable in the early postlatent period (1990-1992). Incidence in females from the 6 most contaminated regions increased in 1992-1998 more than 20-fold as compared to the period of latency. The increased incidence in females and males from the 6 regions started to decline synchronously after 1998, with transition of the most exposed group (aged 0-4 years at the time of the accident) to older age categories.

Since 2001, this group does not include exposed subjects (even those potentially irradiated *in utero*) any more. Incidences in males from the 6 and 21 regions are not significantly different, while that in females from the 6 most contaminated regions is approximately 2-fold higher than in less contaminated regions. Incidence rate for the group aged 0-14 years is widely used in cancer statistics, and the observed values (0.2-0.4 cases per 100,000 person-years) for unexposed Ukrainian population can be compared with data from other countries and other registries. Such a comparison with the ranked data from 28 European countries [11] suggests that the incidence in Ukraine for the group 0-14 years in the period 2003-2010 was about the European average.

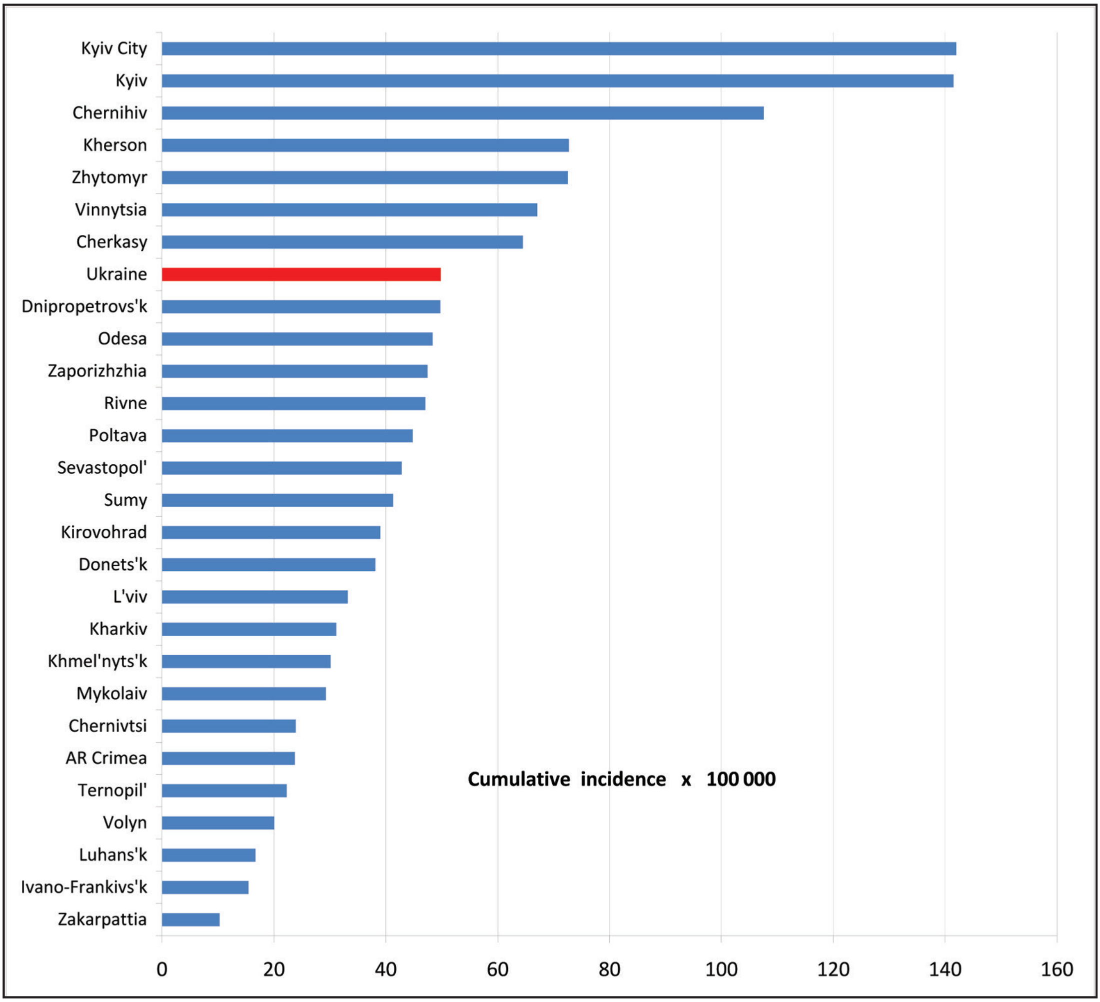

Figure 3.4. Ranking plot of region (oblast) specific cumulative incidence x 100 000 in 1990-2010 for the cohort aged 0-18 years at exposure, both sexes.

In the age group of 15-18 years old at diagnosis, the increasing incidence in the 6 high-dose regions was more gradual compared to the childhood group and reached maximal values both in females and males in 1998-2002 (Table 3.6 and Figure 3.7). Exposed population was not in the group since 2006, after which the incidence in males and females in the 6 and 21 regions became closer.

In the age group of 19+ years old at diagnosis, incidence trends were markedly different from the younger groups (Figure 3.8). This group has no upper age limit, and its size, median age, and age structure change every year. Incidence rates in the four categories (males in 6 regions, females in 6 regions, males in 21 regions, females in 21 regions) show increasing trends. The maximal rates were observed in females from the 6 most contaminated regions, followed by that in females from 21 regions, then in males from the 6 regions and the minimal was in males from 21 regions. It should be noted that in the "adult cohort", the exposed and unexposed populations are "mixed" beginning from 2006 (Table 3.7).

Table 3.7

Thyroid cancer cases and incidence per 100,000 in subjects aged 19+ years at surgery (born before and after Chernobyl)

	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Born before 1987																									
Cases (F)	0	2	3	4	19	19	33	54	65	91	83	113	148	166	165	253	246	233	300	338	400	431	511	531	570
Cases (M)	0	0	1	4	2	7	12	12	9	17	21	26	22	40	34	53	59	54	50	73	85	92	96	100	131
Cases (Both)	0	2	4	8	21	26	45	66	74	108	104	139	170	206	199	306	305	287	350	411	485	523	607	631	701
Incidence	-	0.6	0.4	0.5	0.9	0.8	1.2	1.4	1.5	1.8	1.5	1.9	2.1	2.3	2.1	2.9	2.7	2.4	2.8	3.0	3.7	3.9	4.5	4.7	5.2
6 regions, cases (Both)	-	1	0	3	5	10	13	15	16	39	33	37	68	80	88	133	134	119	141	161	208	213	229	249	256
21 regions, cases (Both)	-	1	4	5	16	16	32	51	58	69	71	102	102	126	111	173	171	168	209	250	277	310	378	382	445
6 regions, incidence	-	1.5	-	0.9	1.1	1.6	1.7	1.6	1.5	3.2	2.4	2.5	4.1	4.5	4.5	6.4	6.0	5.0	5.5	6.0	7.8	8.0	8.5	9.2	9.5
21 regions, incidence	-	0.4	0.5	0.4	0.9	0.7	1.0	1.4	1.4	1.4	1.3	1.7	1.6	1.8	1.4	2.1	1.9	1.8	2.1	2.4	2.6	2.9	3.5	3.6	4.1
Born in 1987 and in subsequent years																									
Cases (F)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	6	7	20	38	49
Cases (M)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	2	5	8	10
Cases (Both)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	7	9	25	46	59
Incidence	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.7	0.5	1.1	1.6	1.7
6 regions, cases (Both)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3	2	9	14	15
21 regions, cases (Both)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4	7	16	32	44
6 regions, incidence	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.5	0.6	1.9	2.4	2.1
21 regions, incidence	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.5	0.5	0.9	1.4	1.6

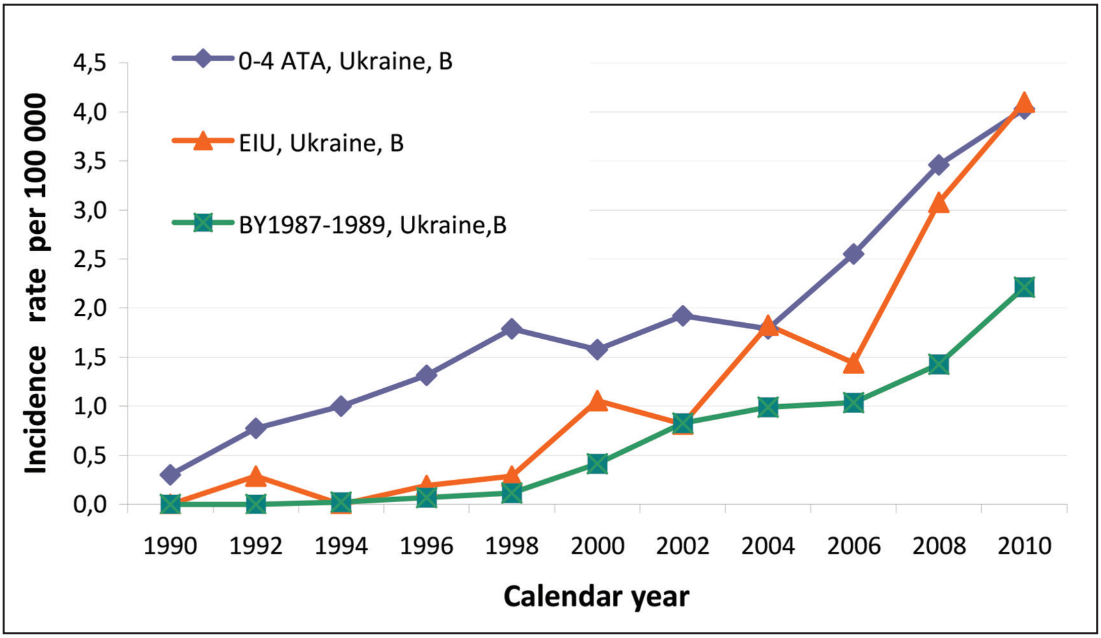

Figure 3.5. Thyroid cancer incidence in 3 birth cohorts, both sexes: aged 0-4 years at exposure (ATA – age at exposure; B – both sexes); exposed *in utero* (EIU – exposed *in utero*, Ukraine – whole Ukraine, B – both sexes); born in 1987-1989 (BY – year of birthday; Ukraine – whole Ukraine, B – both sexes).

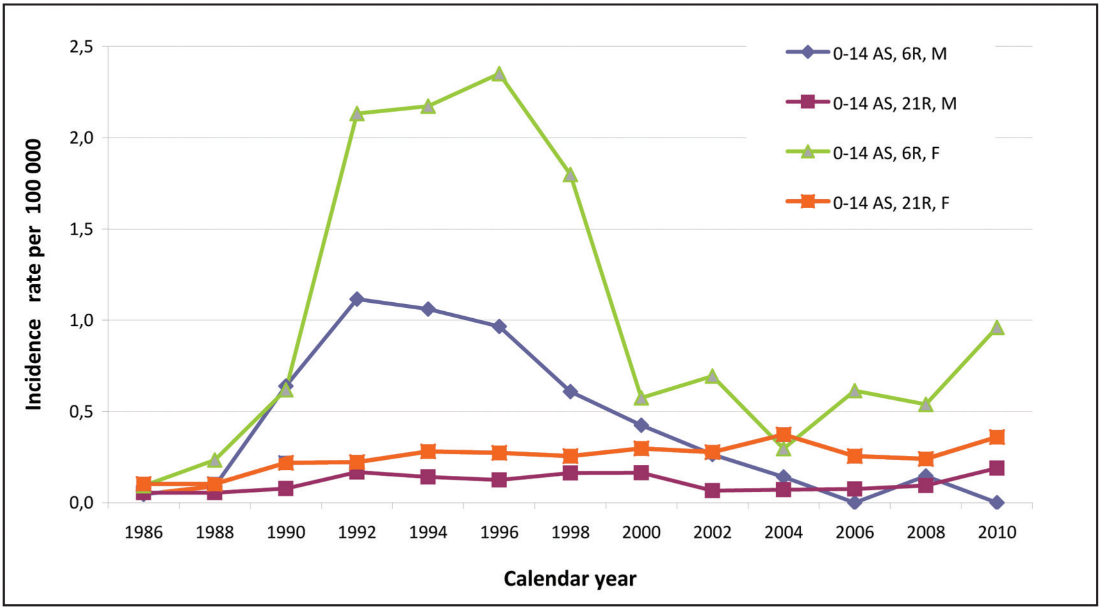

Figure 3.6. Time trends of thyroid cancer incidence among children aged 0-14 years at surgery. AS – age at surgery; 6R – 6 northern regions of Ukraine; 21R – other 21 regions of Ukraine; F – female; M – male.

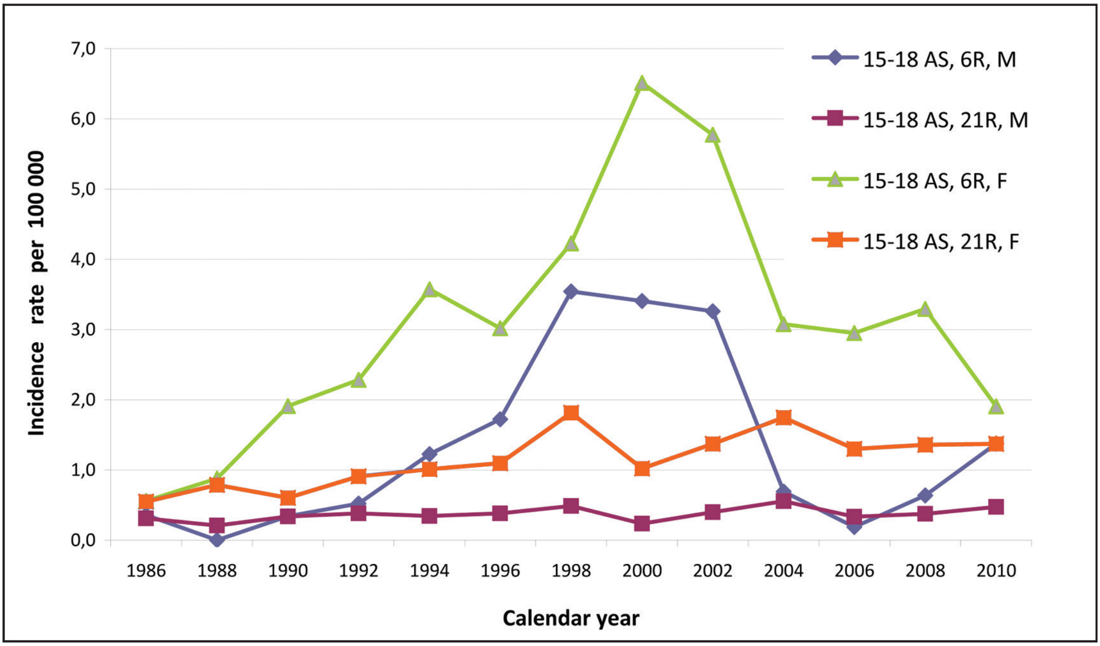

Figure 3.7. Time trends of thyroid cancer incidence among adolescents aged 15-18 years at surgery. AS – age at surgery; 6R – 6 northern regions of Ukraine; 21R – other 21 regions of Ukraine; F – female; M – male.

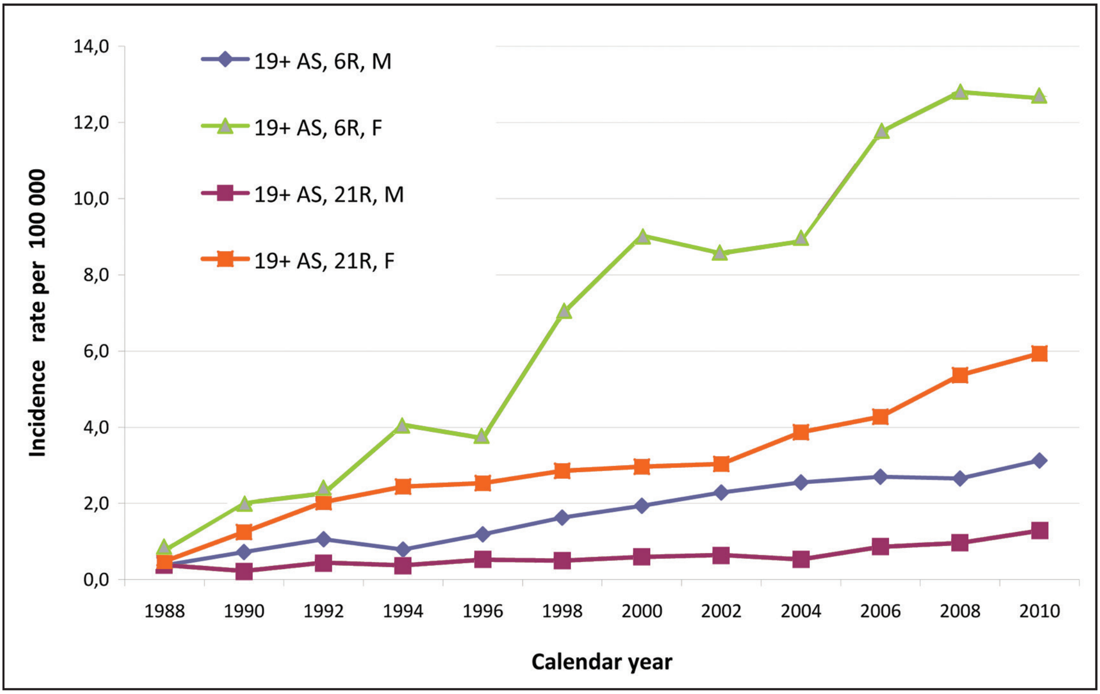

Figure 3.8. Time trends of thyroid cancer incidence among adults aged 19+ years at surgery. AS – age at surgery; 6R – 6 northern regions of Ukraine; 21R – other 21 regions of Ukraine; F – female; M – male.

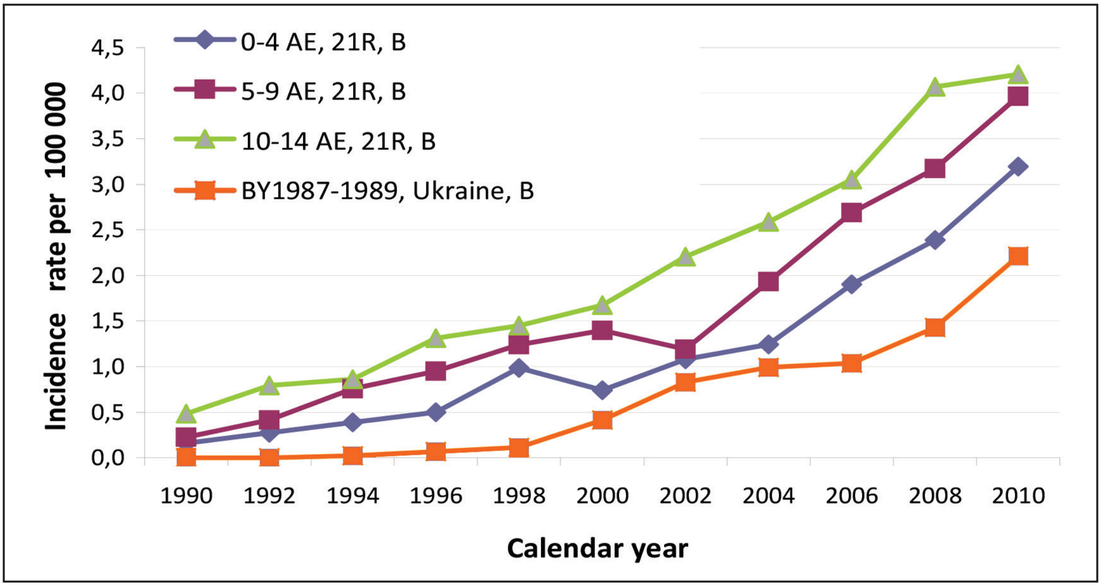

Figure 3.9. Time trends of thyroid cancer incidence in 21 less contaminated regions of Ukraine among 3 exposed and 1 unexposed birth cohorts. AE – age at exposure; 6R - 6 northern regions of Ukraine; B – both sexes; BY – year of birthday; Ukraine – whole Ukraine.

As the next step, we consider in a descriptive analysis the birth cohort effect for exposed and unexposed populations by comparing the incidence trends in the three exposed cohorts (0-4, 5-9, and 10-14 years old at the time of exposure), and in the unexposed cohort (nearest by age to the exposed cohorts) born in 1987-1989. Time trends are considered separately for the 6 regions and 21 regions without subdivision by sex. The size of cohorts (0-4, 5-9, and 10-14 years old at exposure) were 0.75, 0.71 and 0.73 million for high-dose regions, respectively, and about 3 million in each age group for the 21 low-dose regions. The size of the unexposed cohort born in 1987-1989 for the whole of Ukraine was about 2.2 million.

Figure 3.9 presents incidence trends in the postlatent period for these four cohorts in the 21 low-dose regions. At the beginning of the study period (1990-1992), the incidence in each cohort did not exceed 0.5 case per 100,000 person-years. In subsequent years, the cohorts showed a gradual growth of incidence, and at the end of the study incidence rates ranged from 2.2 to 4.1 cases per 100,000 person-years. It is noteworthy that during the analyzed period of time the incidences displayed a strictly ordered character according to attained age. For each fixed period, the cohort born in 1987-1989 showed the lowest incidence; the next higher value of incidence was observed in the cohort aged 0-4 years at exposure (the difference in the attained age with the previous cohort was about 4 years); then in the cohort aged 5-9 years at exposure, and the maximal value was in the cohort of 10-14 years at exposure. The shapes of trends for all cohorts are similar and close to the exponential curves.

Figure 3.10 presents incidence trends in postlatent period for similar four cohorts in the 6 high-dose regions. The trend in the cohort of subjects born in 1987-1989 is the same as in Fig. 3.9, and exponentially increases from 0 to 2.2 cases per 100,000 person-years.

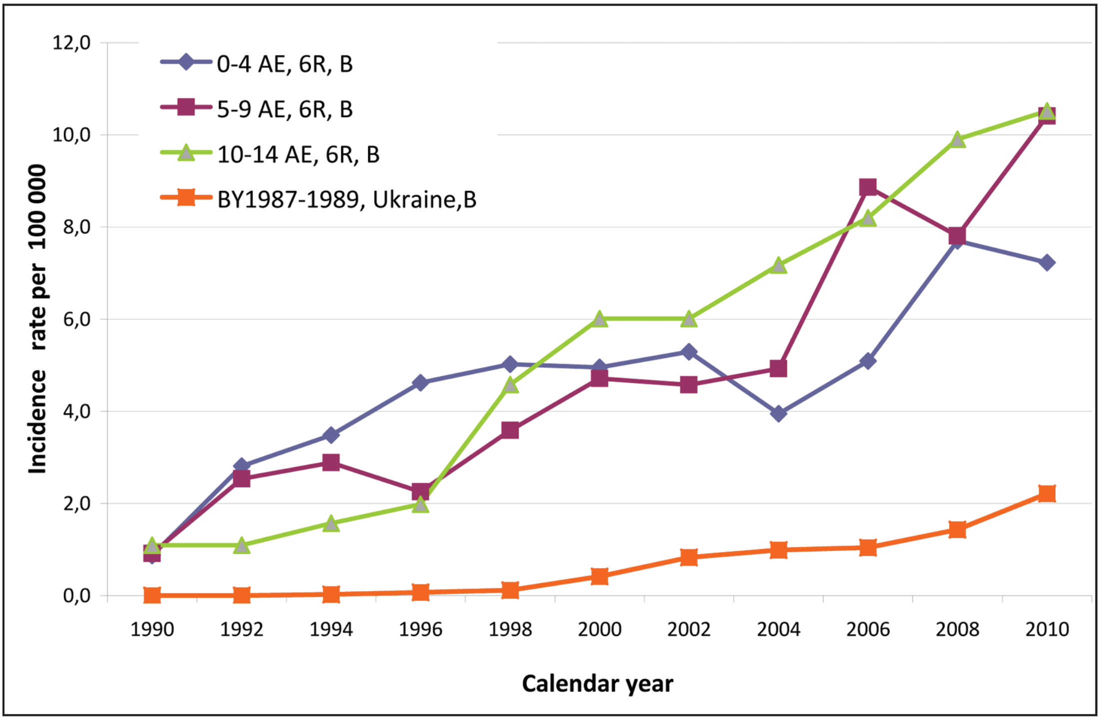

Figure 3.10. Time trends of thyroid cancer incidence in 6 northern regions of Ukraine among 3 exposed, and 1 unexposed birth cohorts. AE – age at exposure; 6R - 6 northern regions of Ukraine; B – both sexes; BY – birtnday year; Ukraine – whole Ukraine.

In the exposed cohorts, the sporadic incidence is supplemented by the radiogenic component and possibly by the factor of screening [58,62]. The trends in the exposed cohort are less "smooth", the values vary within the wide range (from 1 to 10.5 cases per 100,000 person-years) and do not show the "natural" ordering by attained age. Moreover, in the period of 1990-1998, the highest incidence was observed in the youngest cohort of 0-4 years old at exposure, which had accumulated maximal thyroid doses. From 1998 to 2006, the incidence in this cohort was almost stable: about 5 cases per 100,000 person-years, after which it continued to increase.

In the cohort aged 5-9 years old at exposure the incidence began to grow as rapidly as in the younger cohort in 1990, but until 2004 it was lower. The incidence in the older age group (10-14 years old at exposure) was slowly increasing until 1996, after which the growth accelerated and, beginning from 2000, it occupied a "natural" position with the highest incidence rate.

At the end of the study period (2010), the rate ratios in the groups of 0-4, 5-9, and 10-14 years old at exposure for 21 regions to the cohort born in 1987-1989 were 1.4, 1.7, and 1.9 (Fig. 3.9), respectively. The ratios for the 6 high-dose regions are remarkably higher: 3.3, 4.7, and 4.8, respectively.

Thyroid cancer incidence at the level of the whole population according to the data of National Cancer Registry

Finally, we will briefly discuss the incidence and mortality rates for the whole population of Ukraine in the period 1999-2010 according to the National Cancer Registry data [13]. During this period of time, the number of newly reported cases of thyroid cancer increased steadily from 2,093 (360 males and 1,733 females) cases in 2001 to 2,869 (508 males and 2,361females) in 2010. The annual increase in the incidence was 77.6 cases; it was faster in females (62.8 cases) compared to 14.8 cases in males. The sex ratio (the ratio of the number of cases in females to the number of cases in males) was 4.7 on average for the period 2001-2010 ranging from 4.2 to 5.3.

Figures 3.11 and 3.12 represent the trends of thyroid cancer incidence and mortality, respectively, due to thyroid cancer for the whole population of Ukraine for the period 1999-2010 according to the NCR [13]. During this period, the incidence showed an ascending trend both in females (from 6.5 to about 9 cases per 100,000) and males (from 1.9 to 2.5 cases per 100,000). At the same time, mortality rates vary within the ranges 1-1.2 per 100,000 in females and 0.5-0.6 in 100,000 in males with a tendency to a slow decrease. A similar relationship between the incidence and mortality is typical for the registries of other countries [1,8,9]. Such a ratio (declining trend of mortality and increasing incidence) reflects the fact that the increase in incidence is largely due to the growing number of curable well-differentiated tumors, and also due to improvements in the quality of diagnosis over time.

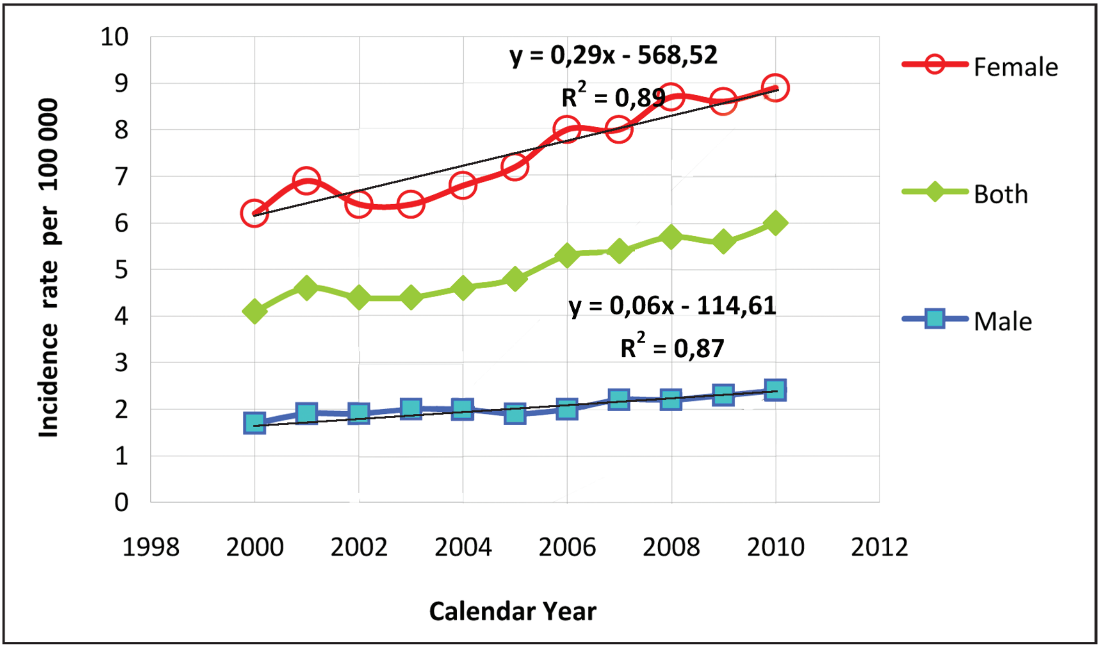

Figure 3.11. Age-adjusted incidence rates of thyroid cancer per 100,000 general population of Ukraine in 2000-2010. Data from ref. [13].

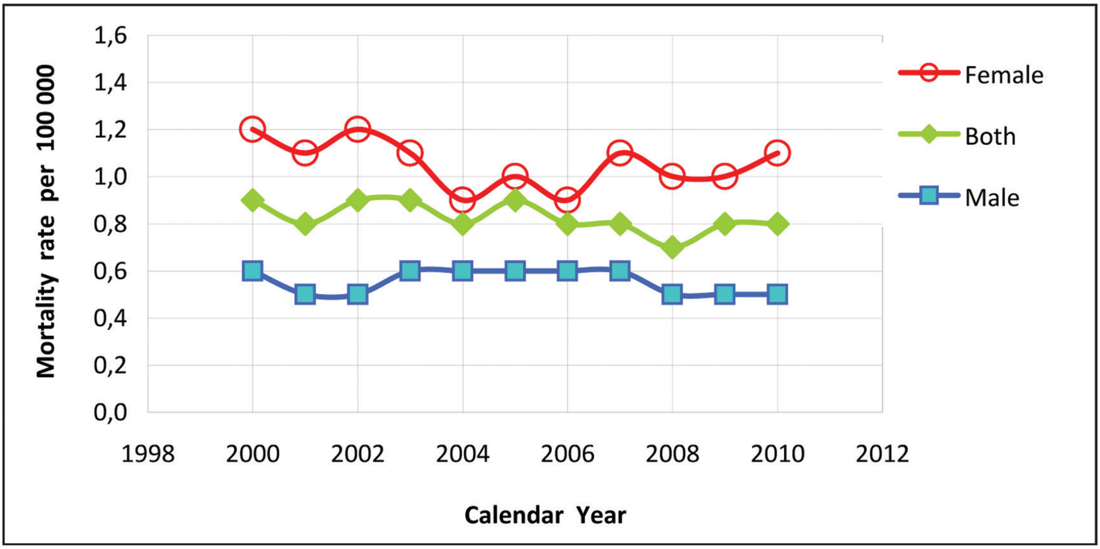

Figure 3.12. Age-adjusted mortality rates of thyroid cancer per 100,000 general population of Ukraine in 2000-2010. Data from ref. [13].

In summary, this chapter demonstrates that among the exposed population of children and adolescents (aged 0-18 years at the time of accident), there has been a significant increase in thyroid cancer incidence after the minimal period of latency; this tendency persists for the period of 20 years (1990-2010). At the same time, incidence rate in the 6 most contaminated regions exceeded that in 21 low-contaminated regions for all postlatent periods of study. However, in both high- and low-contaminated regions, incidence rate displays a descending tendency, perhaps indicating a gradual decrease in the contribution of radiation factor in the increased thyroid cancer incidence in the cohort aged 0-18 years at the time of Chernobyl accident. Among those exposed *in utero*, a significant growth of incidence started after 15 years since accident and continued to grow during the further period.

By age at diagnosis, peak incidences in childhood and adolescent groups were observed in 1995-1997 and 2000-2002, respectively. Since 2002 there are no exposed subjects (including the *in utero* cohort) in the childhood group and since 2006 in the adolescent group. Thus, in these age categories all childhood and adolescent cases of radiogenic thyroid cancer have been realized. In the corresponding groups of unexposed subjects aged 0-14 and 15-18 years at the time of diagnosis, thyroid cancer incidence is comparable to the average rate in European countries.

Incidence of sporadic thyroid cancer markedly increases from the age of 25-30 years old; it may, therefore, be expected that the proportion of radiogenic cancers in Ukraine will decline, even in the regions with relatively high levels of radiation exposure. On the other hand, as shown in a recent study [63], a statistically significant contribution of radioinduced thyroid cancers developing after acute external irradiation can be observed even 50-60 years after exposure. This fact justifies the need for continuous monitoring and analysis of the incidence of thyroid cancer in the population groups exposed as a result of Chernobyl catastrophe.

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