UNSCEAR United Nations Scientific Committee on the Effects of Atomic Radiation

EVALUATION OF DATA ON THYROID CANCER IN REGIONS AFFECTED BY THE CHERNOBYL ACCIDENT

A white paper to guide the Scientific Committee's future programme of work

EVALUATING RADIATION SCIENCE FOR INFORMED DECISION-MAKING

UNITED NATIONS

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EXECUTIVE SUMMARY[1]

At its sixty-third session (27 June–1 July 2016), the Scientific Committee requested the secretariat to prepare an evaluation of data on thyroid cancer in regions affected by the Chernobyl accident. The Committee discussed a paper that recapitulated its previous findings on this matter, reported the latest data provided by the three most affected countries (Belarus, the Russian Federation and Ukraine), summarized key literature of the past several years, and made an assessment of the fraction of the observed incidence of thyroid cancer that could be deemed attributable to radiation exposure of the thyroid:

(a) Both the total number of cases and the crude incidence rate (number of cases per 100,000 person-years) basically increased monotonically over the period 2006−2015. The total number of cases of thyroid cancer registered in the period 1991−2015 in males and females, who were under 18 in 1986 (for the whole of Belarus and Ukraine, and for the four most contaminated oblasts of the Russian Federation), approached 20,000. This number is almost three times higher than the number of thyroid cancer cases registered in the same cohort in the period 1991−2005;[2]

(b) The observed increase in the incidence of thyroid cancer is attributable to a variety of factors: increased spontaneous incidence rate with aging of the birth cohort, radiation exposure, awareness of thyroid cancer risk after the accident, and improvement of diagnostic methods to detect thyroid cancer;

(c) The Committee estimated that the fraction of the incidence of thyroid cancer attributable to radiation exposure among non-evacuated residents of Belarus, Ukraine and the four most contaminated oblasts of the Russian Federation, who were children or adolescents at the time of the accident, is of the order of 0.25. The uncertainty range of the estimated attributable fraction extends at least from 0.07 to 0.5;

(*d*) The increased incidence of thyroid cancer after the Chernobyl accident is a major issue and needs further investigation to determine the long-term consequences of radiation exposure. The ongoing epidemiological cohort studies and research on biomarkers for radiation-induced thyroid cancer may enhance the understanding of carcinogenesis after radiation exposure and contribute to an improved estimation of the fraction of thyroid cancer incidence attributable to exposure.

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[1] Based on the *Official Records of the General Assembly, Seventy-second session, Supplement No. 46** (A/72/46*).

[2] *Sources and Effects of Ionizing Radiation: United Nations Scientific Committee on the Effects of Atomic Radiation 2008 Report to the General Assembly*, vol. II, annex D (United Nations publication, Sales No. E.11.IX.3).

I. INTRODUCTION

1. The Committee has previously assessed in detail the radiation exposures that resulted from the nuclear power plant accident at Chernobyl in 1986 and analysed the associated risks and effects (UNSCEAR 2000 Report, annex J [U1]; UNSCEAR 2008 Report, annex D [U2]; UNSCEAR 2012, annex A [U4]). At the sixty-third session (27 June–1 July 2016), the Committee requested the secretariat to prepare a short paper for its next session (29 May–2 June 2017) on the evaluation of data on thyroid cancer in regions affected by the accident at Chernobyl.

2. The primary objectives of the paper are: *(a)* to provide an authoritative report on the numbers of thyroid cancer cases observed to date, primarily among people who were children or adolescents at the time of the accident; and *(b)* to make an expert judgement of the fraction that can be attributed to radiation exposure resulting from the accident. Secondary objectives are to clarify, where possible, the scientific basis for and the reliability of risk projections, considering the levels and patterns of radiation dose to the exposed populations.

3. This paper is based on data on annual incidence of thyroid cancer as submitted officially under arrangements made by the secretariat with the representatives to the Committee of Belarus, the Russian Federation and Ukraine. In addition, it presents an evaluation of key publications in the peer-reviewed scientific literature up to December 2016, and an assessment of the fraction of the incidence of thyroid cancer attributable to the radiation exposure caused by the accident.

II. RELEVANT PAST REPORTS OF THE COMMITTEE

4. The Committee concluded in its UNSCEAR 2008 Report, annex D [U2] that the 1986 Chernobyl nuclear power plant accident resulted in the release of a significant amount of radioactive material to the atmosphere leading to exposures of nearby populations mainly from beta and gamma radiation. Many of the children and adolescents received elevated doses to the thyroid, almost entirely because they drank fresh milk containing ^{131}I in the first few weeks following the accident. The Committee estimated the average absorbed doses to the thyroid of evacuated children and adolescents, and of non-evacuated children and adolescents (at the time of the accident) in the so-called “contaminated areas” of the former USSR to be about 900 mGy and 170 mGy, respectively [U2]. Average doses to the thyroid of adults were lower, and those of pre-school children were some 2 to 4 times greater than the population average. The average dose to the thyroid of all evacuees was estimated to have been about 500 mGy (with individual values ranging from less than 50 mGy to more than 5,000 mGy). For the more than six million residents of the contaminated areas of the former USSR, who were not evacuated, the average dose to the thyroid was about 100 mGy, while for about 0.7% of them, doses to the thyroid were more than 1,000 mGy.

5. The background rate of thyroid cancer among children under age 10 was approximately two to four cases per million per year. Since 1990–1991, a dramatic increase in the rate of occurrence of thyroid cancer was observed among members of the public who had been infants or young children at the time of the accident. Among those exposed who had been under 14 years of age in 1986, there were 5,127 reported cases of thyroid cancer between 1991 and 2005 (for those who had been under the age of 18 in 1986, there were 6,848 cases). Fifteen cases had proved fatal. The observed pattern suggested that the dramatic increase in incidence for the period 1991–1995 was associated with the accident. There was no evidence for a

decrease in the annual excess incidence of thyroid cancer up to 2005 (the end of the observation period for the report). For those born after 1986, there was no evidence for an increase in the annual incidence of thyroid cancer [U2].

6. The observed increased incidence has been confirmed in several case–control and cohort studies that have related the excess incidence of thyroid cancer to the estimated individual doses to the thyroid due primarily to the radioiodine released during the accident. According to the estimates of Jacob et al. [J1], for the period 1986–2001, about 30% of the incidence of thyroid cancer in the whole of Ukraine—and about one half in the three northern oblasts (including Kyiv City)—was deemed attributable to radiation from the accident; in Belarus, about 60% of the incidence of thyroid cancer was deemed attributable to the accident. Generally, the excess relative rate[3] (ERR) was higher for females than for males.

7. There was little suggestion of an increased incidence of thyroid cancer among those exposed as adults in the general population. Among the recovery operation workers, elevated rates of thyroid cancer compared to those in the general population have been reported, but no clear association with dose from external exposure has been found. In addition, no estimates of doses to the thyroid from inhaled radioiodine to those who worked on the Chernobyl site between April and June 1986 have been available. The influence of annual screenings and active follow-up of these cohorts make comparisons with the general population problematic [U2].

8. The Committee encouraged further investigation [U2] on the conclusion that iodine deficiency might have influenced the ERR per unit dose to the thyroid for thyroid cancer resulting from the incorporation of ^{131}I released during the accident [C1, S2]. However, the conclusion was not statistically significant and the underlying mechanisms were unclear.

9. Studies of large groups of people exposed to moderate and high doses may detect a statistically significant increase in the incidence of thyroid cancer. At lower doses, however, the necessary size of the study group to achieve sufficient power is larger than what could be realized up to now [U4].

10. The Committee in its UNSCEAR 2012 Report, annex B [U4] defined a scenario to estimate the uncertainty in the knowledge on thyroid cancer induced by radiation resulting from the accident. In this scenario, Ukrainians, aged 10 years at the time of the accident, received a hypothetical dose to the thyroid of 200 mGy from the incorporation of ^{131}I. For females, the estimated number of excess thyroid cancer cases during the lifetime of 10,000 exposed was 59 (95% credibility interval from 11 to 200). For males, the excess was about one order of magnitude lower.

11. The Committee in its UNSCEAR 2013 Report, annex B [U3] referred to a cohort study of 13,000 Ukrainians who were children or adolescents at the time of the accident. A first ultrasound screening of the thyroids was conducted in the period 1998–2000 and detected 45 thyroid nodules that were confirmed as malignant after fine needle aspiration. Doses to the thyroid of members of the so-called “Ukrainian-American (UkrAm) cohort” were reconstructed based on measurements of the ^{131}I activity in the thyroid of individuals performed within the first two months after the accident. The ERR per unit dose to the thyroid was assessed to be 5.3 (95% CI: 1.7, 28) Gy^{-1}.

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[3] The excess relative rate (ERR) is strictly a statistic calculated from observed frequencies/rates, while the excess relative risk is a prospective estimate inferred from the data and reasoning [U4].

III. RESULTS OF SCIENTIFIC RESEARCH SINCE THE UNSCEAR 2008 REPORT

12. Monitoring of thyroid cancer continues in the three countries, Belarus, the Russian Federation (four regions) and Ukraine, where there were higher levels of radionuclide deposition after the Chernobyl accident. The data on the incidence of thyroid cancer have been analysed in a large number of epidemiological studies published in peer-reviewed scientific journals. While most of the available and ongoing studies address the incidence of thyroid cancer in those exposed during childhood or adolescence, some studies address other age groups in the exposed population. There is a discussion in the scientific literature about the effects of "over-diagnosis" caused by the application of new highly sensitive screening techniques.

13. Further, substantial efforts have been undertaken to estimate the doses to the thyroid and to quantify their uncertainties. More than 30 peer-reviewed publications have been reviewed in detail during the preparation of this paper, including publications dealing with:

(a) Theoretical modelling of the development of thyroid cancer;

(b) Pathology and molecular biology of thyroid cancer;

(c) Other thyroid diseases (not covered in this report);

(d) Dose assessment methodologies and associated uncertainties.

A. Epidemiological studies and analyses of radiation risk

14. Brenner et al. [B4] evaluated the dose–response relationship for thyroid cancer among 12,514 members of the UkrAm cohort. The arithmetic mean of the dose to the thyroid from the incorporation of ^{131}I was estimated to be 0.65 Gy. After the first screening (prevalence study [T2]), three biennial thyroid examinations were conducted between 2001 and May 2007 [B4]. All individuals with a nodule of ≥10 mm in its largest dimension, or a nodule of 5–10 mm with ultrasound characteristics suggestive of malignancy were referred for fine needle aspiration. By the end of 2008, a total of 65 thyroid cancer cases had been detected during the second, third and fourth screenings and pathologically confirmed after surgery. Of these, 61 were papillary, three follicular, and one medullary thyroid cancer. Excess rates were estimated using Poisson regression models. The linear dose–response model provided an adequate fit of relative rates in different dose groups. Inclusion of an exponential or a quadratic term did not improve the fit significantly. The ERR model described the data better than the excess absolute rate (EAR) model. The ERR per unit dose to the thyroid was 1.91 (95% CI: 0.43, 6.34) Gy^{-1}. It was higher for residents of the Kyiv oblast (2.70 (95% CI: 0.27, 27.52) Gy^{-1}) and particularly of the Chernihiv oblast (4.07 (95% CI: 0.95, 16.80) Gy^{-1}) than for residents of the Zhytomyr oblast (0.06 (95% CI: <−0.02, 1.08) Gy^{-1}). The ERR per unit dose to the thyroid did not vary with time since exposure, the use of iodine prophylaxis, the iodine status, sex, age, or tumour size. The EAR per unit dose to the thyroid was 2.21 (95% CI: 0.04, 5.78) per 10^4 PY Gy [B4].

15. Zablotska et al. [Z1] investigated the effects of screening, iodine deficiency, age at exposure and other factors on the dose–response relationship. The so-called "Belarusian-American (BelAm) cohort" included Belarusians (aged 18 years or younger at the time of the accident) for whom estimated doses to the thyroid due to ^{131}I were available (based on measurements on the thyroids of individuals and dosimetric data from questionnaires). Examinations of the thyroids were performed for 11,903 individuals during the period 1996–2001, and for 67 individuals during the period 2002–2004. The mean dose to the thyroid was

0.56 Gy (range from 0.0005 to 32.8 Gy). The excess odds ratio (EOR) was modelled using linear and linear–exponential functions. A significant dose–response relationship between the dose to the thyroid due to ^{131}I and the incidence of thyroid cancer was observed; the relationship was linear–exponential over the full range of doses. For doses to the thyroid below 5 Gy, the dose–response relationship was linear, and the values of the EOR per unit dose were estimated for pre-screening cases, cases detected by screening, and the combination of both groups (table 1).

Table 1. Excess odds ratio (EOR) per unit dose for prevalent thyroid cancer cases in a cohort of Belarusians with doses to the thyroid of less than 5 Gy [Z1]

Detection	*Dose group (Gy)*	*Cases*	*EOR per unit dose (Gy)$^{-1}$*
Pre-screening	<5	48	8.18 (95% CI: 2.11, 72.71)
Screening	<5	85	2.15 (95% CI: 0.81, 5.47)
Screening	<1	62	4.92 (95% CI: 1.32, 17.12)
Combined	<5	133	3.16 (95% CI: 1.49, 6.95)

16. Ivanov et al. [I3, I4] analysed the incidence of thyroid cancer among members of the population (aged 0 to 17 years at the time of the accident) in the most contaminated territories of the Bryansk, Kaluga, Oryol and Tula oblasts, which were affected by the Chernobyl accident (cohort of 108,166 people; observation period 1991–2013). A total of 86 cases of thyroid cancer were observed in children aged 0 and 4 years at the time of the accident (mean dose to the thyroid of 326 mGy); 60.5% of the cases were deemed attributable to radiation exposure. In the age group 4–9 years at the time of the accident (mean dose to the thyroid of 149 mGy), 78 cases of thyroid cancer were observed; 30% of them were deemed attributable to radiation exposure. In the age group 10–17 years, four out of 152 observed cases of thyroid cancer (2.6%) were deemed attributable to radiation exposure. The value of the ERR for boys was 2.9 times higher than that for girls (aged 0–17 years at the time of the accident). A statistically significant decrease of the ERR with time since exposure (by a factor of 0.37 over 10 years) was observed for the whole cohort and for boys separately. As with the study of Jacob et al. [J2], the results of this study may be subject to ecological bias.

17. Hatch et al. [H1] studied the health effects of in utero exposure to ^{131}I following the Chernobyl accident. The study included 2,582 children born during the two-month period after 26 April 1986. Of these, 1,494 were from the most affected oblasts of Ukraine. The estimated average prenatal dose due to exposure to ^{131}I was 72 mGy (range from 0 to 3,240 mGy). Screening examinations included ultrasound and palpation techniques, clinical examinations and interviews with the mothers. Based on a total of nine cases by 2015, the authors concluded that an elevated risk of thyroid cancer might exist as a consequence of the exposure during pregnancy. The magnitude of the risk was similar to that observed in the main cohort of children exposed at 1–5 years of age. There was a significant dose–response association with thyroid nodules of 10 mm or larger.

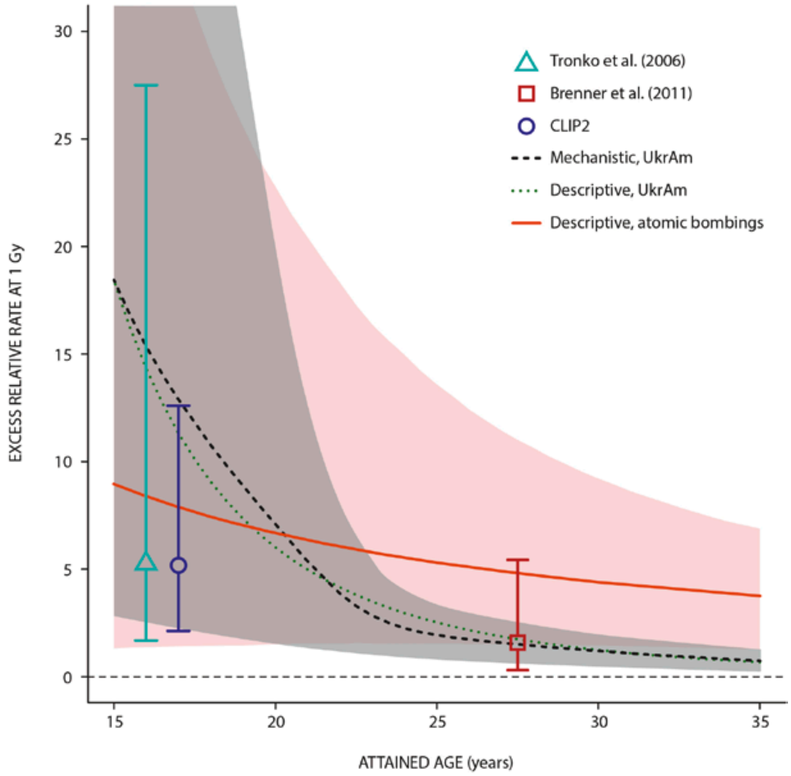
18. In a collaborative case–control study nested within cohorts of Belarusian, Russian and Baltic recovery operation workers, Kesminiene et al. [K2] evaluated the radiation-induced incidence of thyroid cancer. The study included 107 cases and 423 controls. Doses to the thyroid due to external exposure and intake of ^{131}I were estimated for each cohort member. Most of the individuals received low doses (median 69 mGy). A statistically significant dose–response relationship was found with the total dose to the thyroid. The ERR at 100 mGy was 0.38 (95% CI: 0.10, 1.09). The risk estimates were similar when doses from ^{131}I and external exposure were considered separately, although for external exposure, the ERR was not statistically significant.

The ERR was similar for microcarcinomas and larger size tumours, and for tumours with and without lymph-node involvement. Although recall bias and uncertainties in doses could have affected the magnitude of the risk estimates, the findings of this study contribute to a better characterization of the risk of thyroid cancer after radiation exposure in adulthood.

19. Kaiser et al. [K1] included in their study all 115 papillary thyroid cancers reported for the UkrAm cohort that occurred before the screenings, or were detected during the first four screenings. The analysis was based on likelihood functions expressing the different state of knowledge for the prevalent and incident[4] thyroid cancer cases. For an attained age of 27, the ERR per unit dose to the thyroid was estimated to be 1.6 (95% CI: 0.67, 2.6) Gy^{-1}, in good agreement with the result of Brenner et al. [B4] for the incidence in the period 2001–2008. The data do not permit the identification of effects due to age at exposure, age attained or time since exposure. However, a model with a constant EAR per unit dose, which best described the data, resulted in an ERR that depended on the age attained. According to the EAR model, the ERR decreased with increasing age attained. However, the estimate obtained from this model has a very large uncertainty for age below 20 (figure I).

Figure I. Excess relative rate (ERR) per unit dose to the thyroid for cases of thyroid cancer in the UkrAm cohort and among the survivors of the atomic bombings in Japan

The triangle with uncertainty range gives the result for the prevalent cases detected in the first screening [T2], the square with uncertainty range gives the result for incident cases detected in the second to fourth screenings [B4]. The dashed line with darker shading and the dotted line are for papillary thyroid cancer cases detected in all four screenings including those detected among cohort members before the first screening as derived with a mechanistic and a descriptive model, respectively. Results derived from the life span study of survivors of the atomic bombings in Japan (continuous line with lighter shading) are given for comparison. The circle with uncertainty range relates to the ERR for an overexpression of the CLIP2 gene. The ERRs are sex-averaged and 95% confidence ranges are displayed (figure from Kaiser et al. [K1])



[4] Prevalence is the number of cases either reported before a screening (pre-screening cases), or identified during the first screening, while incidence is the number of new cases during a given period, e.g. identified in a screening of persons, who were free of the disease at the previous screening.

20. In summary, the cohort studies in Ukraine and Belarus provide evidence for an ERR per unit dose to the thyroid of the order of 2 Gy^{-1} for the period 2001–2008. There are indications that the ERR was higher during earlier periods after a minimum latent period of a few years.

21. Ecological studies of the incidence of thyroid cancer related to the average regional dose to the thyroid, sex, age at the time of the Chernobyl accident and calendar year are continuing in Ukraine and Belarus. It has been shown that the increase in the incidence rate of thyroid cancer among persons under 18 years old in 1986 was significantly higher in the six oblasts of Ukraine, where the average regional dose to the thyroid was more than 35 mGy, than in the rest of Ukraine [F2]. In subsequent work [B1], the authors provided evidence of a similar effect in those who were adults in 1986. The authors also noted that no significant increase in the incidence rate was observed in persons born after 1986 in these six oblasts.

22. The data in the state registers of Belarus for the period 1978–2015 have also shown a significant increase in the incidence of thyroid cancer in the total population of the country since 1991, which reached a plateau around 2001 and has not declined since then [B3]. The highest incidence was registered in the Gomel and Mogilev regions, where levels of radioactive contamination were higher than in other areas. A strong correlation between the incidence of thyroid cancer and doses to the thyroid was observed. An increased incidence of thyroid cancer occurred also in children and adolescents, especially males, who were evacuated from these areas. No significant increase in the incidence was observed in persons born after 1986. However, both the Ukrainian and Belarusian studies [B1, B3, F2, T3] could not be used to obtain reliable estimates of radiation risk coefficients as they were not free from ecological biases and limitations.

23. Jacob et al. [J3] made calculations predicting the prevalence of thyroid cancer in the first screening in Fukushima Prefecture based on the evidence available from ultrasonic surveys performed in the UkrAm cohort after the Chernobyl accident. In view of the improved technology of ultrasonography and the related detectability of smaller tumours, the detection rate in the Fukushima study was assessed to be a factor of about three higher than in the UkrAm cohort. Based on data from the life span study (LSS) of the survivors of the atomic bombings of Hiroshima and Nagasaki, most of the long-term thyroid cancer risk attributable to the radiation exposure was predicted to accumulate over several decades with the risk during the first years after exposure being a relatively small component of this. Furthermore, the contribution of the first 10 years to the risk over 50 years was predicted to decrease with increasing age at exposure. According to the models applied, the long latency was especially expressed for females: for an age at exposure of 1 year, less than 1% of the attributable risk accumulated during 50 years after exposure would be contributed by the first 10 years.

B. Molecular biology and pathological studies

24. In the past few years, there have been publications that aim to improve the scientific understanding of the development of thyroid cancer. These publications include studies of theoretical modelling of the development of thyroid cancer, and the pathology and molecular biology of thyroid cancer and of other thyroid diseases. The Chernobyl Tissue Bank (CTB) was established in response to the scientific interest in studying the molecular biology of thyroid cancer after the Chernobyl accident [T1]. The project began collecting a variety of biological samples from patients on 1 October 1988, and has supplied material to 23 research projects in Japan, the United States and Europe. Several research groups performed molecular

biological analyses of normal and thyroid cancer tissues from patients who had been exposed during childhood to radiation due to the Chernobyl accident and from non-exposed patients [A1, B4, D2, L1, S1]. A brief overview of possible biomarkers for radiation-induced cancer, which have been identified, is presented here, but further validation is required.

25. Abend et al. [A1] evaluated differential gene expression in thyroid tissue in relation to the dose from exposure to ^{131}I received as a consequence of the Chernobyl accident. They analysed 63 paired RNA specimens from papillary thyroid carcinoma (PTC) that were diagnosed between 1998 and 2008 in the UkrAm cohort. The specimens were taken from fresh frozen tumour and normal tissue provided by the CTB and satisfied the necessary quality control criteria. This study was among the first to provide direct human data on long-term differential gene expression in relation to individual doses to the thyroid due to exposure to ^{131}I and to identify a set of genes that may be important in radiation carcinogenesis.

26. Kaiser et al. [K1] attempted to model molecular data for PTC in the areas affected by the Chernobyl accident making assumptions about the mechanisms for cancer development. They found that an overexpression of the CLIP2 gene could be distinguished statistically for radiation-associated thyroid cancers occurring before age 20 compared to those thyroid cancers that were not radiation-associated. The best estimate of the ERR per unit dose for the CLIP2 overexpression was comparable to the ERR per unit dose for thyroid cancer, and its credibility interval was smaller (figure I). Future research to find and model predictive biomarkers for radiogenic thyroid cancer is warranted; it may shed new light on the pathogenesis.

27. Evidence from pathological analysis showed [Y1] that paediatric PTC was the most prevalent type of thyroid cancer in all studied periods. In recent years, 43.6% of detected PTCs were <10 mm, which reflects the improvement in diagnostic methods. Almost one third of all PTCs were fully encapsulated tumours with minimal invasive properties. A large proportion of them had dominant solid growth patterns. With increasing time after the accident, PTCs with a dominant papillary pattern exhibited more pronounced invasive properties, but, in general, PTCs became less aggressive, which is an important sign for the postoperative prognosis.

C. Dosimetric studies

28. Drozdovitch et al. [D3, D4, D5, D6] described the opportunities and limitations of methodologies used to quantify the absorbed dose to the thyroid gland from various routes of exposure. Because of the short half-lives of the relevant radioisotopes of iodine, measurements covered only a fraction of the population residing in the contaminated regions. A uniform method for dose reconstruction for the population of Belarus and contaminated oblasts of the Russian Federation was described; and the uncertainties of this approach were assessed using Monte Carlo simulation methods. The assessment of doses to the thyroids of individuals took into account the knowledge of their whereabouts and dietary habits (obtained by personal interviews), and information on radionuclide deposition density available for each settlement where they resided after the accident. The dose to the thyroid decreased with increasing age: the median doses were 0.38, 0.37, 0.13, 0.041, and 0.015 Gy for the age groups <2, 2–4, 5–9, 10–14, and 15–18 years, respectively. The doses to the thyroids of young children were found to be higher than those to adolescents. For the same intake of ^{131}I, a child's thyroid receives a higher radiation dose because the same amount of energy is deposited in a smaller thyroid mass. In addition, dairy products, which were the main source of intake of ^{131}I, were reported to be consumed in higher quantities during childhood. The study included an uncertainty analysis: the geometric standard deviation of the dose to the thyroid varied from 1.7 to 4.0 with median values of 2.3 and 2.1 for members of the Belarusian and Russian cohorts, respectively. The

ratios of the “measured” and estimated doses to the thyroid due to ^{131}I were rather wide, both for low and high doses. The mean ratio of dose to the thyroid estimated using the model to that estimated from direct measurements on the thyroid was found to be 2.0 ± 2.2 and the median of the ratios was found to be 1.2. This wide distribution of the ratios shows the relatively large uncertainties involved in the model calculations, which are due to uncertainties in the choice of values for the parameters used in the dosimetry models and in data on individual habits that had been obtained more than 10 years after the accident.

29. Likhtarov et al. [L2] described efforts to improve the estimates of doses to the thyroid for 13,204 members of the UkrAm cohort. All cohort members had at least one direct measurement on the thyroid taken between 30 April and 30 June 1986. These cohort members resided at the time of the accident in the northern parts of the Kyiv, Zhytomyr, or Chernihiv oblasts, which were the most contaminated territories of Ukraine. Doses to the thyroid of the cohort members, which had been estimated following the first round of interviews, were re-evaluated following the second round of interviews. The revised doses to the thyroid ranged from 0.35 mGy to 42 Gy, with 95% of the doses between 1 mGy and 4.2 Gy, with an arithmetic mean of 0.65 Gy, and a geometric mean of 0.19 Gy. Many of the revised estimates of doses to the thyroids of individuals were substantially different from those obtained following the first round of interviews. The responses to the improved questionnaire used in the second round of interviews made it possible to perform a more realistic risk analysis.

30. Skryabin et al. [S3] published a study, which was aimed at determining the volume of the thyroids of children and teenagers (5–16 years of age) living in the Gomel and Mogilev oblasts. The mass of the thyroid is a parameter that accounts for around 50% of the uncertainty in the dose to the thyroid. For a given age and sex, the differences in the dose to the thyroid between children from the Gomel and Mogilev oblasts did not exceed 12%, which is relatively small compared to the differences between individuals in the general population. For children of a given age, the values showed a distribution characterized by a geometric standard deviation of 1.25 to 1.4.

IV. UPDATE OF INCIDENCE RATES OF THYROID CANCER IN BELARUS, RUSSIAN FEDERATION AND UKRAINE

31. A compilation of incidence rates of thyroid cancer between 1982 and 2015 among those exposed under the age of 18 in Belarus, the Russian Federation (the Bryansk, Kaluga, Orel and Tula oblasts) and Ukraine is presented in the annex. It updates table D11 of the UNSCEAR 2008 Report, annex D [U2] with information broken down by age at exposure and for subsequent time periods (usually 5-year intervals).

32. Both the total number of cases and crude incidence rate per 10^5 person-years basically increased monotonically during the last decade (2006–2015). The total number of cases of thyroid cancer registered in the period 1991–2015 in males and females who were under 18 in 1986, for the whole of Belarus and Ukraine and for the four most contaminated regions of the Russian Federation, exceeded 19,000 (table 2). This number is 2.8 times higher than the number of thyroid cancer cases registered in the same cohort in the period 1991–2005 [U2]. On average, the registered numbers of thyroid cancer for females were about four times higher than for males.

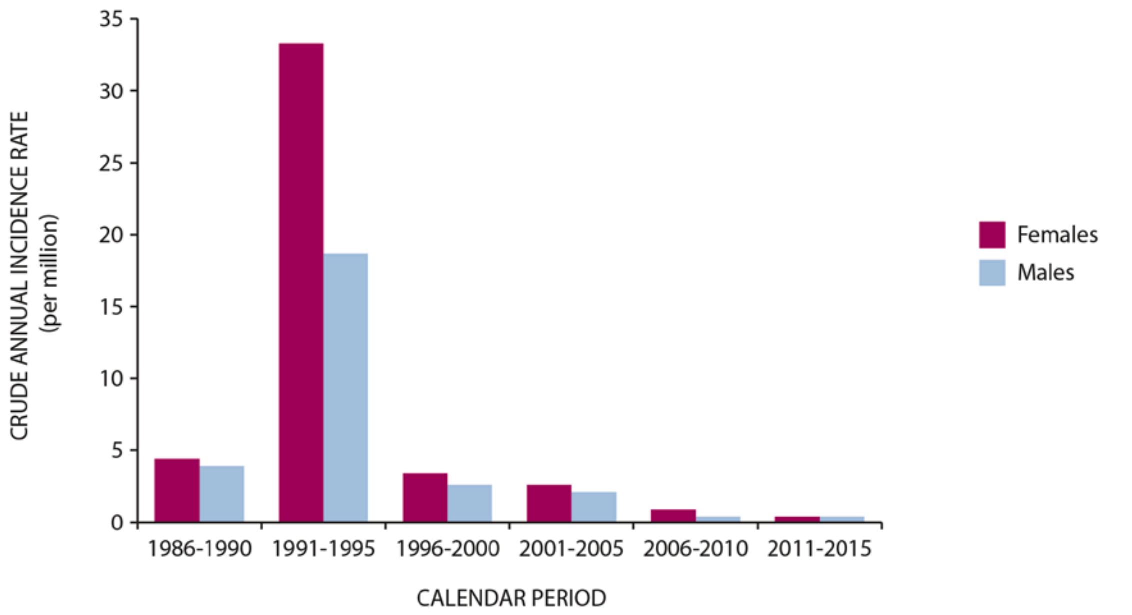
Table 2. Total number of cases of thyroid cancer registered in 1991–2015 among those who were under 18 at the time of the accident

Gender	*Belarus*	*Russian Federation (Bryansk, Kaluga, Orel and Tula oblasts)*	*Ukraine*	*Total*
Females	4 546	1 504	9 393	15 443
Males	1 360	334	2 096	3 790
Total	5 906	1 838	11 489	19 233

33. The observed increase in the incidence of thyroid cancer was influenced by various factors: an increased spontaneous incidence rate with adulthood, radiation exposure, and improvement in diagnostic methods. Discerning the effect of exposure to ionizing radiation contributing to this complicated situation requires both careful epidemiological analysis and basic research into the processes of molecular biology.

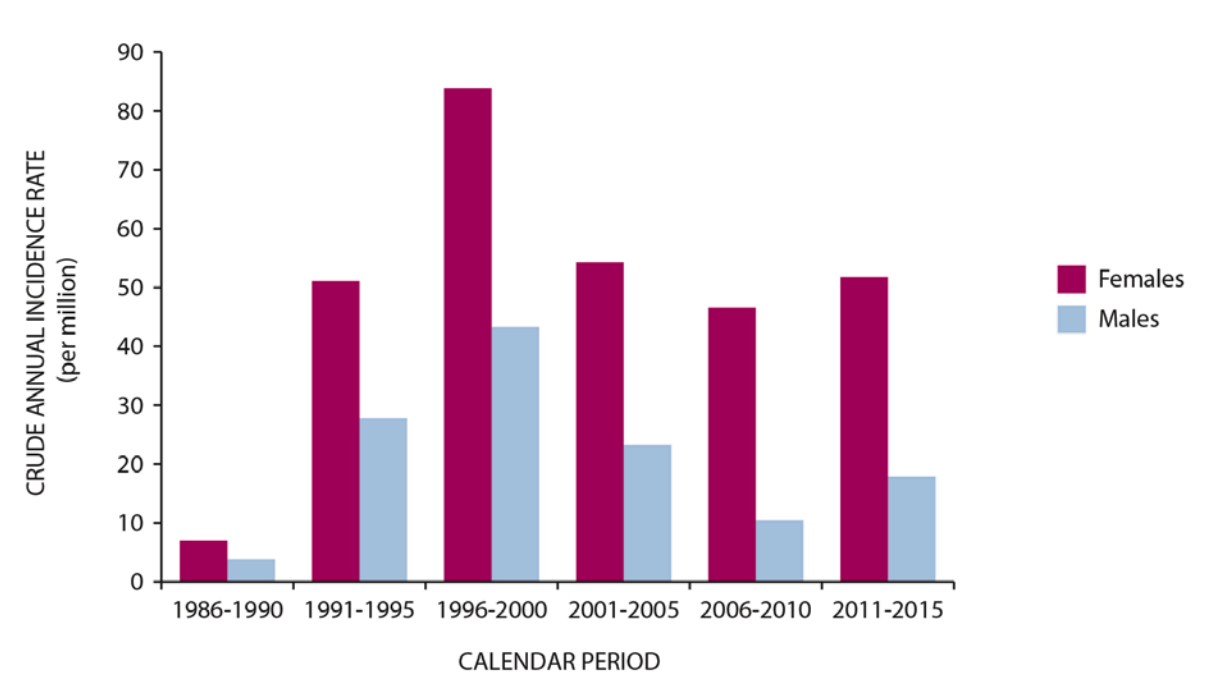
34. The sharp increase in the incidence rate of thyroid cancer among children from about five years after the accident is evident in figure II. The incidence rate of thyroid cancer among Belarusian children up to 10 years old at the time of diagnosis was higher in the period 1991–1995 by about one order of magnitude compared with the incidence rate in other 5-year periods. Both before this period (i.e. before the minimum latent period of 4–5 years) and after this period (i.e. when the cohorts did not include those who were children in 1986), an increase in the incidence rate has not been observed.

Figure II. Incidence rate of thyroid cancer in Belarus for children under 10 years old at diagnosis [D1]



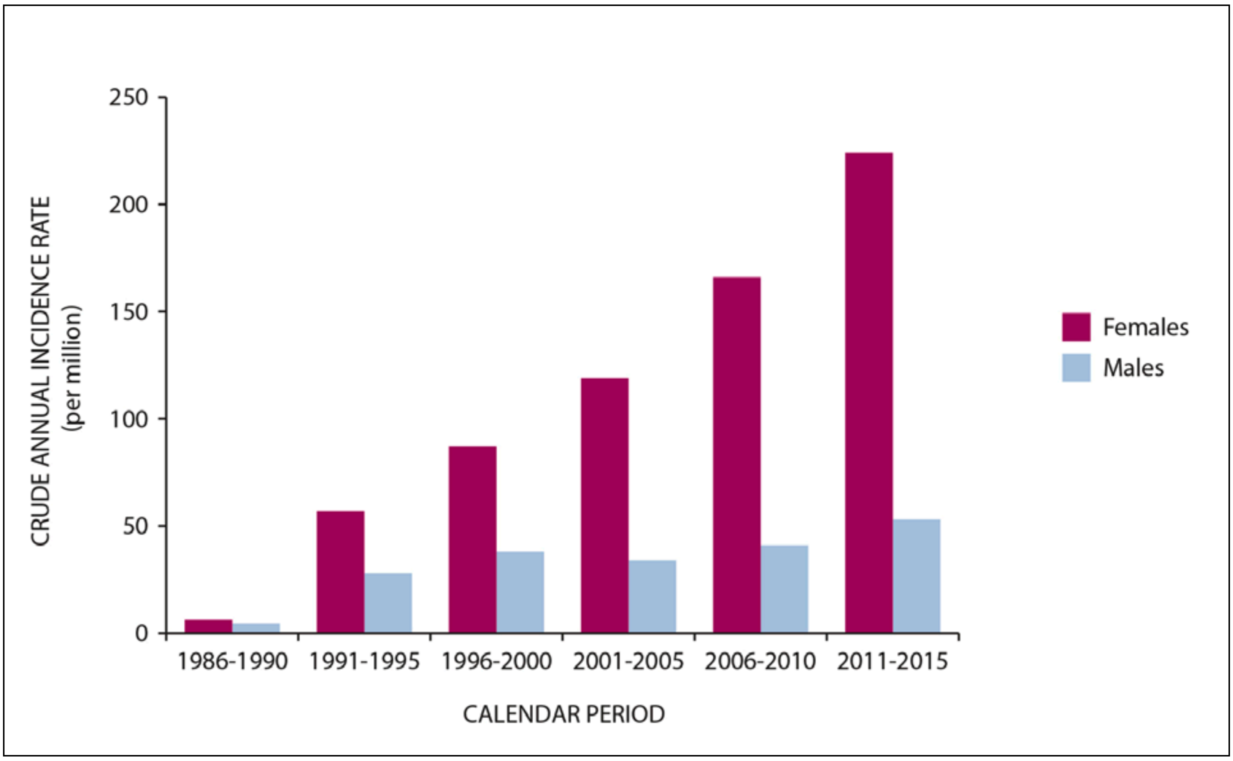
35. A similar, though less pronounced phenomenon, can be observed in cohorts of Belarusian adolescents (aged 10–19 years at diagnosis); see figure III. The incidence rate of thyroid cancer began to increase during the period 1991–1995, reached a peak during the period 1996–2000 and decreased from the period 2001–2005. After 2005, the incidence rate remained higher than that prior to the accident. This apparently reflects the effect of the screening regime. Nevertheless, the incidence rate was significantly lower than in the period 1996–2000 (10–15 years after the accident).

Figure III. Incidence rate of thyroid cancer among adolescents (age at diagnosis 10–19) in Belarus [D1]



36. Figure IV shows the increase in incidence rates of thyroid cancer with time among those exposed as children and adolescents in Belarus at the time of the accident. There is no evidence for a decrease in the excess incidence of thyroid cancer up to 2015. Part of the increase is related to the normal age pattern of spontaneous disease occurrence whereas another part can be deemed attributable to the radiation exposure from the accident.

Figure IV. Incidence rate of thyroid cancer among those in Belarus aged under 18 years at the time of the accident [S4]



V. ASSESSMENT OF THE ATTRIBUTABLE FRACTION

37. The screening in the cohort studies had a significant effect on the absolute incidence rate of thyroid cancer. The crude incidence rate in the UkrAm cohort in the period 2001 to May 2007, for example, was about 100 per 10^5 PY resulting from 65 cases among 12,514 cohort members for an average time of about 5 years between the detection of the new cases and the first screening [B4]. According to the present update of incidence rates of thyroid cancer in the regions affected by the accident, the incidence rate in the same birth cohort and calendar time period in the Ukraine was about 3 per 10^5 PY (see annex). In spite of the large effect on the crude incidence rates, there is no evidence that the ERR per unit dose to the thyroid is significantly influenced by screening. In fact, the confidence bands shown in figure I for the two cohorts, UkrAm and LSS, essentially overlap even though they were subjected to very different screening conditions.

38. An assessment of the fraction of thyroid cancer incidence deemed attributable to radiation due to the accident has been made here based on estimations of average doses to the thyroid, and preconditions that *(a)* the dose–response relationship in the dose range covering the bulk of the doses to the thyroid of the population group of interest is linear, and *(b)* that the estimates of the ERR per unit dose derived from the cohort studies are applicable to the population. Precondition *(a)* might not be true: although there was no evidence for a departure of the dose response from linearity in the UkrAm cohort [B4], there was evidence for a down bending in the BelAm cohort [Z1]. Detailed information on the dose distribution in the population would be necessary to base the estimation of the attributable fraction on a non-linear dose response.

39. As noted before, cohort studies of thyroid cancer among Belarusians and Ukrainians, who were children or adolescents at the time of the accident, indicate an ERR per unit dose to the thyroid of about 2 Gy^{-1} for the period 2001–2008, and a higher value for earlier times after the minimum latent period of a few years. This is consistent with the result of about 6–8 Gy^{-1} in a case–control study of cases in the period 1992–1998 [C1].

40. Estimates of the ERR for thyroid cancer per unit dose to the thyroid from the studies of the survivors of the atomic bombings in Japan showed a decrease with increasing age attained [F1, J3] (see also figure I). For those exposed as children or adolescents and for age attained of about 27, the average age of the UkrAm cohort in the period 2001–2008, the best estimate of the ERR per unit dose of about 2–5 Gy^{-1} was derived, depending on age at exposure [F1]. This value is somewhat higher than that from the cohort studies in Belarus and Ukraine, although the difference is not significant.

41. The average dose to the thyroid of evacuated children and adolescents, and of non-evacuated children and adolescents (at the time of the accident) in the contaminated areas of the former USSR was estimated to about 900 mGy and 170 mGy, respectively [U2]. If it were assumed that for those having been children or adolescents at the time of the accident, the ERR per unit dose was 2 Gy^{-1} for the period 2001–2008, then the ERR for the evacuated and non-evacuated would be estimated to be slightly less than two and about 0.3, respectively.

42. The attributable fraction, AF, is conventionally derived as

$$AF = ERR/(1+ERR)$$

Based on the estimates given above, the fraction of the thyroid cancer cases in the period 2001–2008 attributable to the radiation exposure caused by the accident is assessed to be about 0.6 and 0.25 for the evacuated and non-evacuated children and adolescents, respectively. There is no clear evidence for a value of the ERR per unit dose during other periods. However, there are indications that it was higher in earlier periods and will be slightly lower at later periods. Thus, the estimates of the attributable fraction of 0.6 and 0.25 may be considered to be rough estimates for the whole period 1991–2015.

43. The uncertainty in the estimates is large. Based on only the statistical uncertainty of the ERR per unit dose in the study of Brenner et al. [B4], the estimate of the 95% credibility interval of the attributable fraction for the non-evacuated group would range from 0.07 to 0.5. However, the interval is wider due to other uncertainties including those related to the estimation of average dose, the assumption of a linear dose–response relationship, and the transfer of the result from the UkrAm cohort to the whole population. The width of the credibility interval estimated here—more than a factor of seven (0.5/0.07) between the lower and upper boundaries—is consistent with that obtained in a previous assessment of the Committee of the risk of thyroid cancer among a hypothetical group of Ukrainians exposed to ^{131}I at the age of 10 [U2].

VI. CONCLUSIONS AND RECOMMENDATIONS

44. Various epidemiological studies have shown that the thyroid gland is highly susceptible to the carcinogenic consequences of external exposure to radiation during childhood. Studies of thyroid cancer statistics after exposure to radioiodine released during the Chernobyl accident resulted in comparable estimates of the ERR per unit dose. There are indications of a possible biomarker for radiation-induced thyroid cancer at ages below 20, but independent confirmation is necessary. In the absence of a biomarker, it is impossible to distinguish a radiation-related thyroid cancer from one that develops from other causes. An observed thyroid cancer in an individual among the population of those exposed as children or adolescents at the time of the accident cannot therefore be unequivocally attributed to radiation exposure at the present time.

45. The Committee has estimated the relative fraction of the incidence of thyroid cancer—among non-evacuated residents of Belarus, the four contaminated oblasts of the Russian Federation and Ukraine who were children or adolescents at the time of the accident—attributable to radiation exposure. For the period 2001–2008, the fraction was assessed to be of the order of 0.25. It was probably higher in the first 10 years following a minimum latent period of a few years. Experience from the LSS indicates that it would be smaller after 2008, although the decrease would be expected to be moderate.

46. The uncertainty in the estimated attributable fraction of 0.25 ranges at least from 0.07 to 0.5, which is consistent with that obtained in a previous assessment of the Committee [U2] of the uncertainty related to limitations of the knowledge of the risk of thyroid cancer after exposure to ionizing radiation.

47. Despite the efforts made during the past decade to better understand the risk of radiation-induced thyroid cancer, there are still open questions that require continued follow-up of the health status of the affected populations, as well as basic scientific research on the underlying processes of cancer development. Key scientific questions to be resolved through future research include the continuing need *(a)* to quantify the risk of thyroid cancer after exposure of children to ^{131}I with doses to the thyroid below 500 mGy and for adults at even higher doses; *(b)* to investigate how long any radiation-induced risk of thyroid cancer will persist and how it will reduce with time; *(c)* to improve the understanding of the effects of confounding factors, such as the influence of iodine deficiency on the risk of thyroid cancer; and *(d)* to identify biomarkers for radiation-induced thyroid cancer.

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ANNEX

Incidence rates of thyroid cancer in 1982–2015 among those exposed under the age of 18 in Belarus, Russian Federation (Bryansk, Kaluga, Orel and Tula oblasts) and Ukraine

Update of table D11 in the UNSCEAR 2008 Report, annex D [U2]

***Belarus** [I2, S4]*									
Age at exposure (years)	*Sex*	*Parameter*	*Calendar year periods*						
			1982–1985	*1986–1990*	*1991–1995*	*1996–2000*	*2001–2005*	*2006–2010*	*2011–2015*
0–4	F	Number of cases		11	155	258	209	276	437
		Crude rate per 10^5 PY		0.57	8.02	13.35	10.82	14.52	23.97
	M	Number of cases		9	103	146	79	79	101
		Crude rate per 10^5 PY		0.45	5.21	7.38	3.99	4.01	5.25
5–9	F	Number of cases		9	108	91	169	288	403
		Crude rate per 10^5 PY		0.50	6.02	5.07	9.42	16.57	21.31
	M	Number of cases		10	66	42	59	64	106
		Crude rate per 10^5 PY		0.54	3.59	2.29	3.21	3.66	5.45
10–14	F	Number of cases		8	67	131	202	298	398
		Crude rate per 10^5 PY		0.46	3.85	7.52	11.60	17.46	23.05
	M	Number of cases		7	12	43	60	77	101
		Crude rate per 10^5 PY		0.39	0.67	2.39	3.34	4.67	5.88
15–18	F	Number of cases		15	57	109	223	309	358
		Crude rate per 10^5 PY		1.11	4.21	8.05	16.46	18.23	21.16
	M	Number of cases		5	9	33	40	64	76
		Crude rate per 10^5 PY		0.37	0.66	2.41	2.93	4.0	4.73
Total (0–18)	F	Number of cases	2	43	387	589	803	1 171	1 596
		Crude rate per 10^5 PY	0.04	0.64	5.72	8.71	11.88	16.64	22.38
	M	Number of cases	1	31	190	264	238	284	384
		Crude rate per 10^5 PY	0.02	0.45	2.75	3.82	3.44	4.10	5.34

Russian Federation (Bryansk, Kaluga, Orel and Tula oblasts) *[I1, I2]*

Age at exposure (years)	*Sex*	*Parameter*	*Calendar year periods*						
			1982–1985	*1986–1990*	*1991–1995*	*1996–2000*	*2001–2005*	*2006–2010*	*2011–2015*
0–4	F	Number of cases	0	1	13	36	46	57	96
		Crude rate per 10^5 PY	0.0	0.12	1.5	3.9	5.2	6.3	11.5
	M	Number of cases	0	0	12	26	24	21	15
		Crude rate per 10^5 PY	0.0	0.0	1.3	2.8	2.7	2.2	1.7
5–9	F	Number of cases	1	2	20	37	52	117	133
		Crude rate per 10^5 PY	0.15	0.24	2.4	4.3	6.4	13.4	16.5
	M	Number of cases	0	1	6	10	14	21	19
		Crude rate per 10^5 PY	0.0	0.12	0.69	1.1	1.7	2.4	2.3
10–14	F	Number of cases	0	3	24	48	108	131	178
		Crude rate per 10^5 PY	0.0	0.36	3.0	6.0	13.9	15.3	22.5
	M	Number of cases	0	1	9	9	10	19	40
		Crude rate per 10^5 PY	0.0	0.12	1.1	1.1	1.2	2.3	5.3
15–18	F	Number of cases	1	8	43	61	87	91	126
		Crude rate per 10^5 PY	0.18	1.2	7.2	10.0	13.9	14.4	21.5
	M	Number of cases	0	1	8	14	17	20	20
		Crude rate per 10^5 PY	0.0	0.15	1.3	2.1	2.6	3.3	3.6
Total (0–18)	F	Number of cases	2	14	100	182	293	396	533
		Crude rate per 10^5 PY	0.09	0.44	3.2	5.7	9.5	12.1	17.7
	M	Number of cases	0	3	35	59	65	81	94
		Crude rate per 10^5 PY	0.0	0.09	1.1	1.8	2.0	2.5	3.1

***Ukraine** [B2, I2]*									
Age at exposure (years)	*Sex*	*Parameter*	*Calendar year periods*						
			1982–1985	*1986–1990*	*1991–1995*	*1996–2000*	*2001–2005*	*2006–2010*	*2011–2015*
0–4	F	Number of cases		6	85	202	254	420	957
		Crude rate per 10^5 PY		0.1	0.9	2.2	2.9	4.6	11.0
	M	Number of cases		9	55	91	103	103	183
		Crude rate per 10^5 PY		0.1	0.6	0.9	1.1	1.1	2.0
5–9	F	Number of cases	1	20	106	181	326	601	1 091
		Crude rate per 10^5 PY	0.01	0.2	1.2	2.0	3.9	7.0	14.0
	M	Number of cases		7	40	57	74	121	218
		Crude rate per 10^5 PY		0.1	0.4	0.6	0.8	1.4	2.8
10–14	F	Number of cases	9	35	113	252	496	693	1 148
		Crude rate per 10^5 PY	0.1	0.4	1.2	2.8	5.7	8.3	14.9
	M	Number of cases	7	18	34	55	99	140	248
		Crude rate per 10^5 PY	0.1	0.2	0.4	0.6	1.1	1.7	3.4
15–18	F	Number of cases	15	54	176	277	403	624	988
		Crude rate per 10^5 PY	0.3	0.8	2.6	4.0	5.4	9.7	16.9
	M	Number of cases	7	15	37	53	74	121	190
		Crude rate per 10^5 PY	0.1	0.2	0.5	0.7	1.0	2.0	3.5
Total (0–18)	F	Number of cases	25	115	480	912	1 479	2 338	4 184
		Crude rate per 10^5 PY	0.1	0.3	1.4	2.7	4.4	7.2	13.9
	M	Number of cases	14	49	166	256	350	485	839
		Crude rate per 10^5 PY	0.05	0.1	0.5	0.7	1.0	1.5	2.8

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