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## THYROID SCREENING AND RELIABILITY OF RADIATION THYROID DOSES FOR THE BELARUSIAN *IN UTERO* COHORT

**Objective.** To describe the status and results of thyroid disease screening and assessment of reliability of radiation thyroid doses in the Belarusian *in utero* cohort of 2,965 individuals exposed to Chernobyl (Chornobyl) fallout.

**Materials and methods.** Thyroid screening examinations are currently underway including thyroid palpation by an endocrinologist, ultrasonographic examination by an ultrasonographer and analysis of blood samples for diagnosis of hypo- and hyperthyroidism, autoimmune thyroiditis, thyroid function tests (thyroid-stimulating hormone [TSH], thyroxine [T4], thyroid peroxidase antibody [anti-TPO], and thyroglobulin antibodies [anti-TG]). Reliability of (i) information from 780 pairs of questionnaires obtained during the first and second interviews of the mothers and (ii) thyroid doses, which were calculated for the cohort members using this information, is evaluated.

**Results.** As of 15 August 2021, 1,267 *in utero* exposed study subjects had been screened. A single thyroid nodule was diagnosed in 167 persons (13.2 % of the total) and multiple thyroid nodules in 101 persons (8.0 %): 189 (14.9 %) persons had nodules detected for the first time at the screening while 79 (6.2 %) persons had nodules detected previously (pre-screening nodules). Fifty-nine out of 268 subjects (22.0 %) with a suspicious thyroid nodule were referred to fine needle aspiration biopsy, and among them 33 (55.9 %) were biopsied. Reasonable agreement was observed for *model-based* doses calculated for the Belarusian *in utero* cohort members using data from the two interviews (Spearman's rank-correlation coefficient  $r_s = 0.74$ ,  $p < 0.001$ ), while *measurement-based* doses yielded almost perfect agreement ( $r_s = 0.99$ ,  $p < 0.001$ ).

**Conclusions.** During the thyroid screening, at least one thyroid nodule was identified in 268 of 1,267 (21.2 %) *in utero* exposed cohort members. Seven thyroid cancer cases were identified in the cohort, including 5 pre-screening cases and 2 cases detected during the screening. Ongoing research on this unique cohort will provide important information on adverse health effects following prenatal and postnatal exposure to radioiodine and radiocesium isotopes, for which available epidemiological data are scant.

**Key words:** Chernobyl, Chornobyl, exposure, *in utero*, early life, thyroid cancer, reliability.

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## INTRODUCTION

Understanding both acute and long-term health consequences of exposure to radiation is critical in developing effective countermeasures for preventing adverse health effects following radiation exposure. There is special concern regarding the health of persons exposed during vulnerable prenatal and early postnatal periods. Knowledge of the carcinogenic effects of *in utero* exposure to ionizing radiation derives mainly from the follow-up of the atomic bomb survivors in Hiroshima and Nagasaki [1, 2] and children born to mothers exposed to diagnostic X-rays during pregnancy [3, 4]. While these studies provide information on the effects of external acute gamma- or X-irradiation, there are also two cohorts of subjects exposed prenatally to a mixture of gamma and other types of radiation: the offspring of female workers at the Mayak plant in Russia and those born to mothers living near the Techa River [5–7]. Until recently, the most relevant sources of information on the effects of prenatal radioiodine exposure had been a cohort of 2,582 individuals in Ukraine exposed *in utero* to Chernobyl (Chornobyl) fallout [8, 9]. A remarkably high excess radiation-related risk for thyroid cancer and large thyroid nodules was reported from this study, but the risk estimates were based on a small number of cases with large statistical uncertainty.

From December 2012 through July 2017, the Republican Research Center for Radiation Medicine and Human Ecology (RRCRM&HE, Gomel, Belarus) collaborated with the National Cancer Institute (NCI, Bethesda, MD, USA) to construct a cohort of 2,965 persons exposed *in utero* in Belarus. Since November 2017 the subjects of the Belarusian *in utero* cohort have been undergoing thyroid screening and the reliability of their radiation thyroid dose estimates has been evaluated. However, due to the COVID-19 pandemic, all study field activities involving in-person interaction have been suspended since April 2020, although thyroid screening and re-interview of the mothers on a smaller scale were resumed in August 2020. This paper reports the study progress as of August 15, 2021.

## OBJECTIVES

The objectives of this paper are: (1) to describe the medical screening in progress in the Belarusian *in utero* cohort of individuals exposed to <sup>131</sup>I, focused on thyroid cancer and other thyroid diseases, including follicular adenoma, benign nodules, diffuse goiter, hypothyroidism, hyperthyroidism, and autoimmune

thyroiditis, and (2) to report on the assessment of the reliability of radiation doses for the cohort members using repeated personal dosimetry interviews of their mothers.

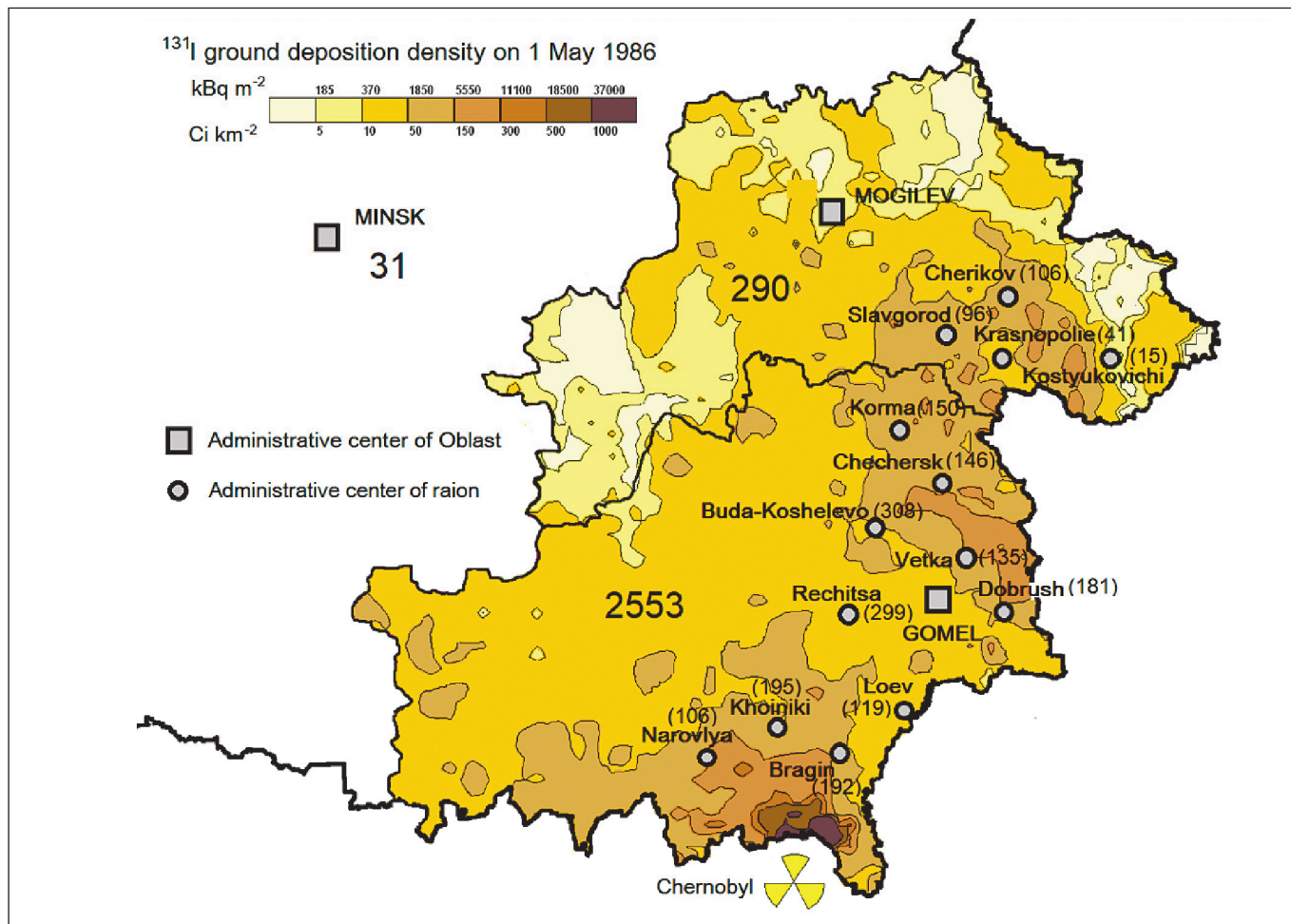
## MATERIALS AND METHODS

### Study population

The Belarusian *in utero* cohort consists of 2,965 child-mother pairs, including 26 pairs of twins, born to 2,939 mothers. The children (referred to here as ‘subjects’) were born between 26 April 1986 and 31 March 1987 so that their mothers were pregnant at some point between 26 April 1986 and 30 June 1986 – the two-month period in which significant <sup>131</sup>I exposure occurred after the Chernobyl accident. At the time of the accident (ATA), mothers of most cohort members (n = 2,553, 86.1 % of the total) lived in Gomel Oblast, while mothers of 290 (9.8 %) and 31 (1.0 %) subjects lived in Mogilev and Minsk Oblast, respectively (Fig. 1). Mothers of 91 individuals (3.1 %) resided outside the study area ATA but had moved into the study area shortly after the accident but before 30 June 1986. For more than 70 % of the study subjects (n = 2,089), mothers lived in raions most heavily contaminated from Chernobyl fallout (as shown in filled circles, Fig. 1).

### Thyroid screening of the Belarusian *in utero* cohort

Because of significant radiation exposure to the thyroid gland from <sup>131</sup>I, medical screening focuses on thyroid cancer and other thyroid diseases, including follicular adenoma, benign nodules, diffuse goiter, hypothyroidism, hyperthyroidism, and autoimmune thyroiditis. Thyroid screening examinations have been performed at the RRCRM&HE since November 2017 in accordance with a modified version of the standardized thyroid screening procedures used in the earlier thyroid screening study of the NCI-supported Belarusian-American cohort of subjects exposed to <sup>131</sup>I in childhood and adolescence (BelAm cohort) [10]. Standardized thyroid screening examinations include thyroid palpation by an endocrinologist and ultrasonographic (US) examination by a trained ultrasonographer. Based on palpation and US findings, a patient could be referred for fine needle aspiration biopsy, and then if indicated, for surgical treatment and histopathological diagnosis. Blood samples are collected for diagnosis of thyroid disorders (e.g., functional thyroid diseases, autoimmune thyroiditis) and medical follow-up. In addition, whole blood samples (10 mL) from study subjects are frozen for future molecular studies.



**Figure 1. Geographical distribution of the Belarusian *in utero* cohort members according to their mothers' residence at the time of the Chernobyl accident and <sup>131</sup>I deposition density.**

Mothers of 91 cohort members, who resided outside the study area, are not shown. Administrative centers of raions most heavily contaminated from the fallout are shown with filled circles, number of cohort members in the raion is given in parentheses.

### Thyroid doses for the cohort members

#### Calculation of thyroid doses

Individual thyroid doses were reconstructed for each cohort member for the following pathways of exposure: (1) prenatal <sup>131</sup>I intake by the mother and postnatal <sup>131</sup>I intake by the infant from breast milk and/or other foodstuffs, if the cohort member was born between 26 April and 30 June 1986; (2) prenatal and postnatal (until 5 years of age) external irradiation from gamma-emitting radionuclides deposited on the ground; and (3) prenatal irradiation from the mother's consumption of foodstuffs contaminated with <sup>134</sup>Cs and <sup>137</sup>Cs and postnatal irradiation (until 5 years old) from the child's consumption of foodstuffs contaminated with <sup>134</sup>Cs and <sup>137</sup>Cs.

Information required for estimation of individual prenatal and postnatal thyroid doses for the cohort subjects was collected during personal interviews of their mothers conducted between 19 December 2012 and 22 July 2017. The study questionnaire included

questions on: pregnancy and term of delivery; mother's and subject's residential history between 26 April 1986 and 31 March 1992; mother's consumption rates and dates of milk from privately owned cows or goats, milk from a commercial trade network, milk products and leafy vegetables between 26 April and 30 June 1986; dates of breastfeeding; mother's consumption rates and dates of consumption of locally produced foodstuffs after 30 June 1986 during pregnancy and/or breastfeeding; and subject's consumption rates of locally produced foodstuffs at age 0–1, 1–2, and 2–5 years old.

Prenatal thyroid doses were estimated using input data specific to the cohort member's mother (personal interview and direct thyroid measurement, when available), and ecological data (<sup>131</sup>I ground deposition in the settlements). Ecological and biokinetic models were used to calculate mother's «model-based» thyroid dose due to <sup>131</sup>I intake with contaminated air and foodstuffs, accounting for individual behavior and con-

sumption reported during the personal interview. The *model-based* thyroid dose for the mother served as the basis for calculating *model-based* thyroid dose to the fetus's thyroid gland using the model from the ICRP Publication 88 [11]. There were 656 subjects born between 26 April and 30 June 1986 who were exposed to <sup>131</sup>I postnatally. Their thyroid doses were estimated considering child's breastfeeding and consumption of locally produced foodstuffs.

Individual radiation measurement data for <sup>131</sup>I thyroidal activity were used to calibrate *model-based* dose and to estimate the most reliable «*measurement-based*» thyroid doses due to <sup>131</sup>I intake. The following three scenarios were utilized to characterize 2,939 mothers of cohort members in relation to the direct thyroid measurements:

1. Direct thyroid measurements were made in April–June 1986 with 286 mothers (9.7 %), including 3 mothers with twins.
2. Direct thyroid measurements were not made in study subject's mother but were made in other 10,430 women of child-bearing age residing in the same settlement or raion. This category included 2,088 women (71.1 %).
3. Mothers of the cohort members residing in areas where direct thyroid measurements were not conducted. This category included 565 mothers (19.2 %).

A detailed description of methodology and results of the thyroid dose calculation for the Belarusian *in utero* cohort can be found elsewhere [12].

### Evaluation of reliability of dose reconstruction

There are uncertainties in the information collected by personal interviews of mothers regarding residential history and individual diet approximately 30 years after the Chernobyl accident. Our previous study among 11,732 persons from the Belarusian–American cohort, who were exposed in childhood [13], showed that if dose-related measurements are unavailable for the study subjects and only modeling is used for dose calculation, high quality individual behavior and dietary data for the study subjects are required to provide realistic and reliable dose estimates. As the direct thyroid measurement data were available only for about 10 % of mothers of the Belarusian *in utero* cohort members, evaluation of uncertainty in thyroid doses due to possibly poor memory recall is especially important in this cohort.

Since the beginning of 2018, a special study has been conducted to re-interview a sample of 1,406 mothers using the same study questionnaire as was used for the

first interview conducted between 2012 and 2017. Information collected from the second personal interviews is being used to estimate thyroid doses to the study subjects and to compare these new estimates with the estimates calculated based on the information from the first interview.

### Statistical analysis

The percentage of agreement, the nonparametric Spearman's rank-correlation coefficient ( $r_s$ ) and the kappa statistics ( $\kappa$ ) were used to measure the degree of agreement of the responses between the two interviews. For the responses with text, i.e., name of settlement, the percentage of agreement between the answers was estimated. Numerical responses were treated in two ways: (a) for whole numbers, i.e., number of settlements of residence, the percentage of agreement and Spearman's rank-correlation coefficients were calculated; and (b) for consumption rates and thyroid dose estimates, i.e., values that could not be expected to be exactly the same, the data were categorized in intervals, and the percentage of agreement in the categories were estimated. Kappa-statistics ( $\kappa$ ) and Spearman's rank-correlation coefficients ( $r_s$ ) were used only for pairs without missing responses, such as «I do not remember». Kappa statistics  $\kappa < 0$  indicates no agreement, while 0–0.20 range corresponds to a slight agreement, 0.21–0.40 to fair, 0.41–0.60 to moderate, 0.61–0.80 to substantial, and 0.81–1.0 almost perfect agreement [14]. The two sets of consumption rates and thyroid doses were also compared using the Wilcoxon test, because values were not normally distributed; here, the  $p_w$ -value represents the significance level of whether data sets differ.

## RESULTS AND DISCUSSION

### Thyroid screening of the Belarusian *in utero* cohort

Between November 2017 and August 2021, 1,901 (64.1 %) of the 2,965 cohort members were contacted and invited for thyroid screening examination. Of these, 1,705 agreed to screening, of whom 1,267 (74.3 %) were examined and 242 (14.2 %) were scheduled for the screening; 105 persons (6.2 %) did not participate in the study because of death, serious physical disability, or migration, while 91 (5.3 %) refused to participate because of life events, pregnancy, etc.

Overall, at least one thyroid nodule was diagnosed in 268 (21.2 %) of the 1,267 Belarusian *in utero* cohort members. Of these, more than two-thirds (189 persons) had a nodule detected during the current screen-

**Table 1**  
**Thyroid nodule pathology detected pre-screening and during the screening of the Belarusian *in utero* cohort**

Diagnosis	Pre-screening		Detected during the screening		Total	
	N	% <sup>a</sup>	N	%	N	%
<b>Solitary thyroid nodule (mm):</b>	<b>39</b>	<b>3.1</b>	<b>128</b>	<b>10.1</b>	<b>167</b>	<b>13.2</b>
< 5	3	0.2	71	5.6	74	5.8
5–10	22	1.7	50	3.9	72	5.7
>10	14	1.1	7	0.6	21	1.7
<b>Multiple thyroid nodules (mm):</b>	<b>40</b>	<b>3.2</b>	<b>61</b>	<b>4.8</b>	<b>101</b>	<b>8.0</b>
< 5 <sup>b</sup>	5	0.4	23	1.8	28	2.2
5–10	14	1.1	27	2.1	41	3.2
>10	21	1.7	11	0.9	32	2.5
<b>Total</b>	<b>79</b>	<b>6.2</b>	<b>189</b>	<b>14.9</b>	<b>268</b>	<b>21.2</b>

Note. <sup>a</sup>Percent is given for 1,267 Belarusian *in utero* cohort members who underwent the thyroid screening examination; <sup>b</sup>size of the largest nodule.

ing while 79 persons had a nodule found prior to the screening (pre-screening) (Table 1). The prevalence of screening-detected nodules of 14.9 % in this Belarusian cohort is slightly higher than that of 13.5 % observed in the Ukrainian *in utero* cohort during the second-cycle thyroid screening in 2012–2015 [9]. Of the 268 persons with nodules, 167 (62.3 %) had a solitary nodule, while 101 (37.7 %) had multiple nodules. Nodules detected during the screening were more frequently solitary than multiple, while pre-screening cases were evenly distributed with respect to single vs. multiple nodularity. In addition, nodules tended to be smaller in those detected during the screening than in pre-screening cases.

Fifty-nine out of 268 subjects (22.0 %) with thyroid nodule were referred to fine needle aspiration biopsy, and among them 34 (57.6 %) were biopsied. Two persons underwent surgery: one for thyroid cancer and one for nodular goiter. To date, 7 thyroid cancers have been identified in the cohort, including 5 pre-screening cases, which were reported prior to screening or through linkage to the Belarusian National Cancer Registry, and 2 cases detected during the screening. It should be noted

that the two screening cycles of the Ukrainian *in utero* cohort identified 8 thyroid cancers [9].

For detection of functional thyroid disorders (e.g., hypo- and hyperthyroidism, autoimmune thyroiditis), thyroid function tests (thyroid-stimulating hormone [TSH], thyroxine [T<sub>4</sub>], thyroid peroxidase antibody [anti-TPO], and thyroglobulin antibodies [anti-TG]) were performed for 1,203 (94.9 %) screened individuals.

#### Thyroid doses for cohort members

Table 2 shows the total (prenatal and postnatal) thyroid doses from <sup>131</sup>I intake, external exposure and ingestion of radiocesium isotopes. The mean thyroid dose from all exposure pathways in the cohort was 137 mGy, including 130 mGy from <sup>131</sup>I intake, 4.9 mGy due to external irradiation, and 2.5 mGy due to ingestion of cesium isotopes. The thyroid doses from <sup>131</sup>I intake ranged up to 14.8 Gy, from external irradiation – up to 102 mGy, while doses due to ingestion of radiocesium isotopes did not exceed 47 mGy.

The mean prenatal thyroid dose due to <sup>131</sup>I intake in the Belarusian *in utero* cohort (123 mGy) was higher than that of 73 mGy for the Ukrainian *in utero* cohort

**Table 2**  
**Thyroid doses from different exposure pathways estimated for the Belarusian *in utero* cohort subjects [12]**

<sup>131</sup> I thyroid dose category <sup>a</sup> (mGy)	N	Mean thyroid dose <sup>a</sup> (mGy) due to			Mean total thyroid dose <sup>a</sup> (mGy)
		Intake of <sup>131</sup> I	External exposure	<sup>134,137</sup> Cs ingestion	
0	338	0	4.0	2.3	6.3
0.001–19.9	1,218	4.8	4.3	2.5	12
20–49.9	392	33	4.5	2.2	39
50–99.9	292	73	4.4	2.1	79
100–199.9	272	142	4.6	2.2	149
200–499.9	290	304	6.4	2.8	313
500–999.9	108	682	9.5	3.6	695
≥1000	55	2,620	12	2.7	2,640
Entire cohort	2,965	130	4.9	2.5	137

Note. <sup>a</sup>Sum of prenatal and postnatal doses

[15]. This could be expected as recruitment of the Belarusian *in utero* cohort members was focused on the most contaminated regions [16], while around 40 % of the Ukrainian *in utero* cohort included individuals from low contaminated regions in Ukraine [8].

**Evaluation of reliability of doses reconstructed for the *in utero* cohort**

One-thousand and fifty (1,050, or 74.7 %) of the 1,406 mothers of the cohort subjects were contacted and invited for a second dosimetric interview. Of these, 988 (94.1 %) agreed to the interview, of whom 780 (79.0 %) were interviewed and 146 (14.8 %) were scheduled for the interview. Thirty-six mothers (3.6 %) were excluded from the study because of death, serious physical disability, or migration; 26 (2.6 %) refused to participate because of life events, etc.

Information from 780 pairs of questionnaires obtained during the first and second personal interviews of the mothers has been analyzed for consistency of respondents' answers. Table 3 shows consistency of the answers on questions about consumption rates of cow's milk, milk products, and leafy vegetables that are the most important information for calculation of thyroid doses due to <sup>131</sup>I intake.

Table 4 provides the prenatal, postnatal, and total thyroid doses from <sup>131</sup>I for the cohort members calculated using individual behavior and consumption data reported by 780 mothers during the two interviews. As noted above, two types of thyroid doses were calculated for

cohort members: (i) using an ecological model, the so-called *model-based* dose; and (ii) the so-called *measurement-based* dose, which was obtained by adjusting the *model-based* dose for <sup>131</sup>I thyroid activity measured in cohort member's mother [12]. A reasonable agreement was observed ( $r_s = 0.74, p < 0.001$ ) for total (prenatal and postnatal) *model-based* doses calculated using data from the two interviews, while *measurement-based* doses calculated using data from the two interviews yielded the better agreement ( $r_s = 0.99, p < 0.001$ ).

Figure 2 compares the prenatal *model-based* thyroid doses due to <sup>131</sup>I calculated for the members of Belarusian *in utero* cohort using information from the first and second interviews. The *model-based* thyroid doses estimated for the same cohort member using the results of different interviews were spread over four orders of magnitude. For 72 % of the *model-based* thyroid doses the two sets of doses agreed within a factor of 3, while for 11 % of the cohort members a difference in the *model-based* doses was less than 10 %. The mean ratio of individual *model-based* doses calculated using data from the second interview to dose calculated using data of the first interview was  $2.0 \pm 4.7$ , and the median of ratios was 0.95.

Better agreement was observed for the prenatal *measurement-based* doses calculated for 105 individuals whose mothers have direct thyroid measurements (Figure 3). For 93 % of the *measurement-based* doses the two sets of doses agreed within a factor of 3. A difference of less than 10 % in the *measurement-based*

**Table 3**  
Consistency of the answers provided by 780 mothers of the Belarusian *in utero* cohort members during two personal interviews

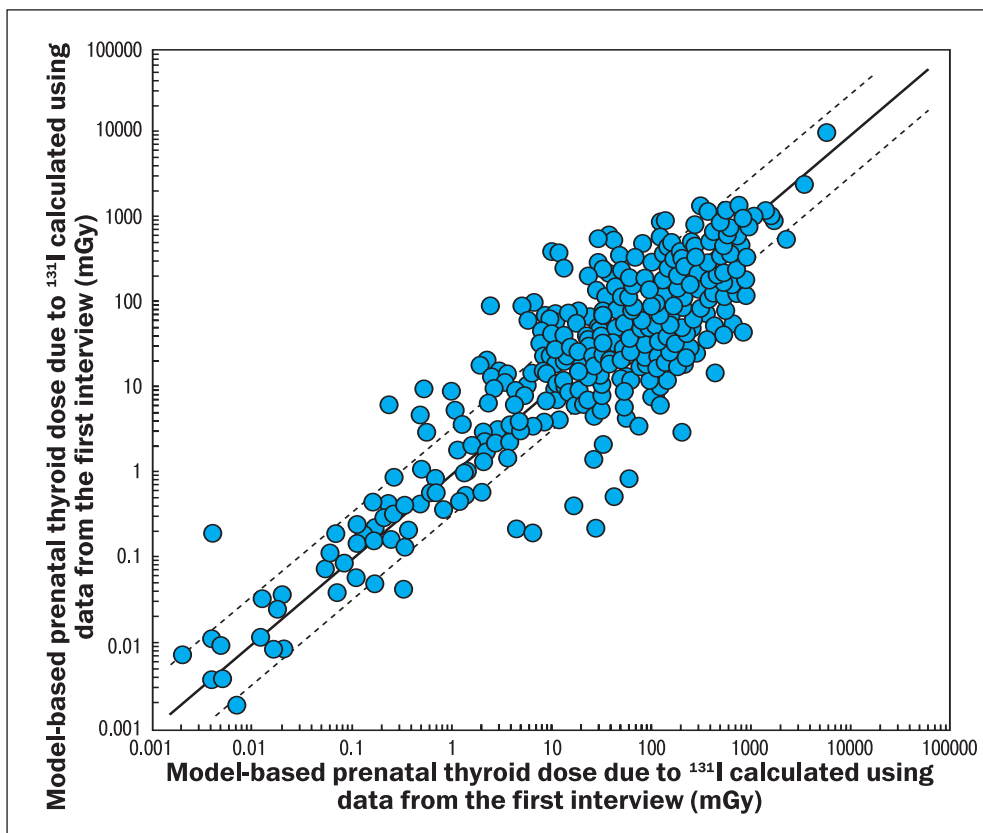
Parameter	First interview		Second interview		$p_{w}$ -value <sup>a</sup>	$r_s^b$	Agreed <sup>c</sup> (%)
	N	Consumption rate (L(g) d <sup>-1</sup> )	N	Consumption rate (L(g) d <sup>-1</sup> )			
<i>Consumption of privately owned cow's milk<sup>d</sup></i>							
Mean ± SD <sup>e</sup>	400	0.54 ± 0.52	407	0.47 ± 0.45	0.001	0.55	61
Median		0.50		0.30		$p < 0.001$	
Range		0.005 – 3.0		0.005 – 3.0			
<i>Mean consumption of cow's milk from a commercial trade network<sup>d</sup></i>							
Mean ± SD	285	0.27 ± 0.24	303	0.24 ± 0.28	0.054	0.41	60
Median		0.21		0.13		$p < 0.001$	
Range		0.01 – 1.1		0.003 – 2.0			
<i>Milk products</i>							
Mean ± SD	662	0.17 ± 0.13	653	0.18 ± 0.12	0.013	0.28	51
Median		0.19		0.20		$p < 0.001$	
Range		0.04 – 1.0		0.002 – 1.0			
<i>Leafy vegetables</i>							
Mean ± SD	565	0.044 ± 0.039	585	0.038 ± 0.040	<0.001	0.19	34
Median		0.025		0.025		$p < 0.001$	
Range		0.001 – 0.3		0.001 – 0.3			

Notes. <sup>a</sup> $p_w$ -value represents the significance level of whether the individual values of consumption rates differ according to Wilcoxon test; <sup>b</sup>Spearman's rank-correlation coefficient and  $p$ -value for the individual values of consumption rates; <sup>c</sup>percent of agreement between two questionnaires for the categories of consumption rates; <sup>d</sup>arithmetic mean of consumption rates between 26 April and 10 May 1986; <sup>e</sup>SD, the standard deviation.

**Table 4**  
**Prenatal, postnatal and total thyroid doses (mGy) for the cohort members from <sup>131</sup>I calculated using individual behavior and consumption data reported by 780 mothers during the two interviews**

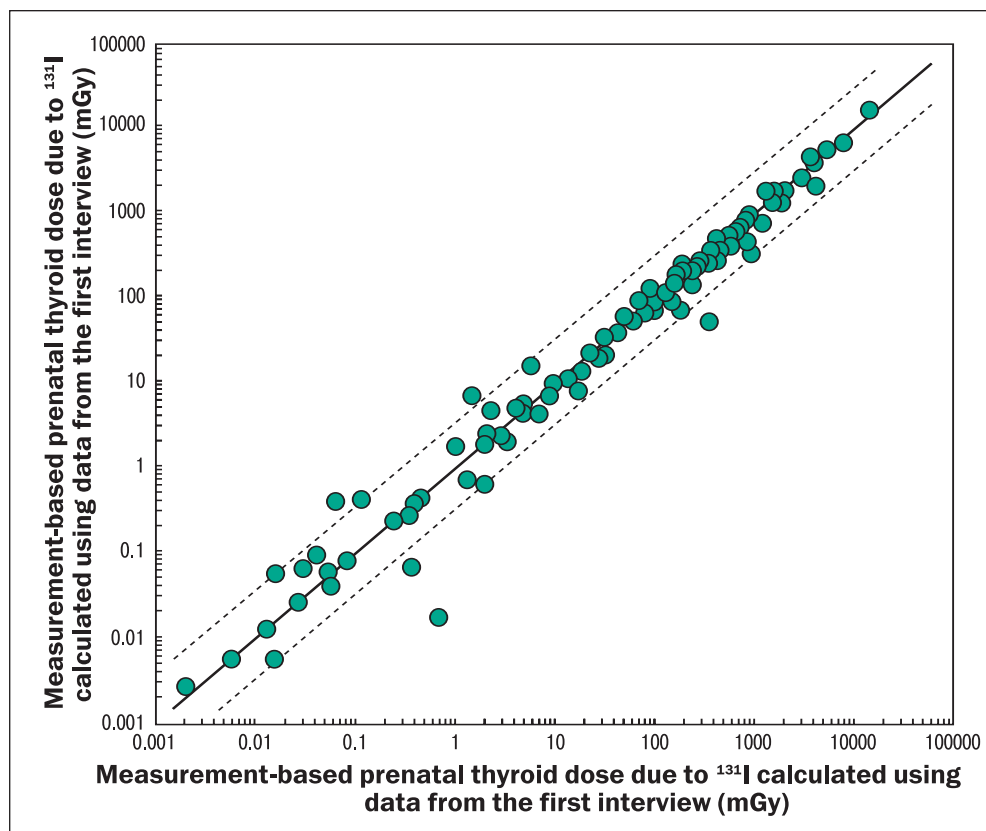
Parameter	N <sup>a</sup>	Thyroid doses due to <sup>131</sup> I intake (mGy) calculated using data reported during		<i>p<sub>w</sub></i> -value <sup>a</sup>	<i>r<sub>s</sub></i> <sup>b</sup>	Agreed <sup>c</sup> (%)
		First interview	Second interview			
<i>Prenatal model-based dose</i>						
Mean ± SD <sup>e</sup>	606	179 ± 334	174 ± 476	0.004	0.79	47
Median		101	72.9		<i>p</i> < 0.001	
Range		0.002 – 5,580	0.002 – 10,570			
<i>Postnatal model-based dose</i>						
Mean ± SD	198	26 ± 65	29 ± 66	0.825	0.84	61
Median		2.4	2.5		<i>p</i> < 0.001	
Range		0.002 – 584	0.002 – 584			
<i>Total model-based dose</i>						
Mean ± SD	765	183 ± 330	180 ± 470	0.007	0.74	47
Median		110	85		<i>p</i> < 0.001	
Range		0.002 – 5,580	0.002 – 10,570			
<i>Prenatal measurement-based dose</i>						
Mean ± SD	105	644±1,760	642±1,940	0.136	0.99	84
Median		88	88		<i>p</i> < 0.001	
Range		0.001 – 14,750	0.003 – 17,500			
<i>Postnatal measurement-based dose</i>						
Mean ± SD	18	175±451	461±701	0.231	0.95	42
Median		1.4	6.7		<i>p</i> < 0.001	
Range		0.006 – 2,040	0.002 – 7,740			
<i>Total measurement-based dose</i>						
Mean ± SD	105	678±1,760	729±2,050	0.286	0.99	83
Median		99	98		<i>p</i> < 0.001	
Range		0.001 – 14,750	0.003 – 17,500			

Notes. <sup>a</sup>Number of cohort members with non-zero prenatal and postnatal doses calculated using two interviews; <sup>b</sup>*p<sub>w</sub>*-value represents the significance level of whether the individual dose-values differ according to Wilcoxon test; <sup>c</sup>Spearman's rank-correlation coefficient and *p*-value for the individual dose-values; <sup>d</sup>percent of agreement between two categories of dose-values, excluding zero prenatal and postnatal doses; <sup>e</sup>SD, the standard deviation.



**Figure 2. Comparison of model-based prenatal thyroid doses due to <sup>131</sup>I calculated using information from the first and second interviews.**

Dashed lines show factor of 3 difference between two sets of doses.



**Figure 3.** Comparison of measurement-based prenatal thyroid doses due to <sup>131</sup>I calculated using information from the first and second interviews.

Dashed lines show factor of 3 difference between two sets of doses.

doses calculated using data collected from two interviews was found for 51 % of cohort members. The mean ratio of the *measurement-based* doses calculated using data from the second interview to doses calculated using data from the first interview was  $1.1 \pm 0.9$ , and the median of ratios was 1.0. This confirmed the previous observation that if measurements of <sup>131</sup>I thyroid activity were available for an individual, the quality of questionnaire data, in general, did not influence the precision of dose estimates [13]. However, there are 5 cohort members for whom the difference between two *measurement-based* doses exceeded 3 times (Fig. 3). The most likely reasons

for this difference are (i) unreliable answers on residential history provided during the personal interviews or (ii) a thyroid measurement was mistakenly assigned to the mother of a cohort member [17].

Pregnancy and childbirth at the time of the Chernobyl nuclear reactor accident was a unique event for mothers of the study subjects. The statistics on agreement, i.e., percent agreed and kappa statistics ( $\kappa$ ), obtained in this study were compared with those in the Belarusian-American cohort of individuals exposed in childhood [13]. Table 5 shows the consistency of answers between two personal interviews of 780 mothers of the

**Table 5**  
Thyroid doses from different exposure pathways estimated for the Belarusian *in utero* cohort subjects [12]

Characteristics	<i>In utero</i> cohort		BelAm cohort [13]	
	Agreed <sup>a</sup> (%)	$\kappa^b$ (or $r_s^c$ )	Agreed (%)	$\kappa$ (or $r_s$ )
<i>Residential history</i>				
Name of settlement ATA	90	–	88	–
Date of first relocation	57	0.720	42	0.329
Name of settlement of first relocation	71	–	49	–
<i>Consumptions of foodstuffs</i>				
Source of cow's milk	57	0.357	56	0.381
Consumption of cow's milk	63	0.327	54	0.334
Consumption of milk products	50	0.127	34	0.099
<i>Stable iodine administration (Yes / No)</i>	88	0.522	75	0.487
<i>Thyroid dose from <sup>131</sup>I intake</i>				
Model-based thyroid dose	47 <sup>d</sup>	0.79 <sup>d</sup>	51	0.66
Measurement-based thyroid dose	84 <sup>d</sup>	0.99 <sup>d</sup>	96	0.97

Notes. <sup>a</sup>Percent of agreement between two questionnaires or dose-values; <sup>b</sup>kappa statistics; <sup>c</sup>Spearman's rank-correlation coefficient; <sup>d</sup>prenatal thyroid dose.



Belarusian *in utero* cohort members and 2,664 pairs of questionnaires for the 1,994 mothers of the subjects in the Belarusian-American cohort (some on the mothers in this cohort were interviewed more than once). Responses from two personal interviews of mothers were found to be more consistent among mothers of the Belarusian *in utero* cohort members than among mothers of the Belarusian-American cohort members. This confirms an earlier study reporting that memory recall can be more accurate if a woman is asked about unique events in her life, like pregnancy [18].

## CONCLUSIONS

The Belarusian *in utero* cohort provides a rare opportunity for elucidating effects of radiation exposure during the gestation period on thyroid cancer and other health outcomes. Standardized thyroid screening examination of the Belarusian *in utero* cohort, includes thyroid palpation by an endocrinologist and ultrasonographic (US) examination by a trained ultrasonographer as well as diagnostic tests for functional thyroid disorders (TSH, T<sub>4</sub>, anti-TPO, and anti-TG), including hypo- and hyper-thyroidism and autoimmune thyroiditis.

A special dosimetry study is in progress to evaluate the reliability of dose estimates for the *in utero* cohort members. For this purpose, repeated interviews of 780 mothers of the cohort members have been conducted to date. Information collected from the second round of personal interviews was used to estimate *de novo* thyroid doses to the study subjects and to compare these estimates with the estimates calculated based on the information from the first round of interviews. It was found that consistency of answers between two personal interviews is better among mothers of the Belarusian *in utero* cohort members than that among mothers of the Belarusian-American cohort members.

Lifelong health consequences of exposure to ionising radiation *in utero* are of special concern after acciden-

tal radioactive releases from nuclear facilities because of the potentially higher radiosensitivity of tissues and organs of the fetus and newborn compared to adults. The Belarusian *in utero* cohort together with the parallel Ukrainian *in utero* cohort provides a rare opportunity to learn about the radiation-related risk of thyroid cancer and other health effects of exposure to ionizing radiation during gestation.

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## Disclaimer

Where authors are identified as personnel of the International Agency for Research on Cancer/ World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy, or views of the International Agency for Research on Cancer/ World Health Organization.

## Conflict of Interest statement

The authors declare that they have no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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