Thyroid cancer incidence trends in Belarus: examining the impact of Chernobyl

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Background While prior studies of thyroid cancer incidence within Belarus have increased since the 1986 Chernobyl reactor accident, the magnitude of increase is not well quantified.

Methods Using Belarussian national cancer registry data, trends in average annual age-adjusted thyroid cancer incidence rates were examined by calendar year and gender. Incidence rates were also examined across specified time intervals, for specific age groups at diagnosis, and in ‘higher exposure’ regions compared with ‘lower exposure’ areas.

Results Age-adjusted thyroid cancer incidence rates (adjusted to the WHO 2000 world population) have increased between 1970 and 2001 from 0.4 per 100 000 to 3.5 per 100 000 among males (+775%) and from 0.8 per 100 000 to 16.2 per 100 000 among females (+1925%). The relative increase among males (+1020%) and females (+3286%) in ‘high exposure’ areas exceeded increases among males (+571%) and females (+250%) in ‘lower exposure’ areas of Belarus. Dramatic increases in thyroid cancer incidence rate ratios were noted among both males and females and in all age groups. The highest incidence rate ratios were observed among people from ‘higher exposure’ areas ages 0–14 yr at time of diagnosis.

Conclusions Marked increases in the incidence of thyroid cancer have occurred over a relatively limited period of observation in all areas of the Republic of Belarus and among all age categories. The greatest increases have occurred among children, suggesting that a high prevalence of pre-existing iodine deficiency in combination with unique susceptibility among younger people might have contributed to potential carcinogenic exposures to the thyroid.

Keywords Thyroid cancer, incidence, epidemiology, ionizing radiation, Chernobyl

The Chernobyl disaster in April 1986 resulted in the release of substantial amounts of radioactive materials over western regions of what was then the Soviet Union, including radioisotopes of iodine, cesium, strontium, and plutonium. The amounts of radioactivity immediately after the disaster exceeded $10^{18}$ becquerels (Bq).1 The most significant contamination impacted the republics of Belarus and Ukraine, as well as the western region of the Russian Federation.1 While exposures varied within each republic, the most heavily exposed areas within Belarus included the Gomel and Mogilev oblasts (Figure 1).2

Major routes of exposure to iodine isotopes, primarily iodine $^{131}I$, occurred via ingestion, primarily of contaminated milk from cows grazing on contaminated grass, and inhalation of airborne radionuclides.3 Because of the magnitude of the radiation doses to the thyroid, especially in children, an increase in the number of thyroid cancer cases was expected. While countermeasures, such as distribution of stable iodine...
potassium iodide), were reportedly implemented, records of activities are not generally available. Further, it is not clear if these efforts were implemented in a timely and uniform manner so as to have an effect on the uptake of radioiodine by the thyroid.4

There was a dramatic rise in childhood thyroid cancer in Belarus between 1990 and 1993, specifically in the birth cohort born 1 January 1971 to 31 May 1986.5 Heidenreich et al. described childhood thyroid cancer incidence rates observed in Belarus during the period 1986–1995 as a function of time after exposure, age at exposure, and gender.6 They noted an increase in incidence rates from 2.8 per 100 000 during the 1986–1989 time period to 21.2 per 100 000 when viewing the longer time interval of 1986–1995.5

In general, prior studies in Belarus have reported on limited periods of follow-up, typically 6–8 yr following the Chernobyl reactor explosion. For example, the most recent calendar year examined appears to be 1996.5,7 Accordingly, these studies were unable to assess either more recent time periods or more extended patterns of thyroid cancer incidence. Also, several of these studies have focused on selected age groups (e.g. children) and/or specific regions; few studies have relied upon a population approach. Lastly, several of these studies focused upon only numerator data rather than incidence rates. The present paper summarizes data on trends in thyroid cancer incidence rates in Belarus, by gender and age group, including areas highly impacted by the Chernobyl accident.

Methods
The republic of Belarus, an independent state since 1991, has a current population of 10 335 000; 69% are between 15 and 64 yr of age with comparable proportions below and above this group. The republic includes a land area of about 80 000 square miles which is slightly smaller than the state of Kansas within the US. Belarus borders Latvia and Lithuania on the northwest, Russia on the northeast and east, Ukraine to the south, and Poland on the west. Assessment of the geographical distribution of radioactive contaminants reveals that there were high levels of contamination across the Gomel and Mogilev regions1,1 in southeastern Belarus.

The Belarusian cancer registry has been operational since 1993; however, data were not considered sufficiently accurate for statistical analyses until the late 1960s. Data are collected from 12 regional cancer centres (oncological dispensaries) distributed throughout the six regions (referred to as oblasts within Belarus). These oncological dispensaries are responsible for registering all cancer patients residing in their service area and obtaining case data from district hospitals. Since 1973, the system has been computerized. Death certificate cases do not exceed 0.4% of all cases (personal communication, Y Averkin, April 2002). The cancer registration system among former Soviet states, including Belarus, has been detailed by Winkelmann et al.8 Data from the Belarusian Cancer Registry also meets the standards for inclusion in publications by the International Agency for Research on Cancer.9 Pathological confirmation of thyroid cancers varied over the 21-year period: 71% during 1980–1986, 76% during 1987–1991, 89% during 1992–1996, and 95% during 1997–2001. There was a dramatic rise in the proportion of papillary thyroid cases: 28% during 1980–1986, 41% during 1987–1991, 71% during 1992–1996, and 81% during 1997–2001.

Analyses were restricted to primary thyroid malignancies (International Classification of Diseases, Eighth Revision [ICD-8], ICD-9 code 193) among residents of Belarus occurring between 1980 and 2001. The analyses were structured as follows:

**Trends in age-adjusted incidence rates**
Annual age-standardized rates (adjusted using the WHO 2000 world population) were examined by gender.10 Denominator data for each oblast represent official counts provided by the Belarusian Ministry of Statistics and Analyses.

While these data are population based, 95% CI are included with rate ratios (RR) to provide an estimate of precision. Average annual age-adjusted incidence rates were also examined across specified time periods: 1980–1986, 1987–1991, 1992–1995, and 1996–2001.

**Trends in age-specific incidence rates**
Annual age-specific incidence rates were compared, by gender and within specified geographical areas, across several categories based upon age at diagnosis: ≤14 yr of age, 15–34 yr, 35–54 yr, and ≥55 yr. These categories were selected to facilitate meaningful analyses. RR and 95% CI were also calculated.11

**Incidence in Chernobyl-related ‘higher exposure’ versus ‘lower exposure’ areas**
As a crude measure of radiation exposure status, the Mogilev and Gomel regions within Belarus were identified as being the most heavily contaminated9 and were designated as ‘higher exposure’ regions; all other parts of this republic were considered to be ‘lower exposure’ regions. Average annual age-adjusted and
age-specific incidence patterns were compared between ‘higher exposure’ and ‘lower exposure’ regions by gender.

Results

As shown in Figure 2, between 1970 and 2001, age-adjusted thyroid cancer incidence rates have increased from 0.4 per 100 000 to 3.5 per 100 000 among males (+775%) and from 0.8 per 100 000 to 16.2 per 100 000 among females (+1925%). The relative increase among males (+1020%) and females (+3286%) in ‘higher exposure’ areas (Gomel & Mogilev oblasts) exceeded increases of +571% and +250% among males and females in ‘lower exposure’ areas of Belarus (Figure 3).

Data in Table 1 summarizes trends in age-specific incidence rates, by gender for thyroid cancers within three time periods: 1980–1986 (pre-Chernobyl), 1987–1991 (immediate, post-Chernobyl), 1992–1996 (post-USSR break-up), and 1997–2001 (delayed, post-USSR break-up). The incidence patterns are generally consistent with the epidemiological characteristics of thyroid cancer—that is, increasing incidence with increasing age and higher incidence among females. While ratios of incidence rates for the 1980–1986 period are generally comparable for ‘higher exposure’ and ‘lower exposure’ regions, RR increased for all of the later time periods among people in the younger age groups; RR among those aged ≥55 yr failed to demonstrate similar dramatic increases.
Table 1: Age- and sex-specific thyroid cancer incidence rates per 100,000 among residents of Belarus, for 'higher exposure' and 'lower exposure' areas, by gender, age at diagnosis, and time period.

<table>
<thead>
<tr>
<th>Year of diagnosis</th>
<th>Age at diagnosis</th>
<th>'Higher exposure area'</th>
<th>'Lower exposure area'</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Rate</td>
<td>n</td>
</tr>
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<td>1980–1986</td>
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<td></td>
<td></td>
</tr>
<tr>
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<td></td>
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<tr>
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<tr>
<td></td>
<td>Female</td>
<td>118</td>
<td>40.64</td>
</tr>
</tbody>
</table>

- The ‘higher exposure’ areas are Mogilev and Gomel oblasts, the ‘lower exposure’ areas are the rest of Belarus.
- Number of cases.
- Rate ratio (incidence rates in ‘higher exposure’ versus ‘lower exposure’ areas).
Table 2 compares ratios of age-specific incidence rates for thyroid cancer by age group and gender across the four time intervals for residents of ‘higher exposure’ areas in Belarus, 1980–2001

### 0–14 years at diagnosis

| Year of diagnosis | Males | | | | | Females | | | | |
|-------------------|-------|-----|-----|-----|-----|-------|-----|-----|-----|
|                   | n     | Rate| RR  | (95% CI) | n | Rate| RR  | (95% CI) |
| 1980–1986         | 1     | 0.08| 1.00| –         | 2 | 0.15| 1.00| –         |
| 1992–1996         | 80    | 48.94| 578.06| (80.44, 4154.28) | 121 | 77.17| 511.39| (126.44, 2068.28) |
| 1997–2001         | 27    | 18.81| 222.13| (127.37, 387.39) | 60 | 43.84| 290.51| (193.50, 436.16) |

### 15–34 years at diagnosis

| Year of diagnosis | Males | | | | | Females | | | | |
|-------------------|-------|-----|-----|-----|-----|-------|-----|-----|-----|
|                   | n     | Rate| RR  | (95% CI) | n | Rate| RR  | (95% CI) |
| 1980–1986         | 12    | 3.64| 1.00| –         | 34 | 10.79| 1.00| –         |
| 1987–1991         | 17    | 7.58| 2.08| (0.99, 4.36) | 68 | 30.93| 2.87| (4.32, 1.90) |
| 1997–2001         | 144   | 72.98| 20.05| (12.13, 33.15) | 329 | 166.61| 15.44| (20.04, 11.89) |

### 35–54 years at diagnosis

| Year of diagnosis | Males | | | | | Females | | | | |
|-------------------|-------|-----|-----|-----|-----|-------|-----|-----|-----|
|                   | n     | Rate| RR  | (95% CI) | n | Rate| RR  | (95% CI) |
| 1980–1986         | 26    | 11.21| 1.00| –         | 76 | 29.69| 1.00| –         |
| 1987–1991         | 26    | 15.71| 1.40| (0.81, 2.41) | 93 | 53.12| 1.79| (1.32, 2.42) |
| 1992–1996         | 46    | 13.39| 1.19| (0.74, 1.93) | 302 | 170.09| 5.73| (4.46, 7.37) |
| 1997–2001         | 118   | 33.30| 2.97| (1.94, 4.54) | 680 | 356.55| 12.01| (9.67, 2.42) |

### 55+ years at diagnosis

| Year of diagnosis | Males | | | | | Females | | | | |
|-------------------|-------|-----|-----|-----|-----|-------|-----|-----|-----|
|                   | n     | Rate| RR  | (95% CI) | n | Rate| RR  | (95% CI) |
| 1980–1986         | 33    | 24.13| 1.00| –         | 118 | 40.64| 1.00| –         |
| 1987–1991         | 32    | 27.07| 1.12| (0.69, 1.82) | 138 | 62.56| 1.54| (1.20, 1.97) |
| 1992–1996         | 66    | 51.62| 2.14| (1.41, 3.25) | 234 | 104.45| 2.57| (2.06, 3.21) |
| 1997–2001         | 65    | 51.73| 2.14| (1.40, 3.27) | 374 | 172.84| 4.25| (3.50, 5.17) |

* The ‘higher exposure’ areas are Mogilev and Gomel oblasts, ‘lower exposure’ areas include the rest of Belarus.
* Number of cases.
* Rate ratio relative to 1980–1986 period.

Table 2 compares ratios of age-specific incidence rates for thyroid cancer by age group and gender across the four time intervals for residents of ‘higher exposure’ areas. Marked increases in RR were noted among both males and females. These increases were most notable among those aged 0–14 yr at time of diagnosis where RR of 578 and 511 were observed among males and females, respectively, when rates for the period 1992–1996 were compared with the period 1980–1986; RR for the 1996–2001 interval are somewhat lower but remain elevated. Nearly all age groups demonstrated increases of twofold or more between 1980–1986 and 1997–2001, with many RR markedly higher. In addition, these data suggest continued increases in thyroid cancer incidence.

Increases in thyroid cancer incidence were also noted in ‘lower exposure’ regions of Belarus, although the magnitude of these increases was less than those noted in ‘higher exposure’ areas (Table 3). Again, the largest increases were noted among those aged 0–14 yr at time of diagnosis, although increases between twofold and eightfold were observed for the age groups.

### Discussion

This study documents marked increases in the incidence of thyroid cancer among residents of both ‘higher exposure’ and ‘lower exposure’ areas within the republic of Belarus. Increases of this magnitude are remarkable over a relatively limited time period.

External exposures to ionizing radiation have been shown to produce DNA damage, yielding increases in cancers such as thyroid, lung, and breast, and for leukaemias. For thyroid cancer, increased risk has been described both among Japanese atomic bomb survivors and among people who received medical irradiation of the head and neck. Reports have typically noted increased thyroid cancer incidence among females compared with males. Also, earlier age at time of radiation exposure is thought to increase susceptibility as a result of higher radiation doses per unit of thyroid tissue and/or through increased metabolic activity of the thyroid gland relative to adults. While 131I was among several radioisotopes...
released at Chernobyl, exposures to this isotope have not been consistently associated with increased risk of thyroid cancer.18

The presentation of some of the thyroid cancers occurring around Chernobyl are considered to be atypical, suggesting that they may be radiogenic. Thyroid cancers are usually confined to the gland at presentation. However, thyroid cancers found in children who were <2 ys of age at the time of the Chernobyl accident and living in exposed areas at the time of the accident tended to have invasion beyond the thyroid gland.19

A recent review by Moysich et al.18 reconfirmed that there is good evidence from descriptive and analytical epidemiological studies to support the existence of an aetiological association between childhood thyroid cancer and Chernobyl-related ionizing radiation exposure. Among adults, such an association was reportedly less clear. Due to the lower metabolic activity of the thyroid gland in adults these authors concluded that longer follow-up of adult cohorts might be needed to observe a carcinogenic effect. Data in this report are generally consistent with the conclusion of Moysich et al. in that the greatest increases are observed among children.

Marked increases were also evident among people ages 15–35 yr and 35–54 yr at time of diagnosis with RR ranging between 1.6 to 7.8 in ‘lower exposure’ areas and 1.2 to 12 in ‘higher exposure’ areas (Tables 2 and 3). Published reports examining thyroid cancer incidence patterns among adults in the former Soviet Union (FSU) following the Chernobyl disaster are less consistent. Thyroid cancer incidence rates have remained stable within exposed areas of the Ukraine20 and in a district in the Russian Federation.21 In contrast, another report noted increased thyroid cancer incidence among adults from contaminated areas within the Russian Federation.22 Bavrestock et al. stated that increases in thyroid cancer support a causal association with Chernobyl radiation exposures and that future increases in thyroid cancer are likely during the next 50 yr.23

Data provided from the present study suggest that exposure to ionizing radiation has resulted in increased thyroid cancer among both adults and children.

Previous studies of thyroid cancer trends in other parts of the world have reported similar increases in incidence. Zheng et al.23 reported increases in age-adjusted incidence in Connecticut, USA, from 1935–1939 and 1990–1992 in both females (+344%) and males (+823%). Cohort analyses showed that these increases came mainly from groups born between 1915 and 1945. This pattern was hypothesized to be consistent with the introduction of radiation therapy for benign childhood conditions of the head and neck (1920–1950). Since 1945, incidence has decreased in parallel with declines in this form of therapy. Liu et al.24 applied the methods of Zheng et al.23 and noted a doubling for thyroid cancer incidence in Canada from 1970–1972 and 1994–1996 in both females and males. This increase was attributed to increased radiation exposure during childhood and adolescence as a result of more intensive radiological diagnostic activities. It is also important to note that these prior associations were observed for external exposures and are different from the Chernobyl-related exposures, which were internal from radiiodine deposited in the thyroid gland.

Increases in thyroid cancer incidence within Belarus have been documented since the Chernobyl accident.5–7,17,19,25–29 A debate exists about whether the reported increase in the number of cases of childhood thyroid cancer in Belarus is real and attributable to radiation from radioactive iodine released following the Chernobyl nuclear accident, or whether it is due to ‘incorrect histological diagnosis, more complete case reporting, and mass screening of children after the accident’.27,28 Aberin et al. examined histological slides from 1986 to 1992 along with time trends and geographical patterns in incidence and tumour characteristics and concluded that the observed increase was in fact real.27 A case-control study among children in Belarus, completed by Astakhova et al., reported a relationship between thyroid cancer and the estimated radiation dose to the thyroid from the Chernobyl accident; the risk of thyroid cancer increased with increasing radiation dose (odds ratio = 5.8, 95% CI: 2.0, 17.3).28 The fact that thyroid cancer incidence has continued to increase during the 1990s argues against an ascertainment bias as the sole explanation for these patterns.

Drozdovitch et al. applied a 131I environmental transfer model to estimate thyroid doses for different population groups.2 After factoring in various parameters, they determined thyroid exposure to be greatest in the southeastern regions of Belarus (areas closest to the Chernobyl power plant) and lowest in the northwestern part of Belarus. The highest average child doses (>1 Gy) were estimated in the Gomel oblast. The model yielded good correlation with direct measurements of 131I activity in thyroid glands.2

Although there have been estimates of regional differences in levels of radiation exposures, these measures may not be accurate for the individual. Since salt was not fortified with iodine, it is likely that a substantial proportion of Belarusian children were iodine deficient at the time of the Chernobyl disaster.30,31 The release of iodine radioisotopes would represent a clear exposure pathway that might be consistent with observed patterns of thyroid cancer incidence.30 Several reports document continued states of iodine deficiency among Belarusian children31–33 lending support to widespread iodine-deficient states at the time of the Chernobyl accident.

The combination of radiation exposure and iodine deficiency has been reported to increase the risk of thyroid cancer by twofold among children and adolescents exposed to 131I from Chernobyl, suggesting a modifying effect for iodine deficiency.34 Iodine deficiency results in thyroid cell hyperplasia and increased uptake of radioiodine when present in the environment. The most direct evidence of iodine deficiency in Belarus comes from Mityukova et al.33 who examined urinary excretion of iodine. Among 472 children from Gomel oblast studied during 1990–1991, 339 (71%) were found to be mildly (27%), moderately (29%), or severely (15%) iodine deficient. Data from Tuuminen et al.32 are also consistent with a high prevalence of iodine deficiency among newborns from Belarus. Since the potassium iodide distribution within Belarus following the Chernobyl disaster was reportedly ‘inconsistent’,35 large numbers of children with iodine deficiency may have taken up iodine radioisotopes as a result of radioactive fallout, potentiating a carcinogenic effect.
The majority of published studies have utilized a descriptive design and few have included estimates of individual radiation doses to the thyroid. Increased thyroid cancer during the period 1990–1993 was reported among Belarussian children born between 1971 and 1986 and an increase of about tenfold in childhood thyroid cancer rates has been described up through 1995. However, radiation doses to the thyroid among children residing in contaminated areas are known to be variable. Among 32 000 Belarussian children studied, doses ranged from <0.02 Gray to >2 Gray, underscoring the high degree of exposure variation within contaminated areas.

While we cannot explain the aetiology of escalating thyroid cancer incidence rates, it appears likely that continued increases could occur if radioiodine exposures served as a cancer-initiating event. It is therefore important that additional research be done to determine successful mitigating factors for radiation absorption in order to optimize future implementation of preventive measures and minimize future thyroid abnormalities. These measures may include uniform addition of iodide in table salt, as well as improved communication systems to ensure timely administration of potassium iodide in times of potential radiation exposure. These data also argue for the systematic implementation of both immediate and sustained countermeasures in the event of a similar situation occurring in the future.

This study documents dramatic increases in the incidence of thyroid cancer among both ‘higher exposure’ and ‘lower exposure’ areas within the republic of Belarus and among all age groups studied. These increases were most notable among people aged 0–14 yr at time of diagnosis, although other age groups also demonstrated striking escalations in incidence rates. The magnitude of increases observed is remarkable given the relatively limited time interval since Chernobyl and argues for continued surveillance in Belarus as well as other affected areas of the FSU.
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KEY MESSAGES

- Between 1970 and 2001 thyroid cancer incidence rates in Belarus increased from 0.4 per 100 000 to 3.5 per 100 000 among males (+775%) and from 0.8 per 100 000 to 16.2 per 100 000 among females (+1925%).
- The relative increases in areas with ‘higher exposure’ from the Chernobyl disaster exceeded those in ‘lower exposure’ areas with marked increases in thyroid cancer incidence rate ratios among both genders and in all age groups.
- The largest increases were observed among people from ‘higher exposure’ areas ages 0–14 yr at time of diagnosis, suggesting that a high prevalence of pre-existing iodine deficiency, in combination with unique susceptibility among younger people, might have contributed to potential carcinogenic exposures to the thyroid.
- The magnitude of increases observed is remarkable given the relatively limited time interval since Chernobyl and argues for continued surveillance in Belarus as well as other affected areas of the Former Soviet Union.

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