Thyroid cancer among Ukrainians and Belarusians who were children or adolescents at the time of the Chernobyl accident

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Thyroid cancer among Ukrainians and Belarusians who were children or adolescents at the time of the Chernobyl accident

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Abstract

Our objective is to assess the regional and temporal dependences of the baseline cases contributing to thyroid cancer incidence among those exposed in childhood or during adolescence in Belarus and Ukraine after the Chernobyl accident. Data are analysed for Kyiv and Sevastopol City and the 25 oblasts (regions) in Ukraine, and for Minsk and Gomel City and the 6 oblasts in Belarus. Average thyroid doses due to the Chernobyl accident were assessed for every birth year in the period from 1968 to 1985. Case data pertain to people who underwent surgical removal of thyroid cancers during the period 1986 to 2001 and who were allocated to their place of residence at the time of the accident. The 35 oblasts/cities were subdivided into an upper, middle and lower group of baseline thyroid cancer incidence. Poisson regressions were performed to estimate age, time and gender dependences of the baseline incidence rates in the three groups. The majority of oblasts/cities with high average doses and the majority of Belarusian oblasts/cities belong to the upper group of baseline thyroid cancer incidence. The baseline in the upper group is estimated to be larger than in the middle group by a factor of 2.3, and by a factor of 4.0 when...
compared to the lower group. The baseline incidence increases with age and with time since exposure. Estimated baseline incidence rates were found to increase from 1988 to 1999 by factors of three and two for the upper and the two lower groups respectively. The estimated thyroid cancer incidence rates in Belarus and Ukraine, and their dependences on gender and age, are consistent with observed rates found in the larger cancer registries of other countries. In conclusion, the baseline cases are found to contribute about 70% to the thyroid cancer incidence in Ukraine, and about 40% to the incidence in Belarus.

(Some figures in this article are in colour only in the electronic version)

1. Introduction

In the areas contaminated with $^{131}$I from the Chernobyl accident during April and May of 1986, a drastic increase in thyroid cancer incidence has been observed among those who were either children or adolescents at the time of the accident [1–4].

Part of the increase in thyroid cancer incidence in Ukraine and Belarus is due to an awareness of the influence of the Chernobyl accident on thyroid diseases, to the introduction of ultrasound devices, and to mass screening [5]. Screening programmes [6–12] detected a total of 64 cases in Belarus and 120 cases in Ukraine (table 1). However, these cases only constitute a small proportion of the cases reported in the two countries among those who were children or adolescents at the time of the accident. Thus, a more dominant role in the increase could be played by radiation and other factors (such as a greater level of attention to the thyroid during general medical examinations such as, for example, annual health checks at schools) rather than specific screening programmes.

Previous investigations [13, 14] which aimed at quantifying how much of the increased thyroid cancer incidence in Ukraine is directly due to radiation exposure and how much is due to the baseline incidence under the conditions of an intensified surveillance of thyroid diseases, were compromised by being based on a small number of cases or by neglecting temporal or regional variations.

It is the purpose of this paper to present thyroid dose estimates and cancer data for the birth-year cohort 1968 to 1985 in the different oblasts (regions) of Ukraine and Belarus, and to estimate the radiation-independent (baseline) component of the incidence.

2. Materials and methods

The present study uses data for two cities and the 25 oblasts of Ukraine and for two cities and the 6 oblasts of Belarus (figure 1). The cities Minsk, Kyiv and Sevastopol are self-administering units which do not belong to any oblast. For the present study, Gomel Oblast has been subdivided into Gomel City and Gomel Oblast (rural), because of the large number of cases in both sub-areas and because thyroid doses in Gomel City were considerably lower than in the remaining highly contaminated part of the oblast.

2.1. Thyroid dose estimates

Ukraine. The assessment of thyroid doses of the Ukrainian population has been described elsewhere [15]. In brief, the study is based on 83,500 measurements performed in the period 20–40 days after the accident. The gamma dose rate was measured in front of the neck of children and adolescents from 748 settlements. The count rates were corrected for the background
Table 1. Number of thyroid cancer cases detected in various screening programmes in Ukraine and Belarus. ATA indicates age at the time of the accident, ATS age at screening.

<table>
<thead>
<tr>
<th>Study</th>
<th>Area</th>
<th>Age group</th>
<th>Period</th>
<th>Number of cases</th>
<th>Prevalence (cases per 10^6 persons)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Kyiv and Zhytomyr</td>
<td>ATS ≤ 15</td>
<td>1992–1994</td>
<td>5</td>
<td>400</td>
</tr>
<tr>
<td></td>
<td>Mogilev</td>
<td>ATA ≤  10</td>
<td>1991–1996</td>
<td>2</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>Kyiv</td>
<td>ATA ≤  10</td>
<td>1991–1996</td>
<td>6</td>
<td>220</td>
</tr>
<tr>
<td></td>
<td>Zhytomyr</td>
<td>ATA ≤ 10</td>
<td>1991–1996</td>
<td>9</td>
<td>310</td>
</tr>
<tr>
<td></td>
<td>Zhytomyr</td>
<td>ATA ≤ 14</td>
<td>1996–2000</td>
<td>11</td>
<td>1300</td>
</tr>
<tr>
<td></td>
<td>Gomel</td>
<td>ATS ≤ 18</td>
<td>2002</td>
<td>2</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2001–2002</td>
<td>21</td>
<td>1800*</td>
</tr>
</tbody>
</table>

* Incidence: new cases among persons who had been screened before.

counts and for the contributions from radiocaesium contained in the human body. Calibration factors were applied in order to convert the net count rate into the 131I content in the thyroid at the time of the measurement. The time integral of the 131I activity was estimated with the help of intake functions that were derived from a total of 14 000 questionnaire responses, which were obtained between 1992 and 1994. These data were processed in order to obtain average thyroid doses for every birth year in the period from 1968 to 1985 and for both genders in the 748 settlements. A radio-ecological model was developed to estimate thyroid doses in the remaining settlements of Ukraine. Ratios of dose estimates based on the radio-ecological model to dose estimates based on the thyroid measurements were used to improve the radio-ecological model.

Belarus. The derivation of thyroid doses for the Belarusian population has been described elsewhere [16–18]. In brief, dose estimates for 125,000 persons, who had the 131I activity in the thyroid measured during May and June of 1986, were derived based on questionnaire responses including information on the consumption of locally produced milk. Dose estimates in settlements with more than ten measurements of the 131I activity in the human thyroid were

- for Minsk and Gomel City in each age group averages of the individual dose estimates of those who lived in their cities in April to May of 1986 (persons for whom it was known that they spent time in contaminated territories were excluded because they were over-represented among the measured persons and because their influence on the average dose was small);
- in the other settlements based on thyroid doses of measured adults (or measured children if enough measurements were available) and generic age dependences of thyroid doses for different radio-ecological conditions.

For settlements with either only a few or no measurements of the 131I content in the human thyroid, average age-dependent thyroid doses were calculated using a modification of the semi-empirical model [16–18]. This model is based on the relationship between the mean thyroid dose of adults and the deposition density of 131I. In settlements with predominantly dry deposition patterns the derived factor is 1.2 × 10^{-7} \text{ Gy Bq}^{-1} \text{ m}^2; for wet conditions the
factor is $1.3 \times 10^{-8}$ Gy Bq$^{-1}$ m$^2$. Intermediate values were used for settlements in which both deposition modes had been prevalent. Reduction factors were applied to doses in settlements with special conditions, for example, where cows were put on pasture after the radioactive fallout had occurred, where residents were evacuated or relocated, where milk consumption had ceased, or where iodine prophylaxis was applied. Doses to children were derived from doses to adults by applying generic factors for the age dependence.

No information was given on differences between doses to girls and to boys in Belarus. Therefore, ratios of gender-specific doses as found in Ukraine were used in the present analysis for Belarus. Gender-specific doses $D_{i,j}^{city}$ for the birth cohort $i$ in Minsk and Gomel City were calculated according to

$$D_{i,j}^{city} = D_{i,j}^{city K} D_{i,j}^{city K} / D_{i,j}^{K},$$

with

$$D_{i,j}^{K} = (PY_{F,j}^{K} D_{F,j}^{K} + PY_{M,j}^{K} D_{M,j}^{K}) / (PY_{F,j}^{K} + PY_{M,j}^{K}).$$

Figure 1. Study area in Ukraine and Belarus: 31 oblasts (regions) and four cities.
where the index $s$ can be $F$ for females and $M$ for males, the index $K$ stands for Kyiv City, and $PY$ for person years. In the same way, gender-specific doses for the oblasts of Belarus were derived using the gender-ratio of the doses in Zhytomyr Oblast, which is the oblast in Ukraine with the largest number of measurements of the $^{131}I$ content in the human thyroid.

There is secondly a radio-ecological approach for estimating age-dependent average doses of the Belarusian settlements [19]. In order to estimate the dependence of the results on dosimetry, alternative calculations were performed with this radio-ecological approach.

Both countries. According to the data, average doses of 32 of the 35 oblasts/cities are estimated to be in the range 0.005–0.2 Gy (figure 2). The minimum value is 0.004 Gy for Vitebsk Oblast, the maximum value is 0.44 Gy for Gomel Oblast.

The ratio of doses calculated for people born in 1985 to those born in 1968 is 6.6 in the six Belarusian oblasts, and 8.0 in Minsk City (figure 3). Similar ratios were found in Ukraine. In Kyiv City, for example, 18 year olds had an average thyroid dose of 20 mGy, whereas 1 year olds had 110 mGy; this corresponds to a dose ratio of 5.5. The same ratio was observed in Zhytomyr Oblast.

The dose estimates have large uncertainties in areas where no measurements of the $^{131}I$ content in the thyroid had been performed. However, in most of these areas doses were quite low (with the exception of Rivne Oblast (0.1 Gy) and Cherkasy Oblast (0.075 Gy)), so that
the dose uncertainty is expected to have a small influence on the estimation of the baseline incidence.

2.2. Population data

All calculations were performed with data for the age-gender structure of the population in 1986. The loss of follow-up during the period 1986–2001 has been neglected, because it was considered to be small compared to the other sources of uncertainty in the analysis.

- The loss of person years due to death is relatively small because the members of the cohort were quite young during the period of observation.
- The loss of person years and cases due to migration is also considered to be small, because thyroid cancers of people who were exposed as children or adolescents by the Chernobyl accident and who underwent surgery in Belarus, Russia or Ukraine should be reported to the registry of the country where the person lived at the time of the accident. Migration to other countries has been neglected.

The age–gender structure in 1989 is known for the oblasts/cities from an All-Union (Former Soviet Union) census [4, 20]. Age–gender-specific death rates for the period from 1986 to 1988 were used to estimate the population structure in 1986. Migration may cause a bias in this calculation. In order to explore this possibility, a linear interpolation of the census data for 1979 and 1989 was performed. The two methods gave similar results for 1986, indicating that neglecting migration is not a major problem in deriving the population in 1986 from the census data in 1989.
Table 2. Microscopically verified thyroid cancer cases by histological type in Ukraine and Belarus (present study) and in the five largest cancer registries of other countries [29].

<table>
<thead>
<tr>
<th>Country</th>
<th>Period</th>
<th>Follicular carcinoma</th>
<th>Papillary carcinoma</th>
<th>Medullary carcinoma</th>
<th>Anaplastic carcinoma</th>
<th>Other or unspecified</th>
<th>Number of microscopically verified cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belarus</td>
<td>1990–2001</td>
<td>4.0</td>
<td>95.0</td>
<td>0.9</td>
<td>0.1</td>
<td>—</td>
<td>1659</td>
</tr>
<tr>
<td>Ukraine</td>
<td>1990–2001</td>
<td>3.9</td>
<td>94.2</td>
<td>1.7</td>
<td>0.2</td>
<td>—</td>
<td>846</td>
</tr>
<tr>
<td>England, UK</td>
<td>1993–1997</td>
<td>24.4</td>
<td>52.2</td>
<td>5.1</td>
<td>4.5</td>
<td>13.6</td>
<td>4280</td>
</tr>
<tr>
<td>Canada</td>
<td>1993–1997</td>
<td>12.0</td>
<td>79.9</td>
<td>2.9</td>
<td>2.1</td>
<td>3.1</td>
<td>7065</td>
</tr>
<tr>
<td>USA, SEER*</td>
<td>1993–1997</td>
<td>25.8</td>
<td>59.7</td>
<td>3.9</td>
<td>5.0</td>
<td>5.8</td>
<td>1763</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>1993–1997</td>
<td>23.1</td>
<td>54.8</td>
<td>10.8</td>
<td>5.3</td>
<td>6.0</td>
<td>1629</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>1993–1997</td>
<td>12.5</td>
<td>81.5</td>
<td>2.4</td>
<td>1.7</td>
<td>1.8</td>
<td>6296</td>
</tr>
</tbody>
</table>

* Surveillance, Epidemiology, and End Results (SEER) programme.

2.3. Thyroid cancer cases

The present study uses data on thyroid cancer cases among the birth cohort of 1968–1985 and for the operation year period 1986–2001. All cases were related to the place of residence at the time of the accident and not to the place of residence at the time of surgery.

The pathological diagnoses of thyroid cancer cases were based on the WHO classification; most diagnoses were confirmed by an international panel of pathologists. In the period from 1990 to 2001, about 95% of the cases were papillary, about 4% follicular, and the remaining medullary or anaplastic carcinomas (table 2).

For some of the cases the full date of birth was missing and only the birth year was available; therefore, throughout the study only birth years were used. Consequently the age at surgery is defined by the difference between the year of surgery and the year of birth.

Ukraine. The clinical-morphological register at the Institute of Endocrinology and Metabolism of the Academy of Medical Sciences of Ukraine has been described elsewhere [3, 21]. According to the Order of the Ministry of Public Health on the Improvement of Endocrinological Help to the Population from 1992, all thyroid cancer cases among persons who were aged up to 18 years at the time of the Chernobyl accident and who received surgery in Ukraine have to be reported to the register. The data have been cross-evaluated with the Ukrainian Cancer Registry.

Belarus. The following three registers were used to establish a data set for the present analysis:

- Belarusian State Chernobyl Register, which was established in 1993 according to a decree of the Council of Ministers of Belarus, containing data about liquidators and citizens of areas with $^{137}$Cs contaminations exceeding 555 kBq m$^{-2}$.
- Belarusian Cancer Register, which was established in 1953 according to a directive of the Ministry of Public Health of the USSR.
- Medical history records for patients of the National Scientific and Practical Center of Thyroid Tumors in Minsk, where all thyroid cancers of Belarusian children have to be treated.
Table 3. Number of person years and of thyroid cancer cases (in the period 1986–2001) in the birth cohort 1968–85 in Belarusian (bold) and Ukrainian oblasts and cities. The regions/oblasts were grouped according to equation (3) with an ERR per dose of 10 Gy\(^{-1}\) and dose estimates in Belarus based on thyroid measurements and the semi-empirical model; ‘u’ indicates upper group, ‘m’ middle group and ‘l’ lower group.

<table>
<thead>
<tr>
<th>Region, group</th>
<th>(10^5) person years</th>
<th>Cases</th>
<th>Region, group</th>
<th>(10^5) person years</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Brest, u</td>
<td>31.2</td>
<td>30.5</td>
<td>105</td>
<td>191</td>
<td>Kirovohrad, m</td>
</tr>
<tr>
<td>Gomel City, u</td>
<td>10.7</td>
<td>10.4</td>
<td>51</td>
<td>125</td>
<td>Kyiv City, u</td>
</tr>
<tr>
<td>Gomel Oblast, u</td>
<td>24.9</td>
<td>24.9</td>
<td>217</td>
<td>332</td>
<td>Kyiv Oblast, u</td>
</tr>
<tr>
<td>Grodno, u</td>
<td>23.2</td>
<td>22.6</td>
<td>32</td>
<td>51</td>
<td>Luhansk, l</td>
</tr>
<tr>
<td>Minsk City, u</td>
<td>33.7</td>
<td>32.2</td>
<td>40</td>
<td>115</td>
<td>Lviv, l</td>
</tr>
<tr>
<td>Minsk Oblast, u</td>
<td>32.6</td>
<td>31.5</td>
<td>31</td>
<td>74</td>
<td>Mykolaiv, l</td>
</tr>
<tr>
<td>Mogilev, u</td>
<td>26.4</td>
<td>26.4</td>
<td>32</td>
<td>118</td>
<td>Odesa, m</td>
</tr>
<tr>
<td>Vitebsk, m</td>
<td>27.3</td>
<td>26.9</td>
<td>11</td>
<td>57</td>
<td>Poltava, m</td>
</tr>
<tr>
<td>Cherkasy, l</td>
<td>28.9</td>
<td>28.5</td>
<td>15</td>
<td>49</td>
<td>Rivne, m</td>
</tr>
<tr>
<td>Chernihiv, u</td>
<td>25.4</td>
<td>24.4</td>
<td>42</td>
<td>100</td>
<td>Sevastopol, l</td>
</tr>
<tr>
<td>Chernovtsi, m</td>
<td>21.2</td>
<td>20.7</td>
<td>6</td>
<td>26</td>
<td>Sumy, l</td>
</tr>
<tr>
<td>Crimea, l</td>
<td>51.1</td>
<td>48.5</td>
<td>8</td>
<td>43</td>
<td>Ternopil, l</td>
</tr>
<tr>
<td>Dnipropetrovsk, m</td>
<td>77.4</td>
<td>76.8</td>
<td>29</td>
<td>128</td>
<td>Vinnitsia, u</td>
</tr>
<tr>
<td>Donetsk, m</td>
<td>102.9</td>
<td>100.2</td>
<td>42</td>
<td>125</td>
<td>Volyn, l</td>
</tr>
<tr>
<td>Ivano-Frankivsk, l</td>
<td>31.8</td>
<td>30.3</td>
<td>7</td>
<td>21</td>
<td>Zakarpattia, l</td>
</tr>
<tr>
<td>Kharkiv, m</td>
<td>63.0</td>
<td>61.4</td>
<td>18</td>
<td>92</td>
<td>Zaporizhzhia, m</td>
</tr>
<tr>
<td>Kherson, u</td>
<td>26.7</td>
<td>26.2</td>
<td>17</td>
<td>78</td>
<td>Zhytomyr, m</td>
</tr>
<tr>
<td>Khmelnytsk, l</td>
<td>30.7</td>
<td>28.6</td>
<td>10</td>
<td>35</td>
<td></td>
</tr>
</tbody>
</table>

Both countries. The largest number of cases has been reported for Gomel Oblast (549 cases). The ratio of the number of cases among females to the number of cases among males (F/M ratio) was 1.5 in Gomel Oblast (table 3). The highest F/M ratios have been reported for regions which are far from the Chernobyl reactor plant and which were not in the main wind directions during the release, for example a value of 8.3 for Odesa Oblast.

2.4. Analysis of data

Grouping of oblasts/cities according to baseline thyroid cancer incidence. The total thyroid cancer incidence rate \(I_k\) in oblast/city \(j\) was plotted against the average thyroid dose \(D_j\) (figure 2). For a grouping according to the baseline incidence rate, a linear risk model with an excess relative risk (ERR) per dose, \(\beta\), of 10 Gy\(^{-1}\) was used:

\[
I_k = a_k (1 + \beta \cdot D), \quad k = 1, 2.
\]

The chosen value of \(\beta\) is intermediate to values which have been reported in [22] and [23]. For a given baseline incidence rate \(a_k\), the risk model is represented by a line in figure 2. Two baseline incidence rates \(a_k\) were chosen in such a way that there was about an equal number of oblasts/cities in the three areas above, between and below the two functions. Accordingly, oblasts/cities were subdivided in an upper, middle and lower group of baseline thyroid cancer incidence.

In order to study the influence of the classification on the final results, all calculations were repeated

• for a value of \(\beta\) of 20 Gy\(^{-1}\), which is an intermediate value of the ERR per dose if also [4] and [14] are taken into account,
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- and for a grouping of the oblasts according to incidence rates for an excess absolute risk (EAR) per dose, \( \alpha \), of two cases per \( 10^3 \) person year Gy [22],

\[
I_k = a_k + \alpha d, \quad k = 1, 2.
\]  

(4)

**Poisson regression.** Poisson regressions were performed for 20,160 records, defined by 35 oblasts/cities, 2 genders, 16 years of surgery and 18 birth years. The preferred model was

\[
\lambda(l, s, ys, la, d) = \lambda_0(l, s, ys, la)[1 + ERR(s, la, d)],
\]  

(5)

where \( \lambda \) is the total incidence rate, \( \lambda_0 \) the baseline incidence rate, \( l \) for the upper, middle or lower group of oblasts/cities, \( s \) the gender,

\[
ys = \text{year of surgery} - 1995,
\]

\[
la = \ln[(\text{year of surgery} - \text{year of birth})/20],
\]  

(6)

and \( d \) the thyroid dose for the corresponding gender–birth-year group in the oblast/city. The baseline risk was modelled by

\[
\lambda_0 = \exp\left\{\eta_0 + \eta_1 ys + \eta_2 ys^2 + \eta_3 \theta_s + (\eta_{1a} + \eta_{1ag} \theta_s)la + (\eta_{2a} + \eta_{2ag} \theta_s)la^2\right\},
\]  

(7)

and the excess relative risk, ERR, by

\[
ERR = \beta_1 d \exp[\beta_2 \theta_s + \beta_3 la] \theta_{\text{90}},
\]  

(8)

where \( \beta \) and \( \eta \) are fit parameters, \( \theta_s \) is \(-0.5 \) for males and \( 0.5 \) for females, and \( \theta_{\text{90}} \) is \( 1 \) for years of surgery in the period from 1990 to 2001 and \( 0 \) for 1986 to 1989. The ERR was modelled to depend only on gender and attained age, because a study of the radiation-related risk showed for fixed attained age only a moderate dependence on age at exposure [24]. In the final analysis, the parameter \( \eta_{2\text{lower}} \) was set equal to zero, because it was neither significant nor did its inclusion improve the fit significantly.

The regressions were performed with the program AMFIT of the software package EPICURE (Hirosoft International Corporation, Seattle, WA).

**Annual number of baseline cases.** Annual numbers of baseline cases were calculated by multiplying the fitted baseline incidence rates according to equation (7) with the numbers of persons in single oblast/cities. Subsequently, the annual number of baseline cases in a country, or in a part of a country, is obtained by summing up the cases in the pertinent oblasts/cities.

3. Results

3.1. Grouping of oblasts/cities according to baseline incidence

The thyroid cancer incidence rate in the period from 1986 to 2001 for the birth cohort of 1968–1985 is, in 31 of the 35 oblasts/cities, in the range 0.4–5 cases per 10^5 person years (figure 2). The minimal value is about 0.1 cases per 10^5 person years (Ternopil Oblast), the maximum value is about 10 cases per 10^5 person years (Gomel Oblast).

**Main analysis.** The oblasts/cities were grouped according to equation (3) with \( \beta = 10 \) Gy⁻¹ and dose estimates in Belarus based on thyroid measurements and the semi-empirical model. The majority of oblasts/cities with high average doses and the majority of Belarusian oblasts/cities belong to the upper group of baseline thyroid cancer incidence (table 3). Exceptions are Zhytomyr Oblast (relatively high dose of 0.12 Gy) and Vitebsk Oblast (Belarus), both belonging to the middle group.
Table 4. Results of different methods of grouping the oblasts/cities and of using the two different dose systems: oblasts/cities in other groups of baseline incidence as in table 3, deviance of fit according to equations (5)–(8).

<table>
<thead>
<tr>
<th>Dose model in Belarus</th>
<th>Grouping according to ERR model (equation (3))</th>
<th>Grouping according to EAR model (equation (4))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta = 10 \text{ Gy}^{-1}$</td>
<td>$\beta = 20 \text{ Gy}^{-1}$</td>
</tr>
<tr>
<td>Semi-empirical plus thyroid measurements</td>
<td>—</td>
<td>Minsk City, m</td>
</tr>
<tr>
<td></td>
<td>Vitebsk, u</td>
<td>Minsk City, m</td>
</tr>
<tr>
<td></td>
<td>Khmelnytsk, Lviv, m</td>
<td>Khmelnytsk, Luhansk, Lviv, Mykolaiv, m</td>
</tr>
<tr>
<td></td>
<td>10059 (Main analysis)</td>
<td>Kirovohrad, Poltava, Rivne, Zhytomyr, l</td>
</tr>
<tr>
<td></td>
<td>10072</td>
<td>10099</td>
</tr>
<tr>
<td>Radio-ecological</td>
<td>—</td>
<td>Vitebsk, u</td>
</tr>
<tr>
<td></td>
<td>Khmelnytsk, Lviv, m</td>
<td>Khmelnytsk, Luhansk, Lviv, Mykolaiv, Vinnytsia, m</td>
</tr>
<tr>
<td></td>
<td>Vinnitsia, m</td>
<td>10142</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
<td>Kirovohrad, Poltava, Rivne, Zhytomyr, l</td>
<td>10161</td>
</tr>
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</table>

Supplementary analyses. For $\beta = 10 \text{ Gy}^{-1}$ (equation (3)), the grouping is independent of the dose model (table 4).

Compared to the main analysis, six oblasts/cities are shifted to other groups for $\beta = 20 \text{ Gy}^{-1}$, and ten oblasts/cities are shifted for the EAR model (equation (4)). The shifts are independent of the dose model in Belarus, with the exception of Minsk City in which the thyroid dose was, according to the radio-ecological dose model, a factor of two smaller than the dose from measurements. In the analyses based on the semi-empirical model (plus direct measurements of the $^{131}$I content in the human thyroid) Minsk City is shifted to the middle group; in analyses based on the radio-ecological model Vinnytsia Oblast is shifted instead.

The quality of fit as expressed by the deviance is significantly better in the main analysis than in the supplementary analyses. Analyses based on the radio-ecological dose model have much higher deviances than analyses based on the thyroid measurements and the semi-empirical dose model.

3.2. Baseline incidence rate

Main analysis. The analysis had 20,144 degrees of freedom; the fit resulted in a deviance of 10,059. The estimated baseline incidence rate in 1995 and at age 20 is 1.65 (95% CI: 1.47; 1.86) cases per $10^5$ person years in the upper group of oblasts/cities (table 5). It is smaller in the middle group of oblasts/cities by a factor of 2.3, and also smaller in the lower group by a factor of 4.0.

For an attained age of 20 years, the incidence rate among females is larger than for males by a factor of 4.2. The difference in the baseline incidence rate of the two genders increases with attained age (figure 4).

For fixed attained age, the estimated baseline incidence rate increased quickly in the upper group before 1993 (figure 4). Later the relative increase slowed down. From 1988 to 1999 the baseline incidence rate increased by about a factor of three. In the middle group, a similar time pattern was observed, however with a smaller increase. In the lower group, the relative increase in rate was more constant. In both the middle and the lower group, the baseline incidence rate increased from 1988 to 1999 by about a factor of two.

The central estimate for the ERR per dose is $15.2$ (95% CI: $12.1$; $18.4$) $\text{ Gy}^{-1}$, which is intermediate to the two values of $\beta$ used in the grouping procedures of the oblasts/cities.
Table 5. Best estimates and 95% confidence ranges of fit parameters according to equations (5)–(8).

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Value</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\exp(\eta_{0upp}))</td>
<td>1.65 (1.47; 1.86) (10^{-5}) PY(^{-1})</td>
<td>Baseline incidence rate in 1995 and at age 20 in upper group of oblasts/cities</td>
</tr>
<tr>
<td>(\exp(\eta_{0mid}))</td>
<td>0.731 (0.650; 0.824) (10^{-5}) PY(^{-1})</td>
<td>Baseline incidence rate in 1995 and at age 20 in middle group of oblasts/cities</td>
</tr>
<tr>
<td>(\exp(\eta_{0low}))</td>
<td>0.415 (0.367; 0.470) (10^{-5}) PY(^{-1})</td>
<td>Baseline incidence rate in 1995 and at age 20 in lower group of oblasts/cities</td>
</tr>
<tr>
<td>(\eta_{1upp})</td>
<td>0.0788 (0.0637; 0.0939)</td>
<td>Coefficient of (ys) in logarithm of baseline incidence rate in upper group(^a)</td>
</tr>
<tr>
<td>(\eta_{1mid})</td>
<td>0.0458 (0.0269; 0.0647)</td>
<td>Coefficient of (ys) in logarithm of baseline incidence rate in middle group(^a)</td>
</tr>
<tr>
<td>(\eta_{1low})</td>
<td>0.0656 (0.0371; 0.0901)</td>
<td>Coefficient of (ys) in logarithm of baseline incidence rate in lower group(^a)</td>
</tr>
<tr>
<td>(\exp(\eta_g))</td>
<td>4.20 (3.53; 4.98)</td>
<td>Ratio of baseline incidence rate among females and males for attained age 20</td>
</tr>
<tr>
<td>(\eta_{a})</td>
<td>1.84 (1.56; 2.12)</td>
<td>Central coefficient of (la) in logarithm of baseline incidence rate(^b)</td>
</tr>
<tr>
<td>(\eta_{ag})</td>
<td>0.77 (0.38; 1.16)</td>
<td>Difference of coefficients of (la) in logarithm of baseline incidence rate for females and males(^b)</td>
</tr>
<tr>
<td>(\eta_{2upp})</td>
<td>0.0073 (−0.0107; −0.0039)</td>
<td>Coefficient of (ys^2) in logarithm of baseline incidence rate in upper group(^a)</td>
</tr>
<tr>
<td>(\eta_{2mid})</td>
<td>−0.00268 (−0.00700; −0.00163)</td>
<td>Coefficient of (ys^2) in logarithm of baseline incidence rate in middle group(^a)</td>
</tr>
<tr>
<td>(\exp(\eta_\theta))</td>
<td>4.20 (3.53; 4.98)</td>
<td>Ratio of baseline incidence rate among females and males for attained age 20</td>
</tr>
<tr>
<td>(\eta_{a})</td>
<td>0.77 (0.38; 1.16)</td>
<td>Difference of coefficients of (la) in logarithm of baseline incidence rate for females and males(^b)</td>
</tr>
<tr>
<td>(\eta_{ag})</td>
<td>0.392 (−0.023; 0.806)</td>
<td>Difference of coefficients of (la^2) in logarithm of baseline incidence rate for females and males(^b)</td>
</tr>
<tr>
<td>(\beta_1)</td>
<td>15.2 (12.1; 18.4) Gy(^{-1})</td>
<td>ERR per dose for attained age 20</td>
</tr>
<tr>
<td>(\exp(\beta_g))</td>
<td>0.495 (0.362; 0.678)</td>
<td>Ratio of ERR per dose for females and males at attained age 20</td>
</tr>
<tr>
<td>(\beta_\theta)</td>
<td>−2.74 (−3.24; −2.25) Gy(^{-1})</td>
<td>Exponent of attained-age dependence of ERR</td>
</tr>
</tbody>
</table>

\(^a\): \(ys\) is: year of surgery — 1995.
\(^b\): \(la\) is: \(\ln((\text{year of surgery} − \text{year of birth})/20)\).

Supplementary analyses. On average, the supplementary analyses lead to slightly lower estimates of the baseline incidence than the main analysis. In general, the results of the supplementary analyses agree with the results of the main analysis within 20% for all ages attained and for all calendar years considered. The analysis based on the grouping according to the EAR model and on the radio-ecological dose model, however, gives lower results for younger ages: for an attained age of 5 years, for example, the estimate of the baseline incidence rate is on average smaller than in the main analysis by 30%.

In summary, differences of results caused by various methods of grouping the oblasts/cities and dose models are small compared to the variability of the estimated baseline thyroid cancer incidence with gender, attained age, year of surgery, or group of oblast/cities.

3.3. Thyroid cancer cases

In Ukraine, the annual number of observed cases increased with a constant slope from 1989 until the end of follow-up (figure 5). In Belarus, a strong increase in the period 1990–94 was followed by a more modest increase. There seemed to be a constant level of the incidence
Figure 4. Best estimates of the baseline thyroid cancer incidence according to equations (5)–(8).

in Belarus in the period from 1996 to 2001; however, the case number reported for 2002 (not analysed in this paper) indicates a continuation of the modest increase since 1995. The time dependence of thyroid cancer incidence in the more contaminated regions (Zhytomyr, Chernihiv and Kyiv in Ukraine (including Kyiv City), and Gomel in Belarus) is similar to the dependence in the whole countries.

According to the estimates of the present analysis, baseline cases in Ukraine contribute about 70% to the total thyroid cancer incidence in the whole country and about one half in the three northern oblasts (including Kyiv City); in Belarus they contribute about 40%. Considering
the period from 1986 to 1989, there is an indication that the true baseline incidence in Gomel is even larger than in the upper group of the present analysis. Generally, the baseline contributes significantly more to the total incidence for females than for males.

The numbers of baseline cases obtained with the supplementary analyses agree within 20% with the numbers given in figure 5. The largest deviation from the main analysis is obtained if the male cases in the three northern oblasts of Ukraine (including Kyiv City) are calculated for grouping according to the EAR model and using in Belarus the thyroid measurements and the semi-empirical dose model: 66 cases are obtained instead of 79.

4. Discussion

4.1. Discussion of the present analysis

Increase of baseline incidence rate with calendar year. The strong increase of the baseline incidence rate in the upper group of oblasts/cities may be related to the fact that most of the higher contaminated oblasts (Gomel, Kyiv, Mogilev) and also Gomel and Kyiv City belong to this group. In the early 1990s there was a heightened awareness of the health consequences of the Chernobyl accident, resulting in the introduction of regular examinations with ultrasound devices in these areas.

Differences between Ukraine and Belarus. The estimated baseline incidence in Belarus and in areas of Ukraine with high thyroid doses is higher than in other parts of Ukraine. This may be partly due to a more effective case detection and reporting in these areas. This explanation is supported by the fact that the frequency of small tumours (≤1 cm) in Belarus is about 35% [25], which exceeds the frequency in Ukraine considerably, where it has been reported to increase from 3.4% in the period from 1986 to 1995 to 7.9% in the period from 1996 to 2000 [26].
Oblast/city-specific baseline incidence. In general, equation (7), the association in table 3 of an oblast/city to a group of upper, middle or lower baseline incidence, and the parameter values in table 5 may be used for an estimate of the baseline incidence rate in the oblast/city. However, there are three limitations of this approach:

- oblasts/cities were only grouped according to the total incidence in the period from 1990 to 2001. A dependence on time has not been taken into account in the grouping procedure of the oblasts/cities;
- there is an indication in figure 5 (period 1986–1988) that the baseline incidence rate in Gomel is higher than in the upper group of the present paper. From the total incidence rates in figure 2 there is also an indication that the baseline incidence rate in Brest is higher than in the upper group, and rates in Ternopil and Zakarpattia are smaller than in the lower group;
- as demonstrated by the supplementary analyses (table 4), some of the oblasts/cities are intermediate to two groups of the present analysis.

Limitations due to use of average doses. Epidemiological studies based on average rather than individual doses can be subject to an ecological bias in estimations of baseline incidence and excess risk values [27]. Adopting an averaging procedure for the dose evaluation may also mean that other important features of the data could remain undiscovered. This is certainly a weakness of the present study. On the other hand, in 27 of the 35 oblasts/cities, the average thyroid dose was below 0.07 Gy, i.e. the excess relative risk was below 1.0. It can be expected that in such a situation the bias for the baseline incidence is smaller than for the excess relative risk. Therefore, the present study has been limited to an estimation of baseline incidence.

4.2. Comparison with other data and analyses

Thyroid cancer in Belarus. The thyroid cancer incidence, as reported in [28], during the period from 1983 to 1987 in Belarus, was about 0.15 cases per 10^5 PY for 10 year olds, and about 0.33 cases per 10^5 PY for 15 year olds. The incidence ratio for 5–19 year old females and males was 2.8. The results of the present study for the baseline incidence in the years 1986–1987 (figure 4; the main part of Belarus belongs to the upper group) are in good agreement with these numbers: 0.12 cases per 10^5 PY for 10 year olds, 0.34 cases per 10^5 PY for 15 year olds, and an incidence ratio of 3.3.

Thyroid cancer in other countries. The five largest cancer registries (England, UK; Canada; USA, SEER (whites); The Netherlands; Czech Republic) show a monotonic increase of the thyroid cancer incidence rate with increasing age for children, adolescents and young adults (figure 6, [29]). For age 20 years, the incidence rate varies between 3.4 cases per 10^5 PY (among whites in the USA) and 0.85 cases per 10^5 PY (in England). However, [29] notes concerning the data for England: ‘As the national data set comprises contributions from all regional registries it necessarily includes material from those with problems of completeness...’. The second lowest value has been reported for The Netherlands (1.0 case per 10^5 PY). According to the results of the present analysis, the baseline incidence rate in Belarus is about in the middle of the range of incidence rates from the five countries but incidence in Ukraine is at the lower end of this range. The pattern of the increase of the thyroid cancer incidence with attained age is consistent in the seven countries.

In the countries with the five largest cancer registries, the ratio of the thyroid cancer incidence rate for females and males varies at age 20 years between 2.4 (The Netherlands)
Figure 6. Baseline thyroid cancer incidence in 1993–1997 as reported by the five largest cancer registries in [29] (England, UK; Canada; USA, SEER (whites); The Netherlands; Czech Republic), and as derived in the present analysis for members of the birth cohort 1968–1985 in Belarus and in Ukraine.

and 6.3 (among whites in the USA) [29]. Again, the result of the present study (ratio of 4.2) falls in the middle of this range.

It was not possible to identify the distributions of baseline and radiation-induced thyroid cancer cases separately by histological type in the present study. It is obvious that the distribution of all microscopically verified cases in Belarus and Ukraine differs from the distribution in countries not directly affected by the Chernobyl accident (table 2). Whereas papillary carcinomas constitute 95% of the cases in Belarus and Ukraine, they constitute between 52% and 82% in the countries with the five largest cancer registries. Part of this difference is due to the different age distribution (i.e., for the birth cohort of 1968–1985 in the period from 1990 to 2001 for the present study, whereas the data for other countries are for all microscopically verified cases during the period from 1993 to 1997). The difference is an indication of the radiation effect. Papillary cancers are known to be associated with radiation exposure.

Other studies after the Chernobyl accident. Jacob et al [22] estimated that the baseline incidence in the Belarusian area highly contaminated by the Chernobyl accident was a factor of 3 (95% CI: 1–5) larger for the period from 1991 to 1995 than the data covering the period from 1983 to 1987 in [28]. According to the present analysis, the baseline incidence rate in Belarus was 0.85 cases per 10^5 PY for 15 year olds in the period from 1991 to 1995. This is by a factor of 2.5 larger than the value in [28], confirming the assumptions of [22]. In two other papers [4, 14], lower baseline risks were assumed, and this explains why those studies obtained high estimates of relative risk.

Three case-control studies [30–32] showed a strong relation between thyroid cancer and estimated radiation dose from the Chernobyl accident. In one of these studies [32], excess thyroid cancer risk was observed to be higher in rural areas which had a lower content of stable iodine in the soil. In contrast to the rural areas, the populations of large cities have been assumed to be iodine sufficient. In the present study, two of the larger cities considered (Kyiv and Gomel) were in the upper group of baseline thyroid cancer incidence, one (Minsk) in the
middle group, and one (Sevastopol) in the lower group. Thus, no significant difference could be observed between the baseline thyroid cancer incidence rate in the larger cities and in the rural areas.

Acknowledgments

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Thyroid cancer after Chernobyl accident

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