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Time Trends of Thyroid Cancer Incidence in Belarus after the Chernobyl Accident

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The rates of childhood thyroid cancer incidence observed in Belarus during the period 1986 to 1995 are described as a function of time after exposure, age at exposure, and sex. Conclusions are drawn for the excess absolute risk function. After a minimum latent period of about 3 years after exposure, this risk function has a linear increase with time for at least 6 years. After correction for the dependence of average doses on age, the radiation-induced absolute thyroid risk in Gomel is about a factor of 3 higher for children up to age 10 at exposure compared to older ones; this may be due in part to different case-collection quality. In addition, in the group up to 10 years at exposure, the thyroid of girls is more sensitive to radiation by a factor of about 1.5 than the thyroid of boys on an absolute scale. Risk estimates from external exposure are consistent with risk estimates from Gomel assuming that the increase in excess cases reaches a plateau soon.

INTRODUCTION

Information on the risk of thyroid cancer after incorporation of ^{131}I during childhood is limited (*1, 2*). Data on thyroid cancer after diagnostic administration of ^{131}I suggest that protraction of the dose may result in a lower risk than an acute exposure to the same dose of X rays (*3*). However, animal studies show similar risks for incorporated ^{131}I and external photon irradiation (see ref. *4*). New data have become available since the Chernobyl accident in 1986 (*5, 6*). The spontaneous rates of childhood thyroid cancer are very low, and they vary a great deal between countries and over time (*7*). For example, in the age group of 1–25 years during the period 1983–1987, the incidence of thyroid cancer in the U.S. (SEER white) was a factor of more than 4 larger than in England and Wales. In the German Democratic Republic, it increased by a factor of about 3 between 1961 and 1989 (*8*). However, in the areas of Belarus most affected by the Chernobyl accident, the recent rates of incidence of childhood thyroid cancer (*5, 9, 10*) are far above the spontaneous rates observed elsewhere (*11*). In the Belarus cancer registry, data on spontaneous risk exist for the time before the accident (*11*), so the data after 1986 can give detailed information about the onset of an additional exogenic risk for a solid tumor in humans. Individual dosimetry for the affected persons is uncertain unless direct thyroid measurements exist. From such activity measurements, of which about 300,000 were performed in Belarus in May and June 1986 (*12*), it is known that the range of doses for persons in one settlement who are of the same sex and age can vary by a factor of more than 100. This is attributed to individual behavior during the first weeks after the accident, such as the quantity of milk consumed, the iodine contamination of the consumed milk, and possibly the intake of stable iodine.

Under these conditions, a long-term cohort study of persons measured directly should supply the most reliable risk coefficients (*13*). However, the number of cases in this group (26 up to 1995 in the group up to age 14 in 1986) is small, and therefore such a study cannot provide detailed information about the early years after exposure. In spite of this small number, long-term follow-up of the cohort of measured persons may well be highly informative and more reliable than other approaches. A case–control study with the aim of deriving information on radiation risk would require a larger number of cases and therefore would have to cope with the uncertainties of individual dosimetry.

Under these special conditions, a geographical study that uses the full number of registered cases may provide useful information that could not be obtained otherwise and can supplement more controlled, conventional epidemiological studies. Some of the potential pitfalls of geographical studies (*14*) are of minor importance here: The excess number of cases is large compared to the expected spontaneous number of cases. In this respect, the situation here is radically different from lung cancer risk due to indoor radon, where a small effect has to be separated from the large risk factor related to smoking. Furthermore, differences in case collection due to different regional procedures are largely avoided. Possible age-dependent differences in diagnosis

TABLE 1
Number of Persons and Thyroid Cancer Cases in the Birth Cohort 1968 to 1986, and Rates in These Regions, as Well as Expected Rates based on Other Registries, 1983–1987

Region	Persons (10^6)	Cases 1986–1995	Cases 1986–1989	Rates per 10^6 PY 1986–1995	Rates per 10^6 PY 1986–1989	Female/all 1986–1995
Belarus (total)	3.1	657	35	21.2	2.8	0.66
Gomel	0.50	301	13	60.2	6.5	0.63
Belarus (excluding Gomel)	2.6	356	22	13.7	2.1	0.69
Belarus 1983–1987				2.8	1.9	0.77
German Democratic Republic 1983–1987				4.8	2.5	0.76
United States 1983–1987				11.7	6.7	0.83
England and Wales 1983–1987				2.5	1.5	0.73

are discussed below in conjunction with the specific numbers.

In the present paper, epidemiological techniques are adapted for analyzing new data from Belarus to derive information on the risk of thyroid cancer after incorporation of ^{131}I. The aim is to extract from the available data those features of the risk function that can be determined most accurately. As the dose reconstruction is difficult and incomplete, features of the risk function which can be extracted with less dosimetric information are done first. For the dependence of the absolute risk function on time since exposure, the only necessary items of dosimetric information are that the overwhelming fraction of exposure to the thyroid occurred within a period of about 1 month after the accident and that excess risk depends linearly on dose. Data on thyroid cancer after external irradiation are consistent with a linear dose response (*2*).

For comparing different age-at-exposure groups, relative average doses are used. Reliable collective dose estimates for some population group are necessary only for the normalization of the excess absolute risk function. Information on individual doses is useful for showing that the dose is responsible for the excess cases and for testing for a linear dose response, but once these facts are accepted, average or collective doses are equally useful. The emphasis in the present approach is on those features of the risk function that can be obtained reliably even with incomplete dosimetric information.

MATERIALS AND METHODS

All thyroid cancer cases in children up to 18 years of age in the year of exposure (i.e. for the birth years 1968 to 1986) are being collected at the Research Clinical Institute of Radiation Medicine and Endocrinology in Minsk. The sources of information on birth year, operation year, sex and place of residence at the time of the accident were the databases of the Belorussian Cancer Registry. Medical histories were obtained from the clinics where the children were operated on and examined after the surgery. Some overall numbers of cases are given in Table 1.

From the census of 1989, the total number of children up to 15.0 years of age is known in each of the six oblasts of Belarus and in the city of Minsk. From this, the approximate number of persons of each sex and in each birth year from 1968 to 1986 was calculated, assuming all are equal. It is also assumed that changes due to emigration from Belarus and due to death are negligible for the period studied here. This crude procedure should give approximate numbers for the actual person-years at risk in Belarus in the various cohorts defined by birth year, sex and place of residence at the time of the accident. By comparing with population numbers from Belarus (*11*), we estimate that this procedure could introduce errors of less than 10%. This uncertainty is small compared to the uncertainties of background rates and affects the findings only in a minor way. Table 2 provides an example of the raw data for Belarus, with both sexes combined.

The absolute risk function describing the additional rates of thyroid cancer incidence by radiation exposure is preferred here to the relative risk function mostly for practical reasons: For example, in the Gomel oblast, there have been 301 cancer cases between 1986 and 1995 for the birth years 1968 to 1986. Approximately 14 cases would be expected on the basis of the incidence rate in Belarus during the period 1983–1987. Uncertainties of this expected number, which are hard to estimate, influence the estimated absolute number of excess cases (about 287) much less than the estimated relative risk (of about 21.5). Also, there are indications that for thyroid tumors (and also for all solid tumors) in young persons, the absolute risk due to radiation exposure (at least for acute external irradiation) tends to vary less over time since exposure (for 15 years after exposure and later) than the relative risk (*15*).

The birth cohorts received the overwhelming proportion of their thyroid dose in the first month after the accident. Therefore, the dependence of absolute risk on time since exposure follows from the corresponding dependence of the number of excess cases. The dependence of the excess absolute risk on age at exposure and sex requires additional (relative) dosimetric information. The average age-specific doses relative to the average doses of adults are taken from published data for the Ukraine, where the analysis of direct measurements is further advanced. The risk function is normalized by comparing with the risk coefficient for a cohort of children from the area of Belarus with the best dosimetric information. Details of these methods are given below.

To simplify comparison between age cohorts and birth cohorts, a power function of age a was fitted to the published information on spontaneous hazard rates of thyroid cancer from various registries. The parameters c_s p_s of the hazard function

$$h(s, a) = c_s a^{p_s} \quad (1)$$

were obtained using Poisson regression to compare observed cases with expected cases from

$$N(s, a) = PY(s, a)h(s, a), \quad (2)$$

where $N(s, a)$ is the expected number of cases of sex s (male, female or both) at mean age a for $PY(s, a)$ person-years at risk. Only the age group from 1 to 30 years was used to avoid distortions by age intervals, which play no role in the group considered here. The parameters found are given in Table 3. Note that the exponents are quite different for the various

TABLE 2
Number of Persons and Number of Cases in Each Year of Registration for Belarus

Birth year	Persons	Number of cases										
		1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	Total
1986	161,587	0	0	0	0	2	2	2	4	3	3	16
1985	161,587	0	1	0	1	3	6	8	17	19	22	77
1984	161,587	0	0	0	0	0	11	6	10	10	20	57
1983	161,587	0	1	0	0	4	11	8	18	6	16	64
1982	161,587	0	0	0	0	4	4	4	9	12	9	42
1981	161,587	0	0	0	1	4	5	7	13	13	11	54
1980	161,587	0	0	0	0	3	5	3	6	16	15	48
1979	161,587	0	0	2	2	0	3	13	7	6	3	36
1978	161,587	0	0	0	0	2	5	8	12	5	9	41
1977	161,587	0	1	0	0	1	4	5	6	6	3	26
1976	161,587	1	0	1	2	1	5	3	5	6	2	26
1975	161,587	0	0	1	0	2	2	3	2	4	3	17
1974	161,587	0	1	1	0	0	2	0	2	4	3	13
1973	161,587	0	0	0	0	2	2	3	4	6	4	21
1972	161,587	0	2	0	1	0	2	4	3	3	5	20
1971	161,587	0	0	0	1	0	4	1	2	7	3	18
1970	161,587	1	3	1	1	0	1	4	5	7	6	29
1969	161,587	0	2	2	2	2	3	6	0	7	4	28
1968	161,587	1	2	0	0	3	1	3	2	9	3	24
Total	3,070,153	3	13	8	11	33	78	91	127	149	144	657

cases. For females they tend to be higher than for males, as the sex ratio depends on age (7). There is no easy ordering, except by plotting the functions. The rates for the U.S. are usually the highest, and the ones for Belarus and England and Wales are at the low end. The coefficients c depend strongly on changes in the exponents p.

RESULTS OF DESCRIPTIVE ANALYSES

General Description of the Observed Number of Cases

Table 1 gives the number of children used in this analysis, the registered number of thyroid cancer cases in 1986–1995 and in 1986–1989, and the rates. For comparison, we calculated the expected rates for the model population of Belarus using the spontaneous rates of other registries (Table 3). While the rates up to 1989 are not exceptional outside the Gomel oblast, in Gomel, they appear to have increased. From the more detailed distribution, this could be interpreted as a screening effect in the older age portion of the population, or as an early radiation-induced increase in the year 1989. For the whole period 1986 to 1995, the rates in Belarus, especially in Gomel, exceed all comparable numbers from earlier registries by a wide margin. The fraction of female cases tends to be a little lower after the accident than in the registries used for comparison.

In Fig. 1 the total number of cases is plotted for Belarus and for the Gomel oblast together with the expected numbers calculated by using the parameters of Table 3 for Belarus. The figure also gives the observed numbers for the two sexes. The observed numbers in 1990 and later are much higher than the expected numbers. Using 2-year averages would smooth the lines. The numbers suggest a description of the excess cases by a linear increase with calendar time from about 1989 to 1995. The number of female cases in 1991 and 1992 in Gomel suggests an "earlier operation effect", as a statistical fluctuation of that size is very unlikely.

The influence of the unknown spontaneous rates on the excess cases was tested using the various hazard functions of Eq. (1). The influence is small for young children, especially in Gomel, but becomes quite important for older children in Belarus as a whole. Figure 2 shows these extreme situations.

Future knowledge of the numbers of cases of children

TABLE 3
Parameters for the Power Law of Eq. (1) for the Age Group of 1–30 Years

Registry	Male		Female		Both	
	$c_m \times 10^8$	p_m	$c_f \times 10^8$	p_f	$c_b \times 10^8$	p_b
Belarus 1983–1987	2.44	1.49	1.14	2.19	1.20	2.02
German Democratic Republic 1983–1987	2.49	1.69	1.52	2.27	1.53	2.12
England and Wales 1983–1987	1.23	1.75	0.342	2.55	0.442	2.33
United States 1983–1987	0.542	2.45	1.43	2.63	0.938	2.60

Note. More digits than justified by the uncertainties are given for numerical reproducibility.

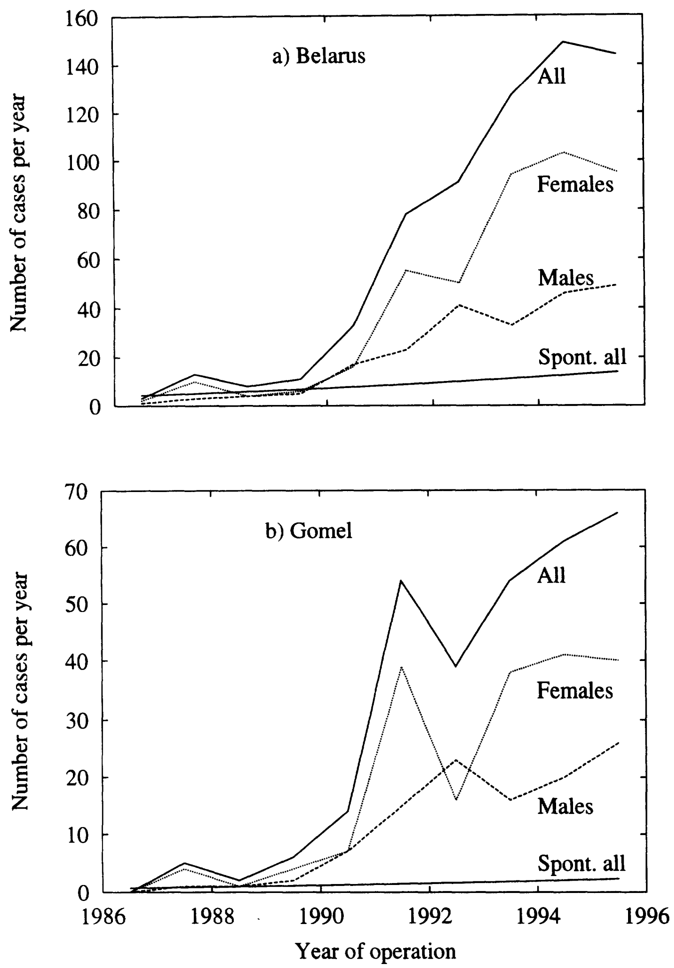

FIG. 1. Thyroid cancer cases in Belarus (panel a), and in Gomel (panel b), as a function of year of operation for children aged 0–18 in 1986 (i.e. birth years 1968–1986). Also plotted is the expected number of cases based on the parameters from Table 3 for Belarus. Spont., spontaneous.

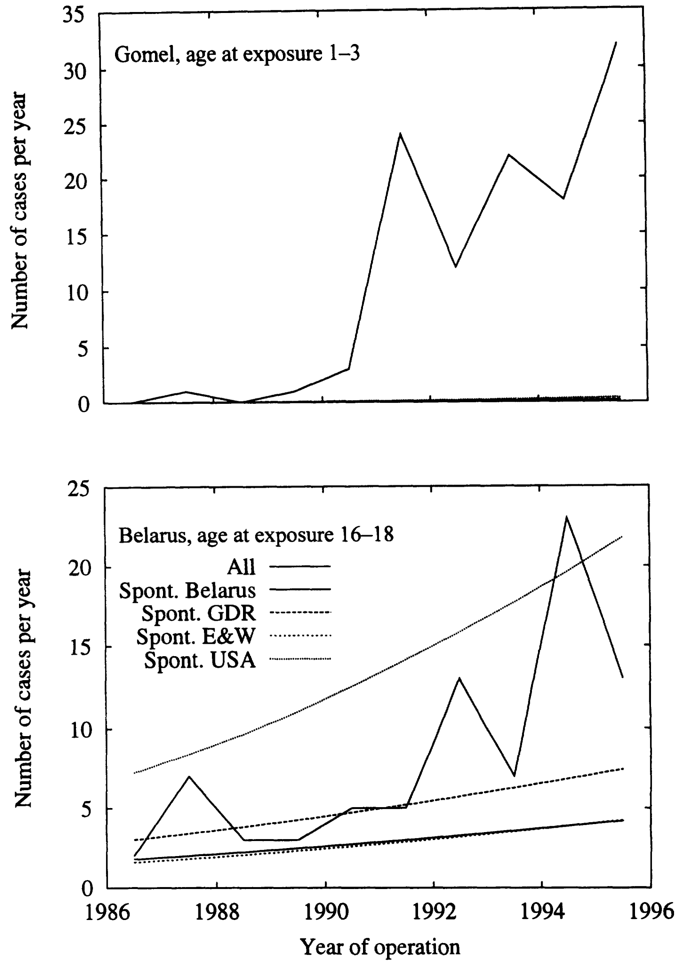

FIG. 2. Observed cases (number of operations per year) and expected numbers as a function of year of operation based on the parameters from Table 3 for different choices of background rates. Shown are the two situations where the difference between the observed and expected number of cases is largest and smallest. Spont., spontaneous; E&W, England and Wales.

born after the accident will allow improvement in the estimates of these rates, which may have to allow for a calendar-time effect.

Dependence on Age at Exposure and Sex

A simple model was fitted for the excess cases $N(t) - N_0$, using the assumption of a minimum latent period t_l before the expression of the radiation-related additional risk and a linear increase with time t afterward:

$$N(t) = N_0 + \theta(t - t_l) \times n_{a_e} \times N' \times (t - t_l). \quad (3)$$

Here N_0 is the expected number of spontaneous cases, and n_{a_e} is the number of birth years considered. The theta function $\theta(x)$ is zero for negative arguments and one for positive ones. The two empirical parameters, minimum latent time t_l and the annual increase in excess cases per year and per birth year N', can depend on age at exposure and on sex. From Fig. 1, it can be seen that the sex dependence of t_l is small, while N' depends strongly on sex. Calendar time t is used here, but it can easily be converted to time since the accident. Later, we will use the rates of annual increase of excess cases per birth year,

$$r' = n_{a_e} \times N'/PY. \quad (4)$$

To investigate the dependence of t_l on age at exposure, the model of Eq. (3) was fitted for various age-at-exposure groups; the results are given in Table 4. The range of t_l was limited to the period 1988–1991 to avoid numerical instability in the fitting procedure in some of the groups. No systematic age-at-exposure dependence of t_l was found. The Gomel oblast has a tendency for a smaller t_l, but since only the operation year was used (and no information on the size of the tumor at operation), the precision of t_l should not be overrated. The results for the young age-at-exposure groups are less sensitive to the actual choice of the spontaneous rates. When calculating an average value for t_l, the data for younger age-at-exposure groups were weighted more than those for older groups. In the following, a common value of

$$t_l = 1989.25 \quad (5)$$

TABLE 4
Estimated Parameters for Minimum Latent Period and Annual Increase in Excess Cases per Year and Birth Year

	Belarus			Gomel		
Age	Male	Female	Both	Male	Female	Both
			Minimum latent period t_l in years since 1900			
0–18	88.4 ± 0.4	89.6 ± 0.2	89.3 ± 0.2	88.5 ± 0.4	88.9 ± 0.4	88.8 ± 0.3
1–6	89.4 ± 0.2	89.5 ± 0.2	89.4 ± 0.2	89.2 ± 0.2	89.2 ± 0.3	89.2 ± 0.3
7–12	88.0 ± 0.2	89.8 ± 0.5	88.1 ± 1.9	88.5 ± 0.8	88.0 ± 2.8	88.1 ± 1.6
13–18	88.0 ± 2.0	90.3 ± 0.5	89.8 ± 0.4	88.0 ± 2.0	88.6 ± 0.8	88.0 ± 3.0
			Annual increase N' per birth year			
0–18	0.37 ± 0.04	0.94 ± 0.08	1.33 ± 0.09	0.20 ± 0.03	0.37 ± 0.05	0.57 ± 0.06
1–6	1.01 ± 0.08	1.57 ± 0.16	2.58 ± 0.20	0.55 ± 0.07	0.83 ± 0.11	1.37 ± 0.14
7–12	0.26 ± 0.04	0.70 ± 0.14	0.70 ± 0.12	0.15 ± 0.05	0.18 ± 0.04	0.32 ± 0.07
13–18	0.06 ± 0.02	0.75 ± 0.16	0.72 ± 0.09	0.015 ± 0.011	0.12 ± 0.04	0.12 ± 0.03
			Annual increase N' per birth year, for t_l = 1989.25			
0–18	0.46 ± 0.03	0.85 ± 0.05	1.30 ± 0.06	0.25 ± 0.02	0.41 ± 0.03	0.65 ± 0.04
1–6	0.98 ± 0.09	1.45 ± 0.11	2.43 ± 0.14	0.56 ± 0.06	0.83 ± 0.08	1.39 ± 0.10
7–12	0.35 ± 0.05	0.60 ± 0.07	0.94 ± 0.09	0.18 ± 0.04	0.25 ± 0.04	0.43 ± 0.06
13–18	0.08 ± 0.03	0.55 ± 0.07	0.63 ± 0.08	0.018 ± 0.014	0.14 ± 0.04	0.16 ± 0.04

is used. It corresponds to a minimum latent period of a little less than 3 years, as the major part of thyroid exposure occurred within a month after the accident on April 26, 1986 (i.e. about 1986.4).

The observed numbers of cases in 3-year age-at-exposure intervals are given in Figs. 3 and 4, as well as the expected numbers based on Eq. (3). The lines correspond to the best estimate of N' with one standard deviation in the Poisson distribution of expected cases. The agreement with this simple model is remarkably good, except for the group of children aged 7–9 in 1986. For them the observed numbers are exceptionally high when they reach about age 14, and then they become unusually low until age 18; the values at around age 18 are comparable to those found for the older age-at-exposure groups. Following the groups for longer periods should show whether this is a real effect or just a random fluctuation.

Note that the data collection procedure may be different for different age groups. To analyze this effect further, the number of cases per birth year and per observation year in Belarus and in Gomel (in the data set used) is plotted as a function of age at operation in Fig. 5. The steep decrease by a factor of about 2 between age 15 and age 16 in both sexes could come about because children (up to age 15) are operated on centrally in Minsk, while older persons are operated on in several clinics. There could be, for example, under-reporting in the older group, earlier diagnosis due to better screening in the younger group, or a mixture of both. Children in school undergo screening programs; such screenings are less frequent for older persons. There is a large difference in the observed number in the females and males older than 16 years. We are not aware of any systematic differences in the collection of cases between the sexes. The situation in the Gomel oblast is not qualitatively different from Belarus as a whole. The smaller increase in the older ages comes from the smaller influence of spontaneous rates.

Such effects of earlier diagnosis or under-reporting do not affect the groups up to age 6 in 1986, as they are 15 or younger in the last observation year 1995, and they barely affect the groups of age 10 and older in 1986, as they are mostly older than 15, when the increase in observed cases becomes important. For the group aged 7–9 years in 1986, the best estimate with all data gives $N' = 1.33$ per birth year for Belarus and both sexes. When restricted to children up to age 15 in the year of operation, the estimate is $N' = 1.81$, and when restricted to older ones, it is $N' = 0.83$. If the differences are due to earlier diagnosis, the best estimate is not affected much. If it actually turns out that case-collection quality plays a major role, the two separate numbers could be used with the respective intervals. In this case comparisons between the older and younger children at exposure would be complicated.

In Fig. 6 the estimated values for N' are given for the six intervals of age at exposure used in Figs. 3 and 4 and for both sexes separately and combined in Belarus and in the Gomel oblast. As can be seen for children aged 1–12 in 1986, the $N'(a_e)$ decreases approximately linearly to a small value and then stays fairly constant for children up to 18 in 1986. For this latter period, the dependence on spontaneous rates is too large to allow more precise statements at present. For children born in 1986, N' is much smaller, about a third to a quarter of those born in 1985. Ten of the 16 children born in 1986 were born in the first 4 months, five in the next 4 months, and only one in the last 4 months. This rapid decrease is a strong indication for causation of the excess by the accident.

The female fraction N'_{female}/N'_{all} is about 0.6 for ages at exposure up to about 10 years. At older ages at exposure it becomes larger for Belarus and smaller for Gomel; this

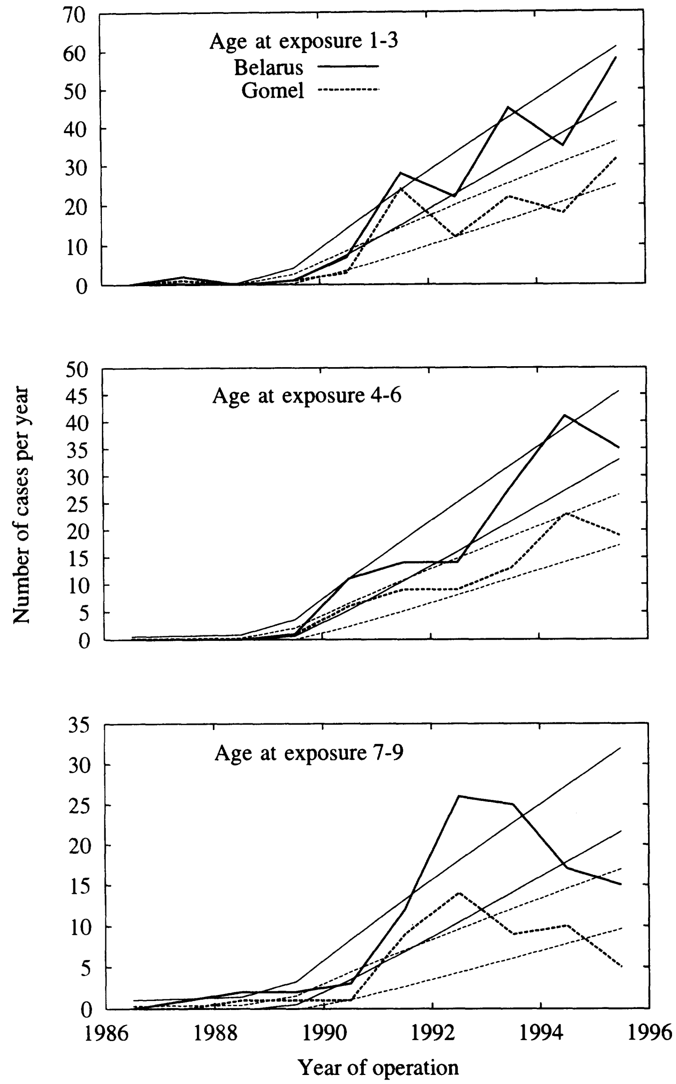

FIG. 3. Thyroid cancer cases (number of operations per years) in Belarus and in Gomel as a function of year of operation for children in various age-at-exposure groups. Also plotted are the boundaries of the expected number of cases given by one standard deviation of a Poisson distribution around the best estimate of the model.

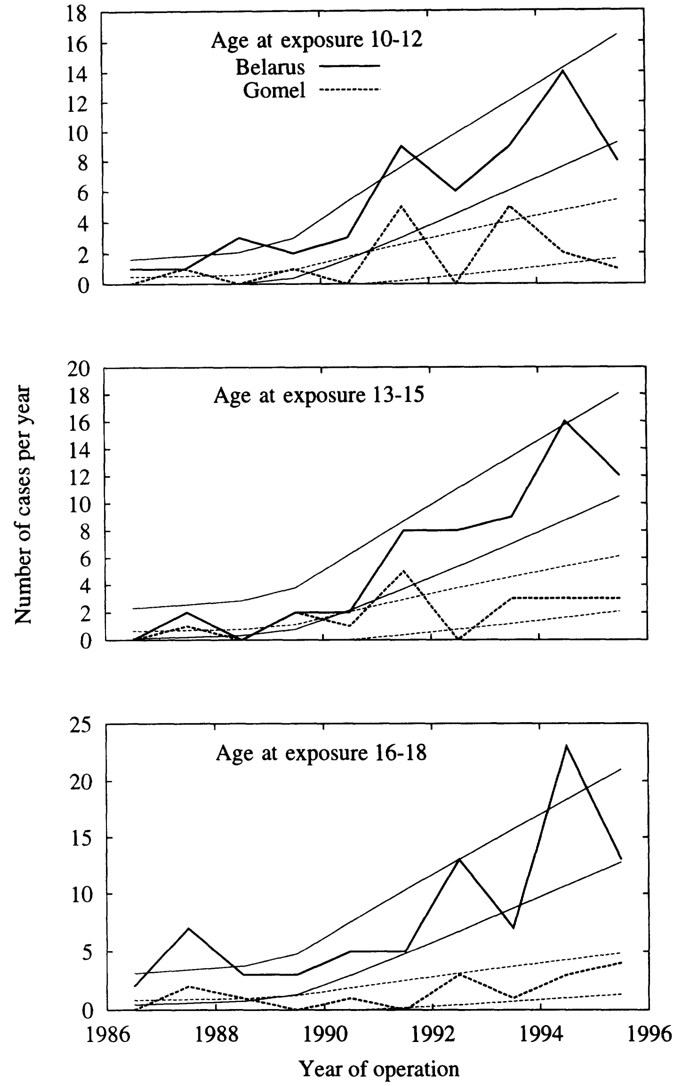

FIG. 4. Thyroid cancer cases (number of operations per year) in Belarus and in Gomel as a function of year of operation for children in various age-at-exposure groups. Also plotted are the boundaries of the expected number of cases given by one standard deviation of a Poisson distribution around the best estimate of the model.

may be due to the relative importance of radiation-induced tumors, but again the uncertainties are large, and definite conclusions in this range will require analysis of further data.

RISK FUNCTION

Dependence on Time since Exposure

The thyroid exposure was accumulated in a short period compared to the minimum latent period. Therefore, the quantity age at exposure is well defined for each individual. For the further analysis, it is assumed that the excess number of cases is linearly related to the dose received, and that the population is homogeneously susceptible to radiation-induced thyroid tumor, except for differences in sex s, age at exposure a_e, and calendar time t. (Linearity in dose is only needed later, but the usual definition of K assumes it; calendar time is easily converted to time since exposure.) A descriptive tool for the summary of radiation-induced risk is the absolute risk function $K(s, a_e, t)$. K is defined for a given population by the equation

$$N(s, a_e, t) = PY(s, a_e, t)[h_0(s, a_e, t) + D(s, a_e) \times K(s, a_e, t)]. \quad (6)$$

In this formula,[1] N is the observed number of cases, PY is the number of person-years at risk in the population, h_0 is the spontaneous thyroid cancer hazard function, and D is the average dose. One aim of our work is to estimate the excess absolute risk function K as well as possible. Alternatively, one could consider the relative risk function. This

[1] To be more precise, integrals over the relevant intervals of a_e and t ought to be written; however, the equation given here is a good approximation if 1-year intervals and mean values are used.

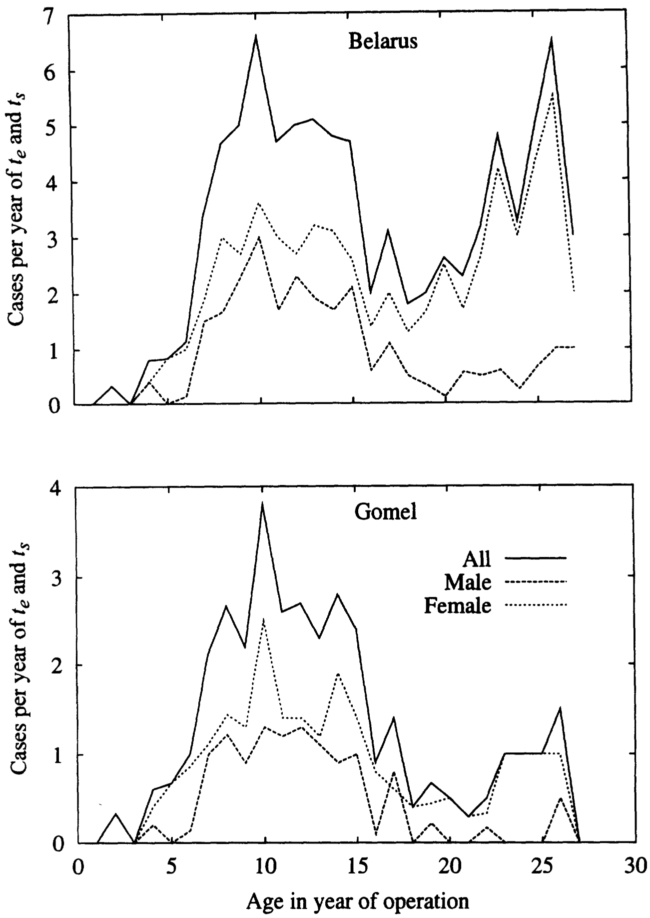

FIG. 5. Number of cases of thyroid cancer in Belarus and in Gomel for birth years 1968 to 1986 per year of age at exposure and year since exposure as a function of year of operation minus birth year.

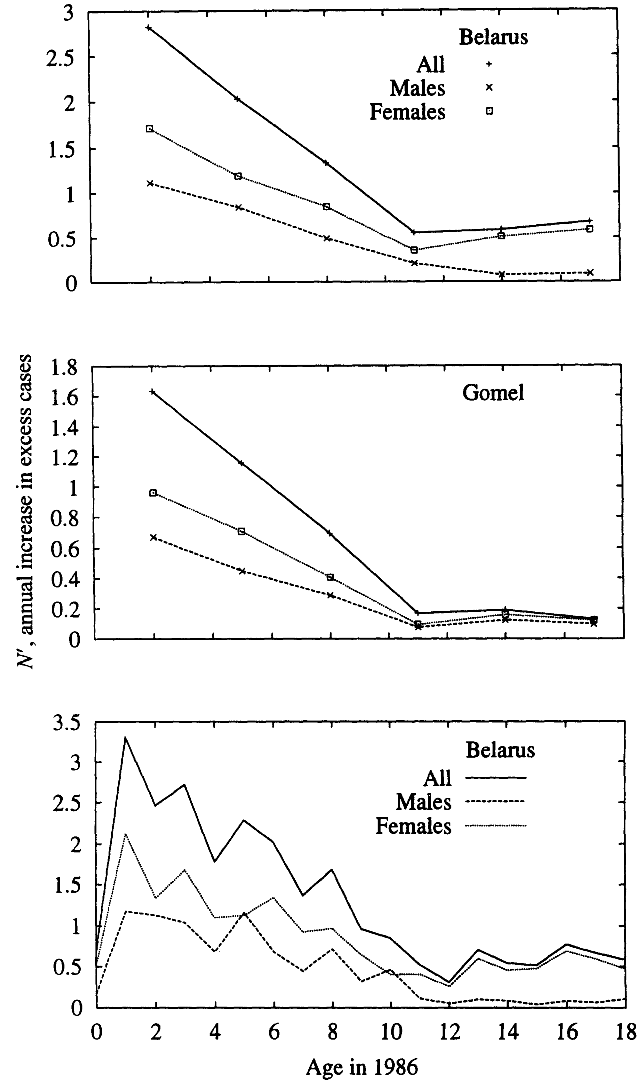

FIG. 6. Annual increase in excess cases per year in Belarus and in Gomel as a function of age at exposure and sex using a minimum latent time of 1989.25 and best estimates of N' in Eq. (3). In the bottom panel an estimate of N' for each birth year is plotted.

would be mathematically equivalent. However, in our case the spontaneous hazard is not well known, and for the most part it is small compared to the total hazard. As mentioned before, the absolute risk function can be determined more precisely under these conditions. If needed, the relative risk function can be calculated from it.

In the present analysis, it was assumed that

1. The person-years PY do not depend on sex, a_e and t (improvements are easily possible, but do not influence the results greatly).
2. The spontaneous hazard function h_0 depends on sex and age only (calendar-time dependence can be included when data on children born after the accident become available).
3. The average dose D after the initial month of intake is independent of calendar time t (no dose-dependent migration or death is to be expected beyond the occurrences of thyroid tumors).

Under these assumptions, the dependence of K on time since exposure can be calculated from Eq. (3) for the observation period up to 9 years after the accident, with the result

$$K(s, a_e, t) = \theta(t - t_l) \times k(s, a_e) \times (t - t_l). \qquad (7)$$

The reduced risk function $k(s, a_e)$ is related to the annual increase of excess absolute risk $r'(s, a_e)$ from Eq. (4) by

$$D(s, a_e) \times k(s, a_e) = r'(s, a_e). \qquad (8)$$

After a minimum latent period of about 3 years, K increases linearly for up to at least 6 years. The minimum latent period is independent of sex and a_e.

This is a more detailed form of the dependence on t than a step function 5 years after exposure, which is used in other risk estimates (*16*).

Dependence on Age at Exposure and Sex

The dependence of k on sex and a_e can be obtained only if we know the dependence of average dose on sex and a_e. Relative average doses can be calculated from the direct thyroid dose measurements. Due to the large numbers (*12*), the statistical errors after averaging become small, but it is

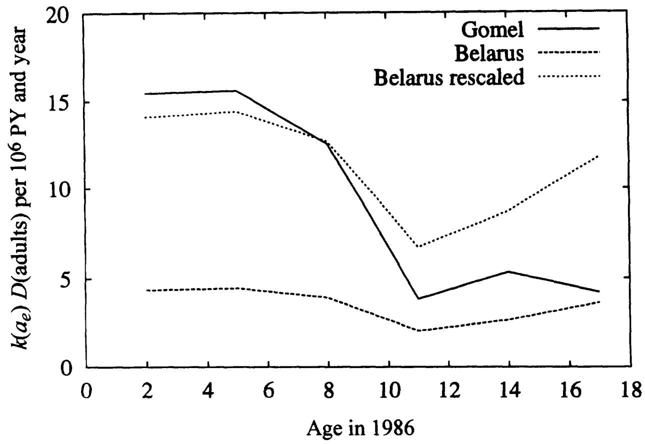

FIG. 7. Dependence of the reduced risk function on age at exposure for both sexes combined, using the relative doses from Chernigov city. For better comparison, the line for Belarus is also rescaled such that at 8 years of age it agrees with the line for Gomel; this corresponds to correcting for different average doses.

necessary to use relative doses from one population for another population. This may be possible, as it essentially has to do with the behavior patterns in the populations in question. Typically, the average doses to children decrease with increasing age at exposure, thus reducing the dependence of k on a_e compared to that of r'. As a demonstration of this proposed method, we use the same function for the age dependence (in years) of average doses (in grays) as that given for Chernigov city, Ukraine (*17*),

$$D_C(a_e) = 0.03 \times 10^{\exp(-0.064 \cdot a_e)}. \quad (9)$$

This formula is proposed for ages up to 20 years for both sexes. The value at age 20 is considered to be applicable to all adults. The relative dose is

$$D_r(s, a_e) = D_C(a_e)/D_C(20). \quad (10)$$

For other areas it is assumed that the age-at-exposure-dependent doses can be expressed by the adult dose for the area as

$$D(s, a_e) = D_r(s, a_e) \times D(\text{adults}). \quad (11)$$

If used in Eq. (8), this gives

$$D(\text{adults}) \times k(s, a_e) = \frac{r'(s, a_e)}{D_r(s, a_e)}. \quad (12)$$

In Fig. 7, these functions are plotted for Belarus and Gomel with both sexes combined. Also plotted is a rescaled curve for Belarus. In this way, the two calculations of $k(a_e)$ can be compared more easily. Up to about 10 years at exposure, the two curves are quite consistent, with Gomel higher than Belarus, as it has higher average doses. For older children, the uncertainties addressed above become more important; as the influence of background estimates is less important in Gomel, the curve for Gomel is considered to be more reliable. For Gomel the reduced risk function is about a factor of 3 higher for children up to age 10 at exposure than for older ones. The relative dose for boys and girls of same age is close to 1 (*17*). Therefore the sex dependence of k is close to the sex dependence of r'; i.e., up to about 10 years age at exposure, it is $k(f)/k(m) \approx 1.5$. This number can be compared with the sex ratio of spontaneous rates: When combining many registries, a female/male ratio of 0.2, 1.2 and 3.6 holds for children aged 1–5, 6–10 and 11–15 years, respectively (*7*). For radiation-induced thyroid tumors, neither the sex ratio of age at exposure nor that of age at operation appears to apply, but rather a value in between. For children older than 10 years at exposure, the uncertainties are too large to draw conclusions at present. We expect to extract relative age- and sex-dependent collective doses from the persons with direct measurements to determine the dependence of k on s, a_e more precisely.

Normalization

If we want to calculate the excess absolute risk per PY Gy of a collective given by birth years and observation period, some calculation gives

$$\frac{\text{Excess cases}}{\text{Collective dose}} = \frac{\sum_t \theta(t - t_l) \times (t - t_l)}{\sum_t 1} \frac{\sum_{a_e} D_r(a_e)k(a_e)}{\sum_{a_e} D_r(a_e)}, \quad (13)$$

where Σ_t 1 is the number of years of the observation period. If there is a reliable risk coefficient for a range of age at exposure and time since exposure, this equation can also provide the normalization of the risk function. For demonstration of this method, we use an EAR of 2.9 per 10^4 PY Gy for children born between 1971 and 1986 for the period 1991 to 1995. This number was calculated by pooling areas with relatively reliable information about collective doses from Belarus (*18*). Using Eq. (13) and the numerical values of Fig. 7, the reduced risk function k and the excess absolute risk function K are fixed. In Fig. 8 we plot the results obtained from Gomel. Also plotted is the excess absolute risk coefficient per gray of 4.4 per 10^4 PY Gy of ref. (*2*) for children exposed externally before 15 years of age. This number is consistent with the risk function derived here. Therefore, it is consistent with a relative biological effectiveness of 1 between external and internal irradiation of the thyroid. This agreement of risk estimates could be an indication that the observed rapid increase in excess cases may reach a plateau soon. We expect that the time-since-exposure pattern will eventually become similar to what has been seen for solid tumors in the atomic bomb survivors (*15*). It can also be seen that the dependence of excess absolute risk on age at exposure and time since exposure is strong, and that the thyroid tumor registries around Chernobyl are a unique resource for studying it.

CONCLUSIONS

The data set for thyroid cancer cases in Belarus among children exposed as a result of the Chernobyl accident has

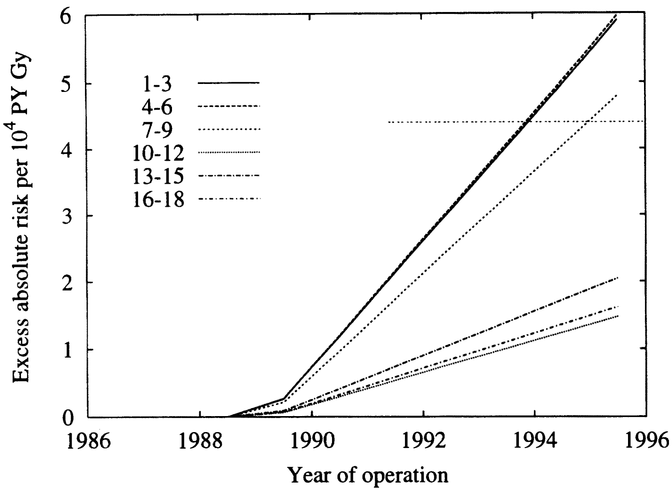

FIG. 8. Excess absolute risk function $K(a_e, t)$ for both sexes combined for various age-at-exposure intervals. The horizontal line at $K = 4.4$ per 10^4 PY Gy represents the estimation for children aged 0–15 years at exposure; see text.

a large number of excess cases. Due to the difficulties of estimating individual doses for the persons at risk, specific methods of extracting information on the radiation risk have been developed.

For the dependence of risk on time since exposure, it is crucial that case-collection quality for the relevant birth years 1968 to 1986 remain high. For the dependence of risk on age at exposure and sex, relative doses were used, which can be determined more accurately than collective or individual doses. For the normalization of the risk function, a group of persons with a reliable collective dose is needed. However, we stress that uncertainties in the estimates of the risk function progressively increase in the following sequence: time-since-exposure dependence at young age, time-since-exposure dependence at older age, age-at-exposure dependence, sex dependence, and normalization. Following the cohorts in the future should give information on the shape of the expected leveling off of excess absolute risk with time since exposure.

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