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Dietary habits during the 2 months following the Chernobyl accident and differentiated thyroid cancer risk in a populationbased case–control study

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Abstract

Conflict of interest statement

The authors declare no conflicts of interest.

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Authorship contribution statement

Elisabeth Adjadj, Florent de Vathaire designed the study. Françoise Borson-Chazot, Geneviève Sassolas, Claire Schvartz, Marc Colonna, Brigitte Lacour, Anne-Sophie Woronoff, Emilie Marrer, Michel Velten, Laurent Bailly and Eugènia Mariné Barjoan were in charge of data collection and cases recruitment for the study.

Constance Xhaard, Carole Rubino, Stéphane Maillard conducted the study. Constance Xhaard, Vincent Souchard and Florent de Vathaire analyzed the results and Constance Xhaard wrote the article. Carole Rubino, Jacques Orgiazzi, Martin Schlumberger, Yan Ren, Emilie Marrer, Laurent Bailly, Brigitte Lacour and Vincent Souchard reviewed and criticized the manuscript. All authors read and approved the final manuscript.

Background: The Chernobyl nuclear power plant accident occurred in Ukraine on April 26th 1986. In France, the radioactive fallout and thyroid radiation doses were much lower than in highly contaminated areas. However, a number of risk projections have suggested that a small excess in differentiated thyroid cancer (DTC) might occur in eastern France due to this low-level fallout. In order to investigate this potential impact, a case–control study on DTC risk factors was started in 2005, focusing on cases who were less than 15 years old at the time of the Chernobyl accident. Here, we aim to evaluate the relationship between some specific reports of potentially contaminated food between April and June 1986 – in particular fresh dairy products and leafy vegetables – and DTC risk.

Methods: After excluding subjects who were not born before the Chernobyl accident, the study included 747 cases of DTC matched with 815 controls. Odds ratios were calculated using conditional logistic regression models and were reported for all participants, for women only, for papillary cancer only, and excluding microcarcinomas.

Results: The DTC risk was slightly higher for participants who had consumed locally produced leafy vegetables. However, this association was not stronger in the more contaminated areas than in the others. Conversely, the reported consumption of fresh dairy products was not statistically associated with DTC risk.

Conclusion: Because the increase in DTC risk associated with a higher consumption of locally produced vegetables was not more important in the most contaminated areas, our study lacked power to provide evidence for a strong association between consumption of potentially contaminated food and DTC risk.

Keywords

Differentiated thyroid carcinoma; Case–control study; Chernobyl fallout; Contaminated food; Leafy vegetables; Dairy products

1. Introduction

Thyroid cancer, the most common malignancy of the endocrine system, accounts for less than 2% of all cancers diagnosed worldwide [1]. However, in recent decades its incidence has grown rapidly in many regions, including in Europe [2,3] and North America [4]. In France, thyroid cancer incidence per 100 000 has risen from 1.1 to 2.8 in men and from 5.5 to 13.8 in women between 1980 and 2012 [5]. This trend over time is due mostly to an increase in the incidence of differentiated thyroid carcinoma (DTC), which can be attributed to an increased use of diagnostic procedures [6,7]; however, environmental and lifestyle factors could also play a role [8].

The Chernobyl nuclear power plant accident occurred in Ukraine on April 26th 1986. In France, the radioactive fallout and thyroid radiation doses were considerably lower than in highly contaminated areas such as Ukraine, Belarus, and Russia. A number of risk projections, using risk coefficients estimated for moderate and high doses [9,10], suggested that a small excess in thyroid cancer might occur in eastern France as a result of this low-level fallout [11,12]. Since these estimations, large-scale studies examining radiation doses from CT scans have reported that, for breast and brain cancers, risk coefficients for

a low dose may be higher than for a high dose [13,14]. Lastly, the largest meta-analysis performed up to now – using individual data within cohorts of patients with documented thyroid radiation dose estimation, and including 12 studies and 1070 thyroid cancers – evidenced a supralinear dose response up to 2–4 Gy, and a significant dose response was observed within the range of radiation doses lower than 0.1 Gy [10]. Therefore, predictions from Cardis et al. [11] could have been underestimated.

In order to investigate the potential impact of Chernobyl radioactive fallout on DTC incidence in eastern France, a case–control study on DTC risk factors was started in 2005, focusing on cases who were less than 15 years old at the time of the Chernobyl accident.

The evaluation of the radiation dose received by the thyroid about 30 years ago for cases and controls in France presents a number of challenges: individual thyroid radiation dose reconstruction has to be based not only on radioactive fallout, meteorological data in the residential area, and demographic characteristics, but also on a number of lifestyle and food-consumption parameters, which have to be assessed by interview [15].

Radiation doses were received by the thyroid from two modes of exposure: external irradiation from radionuclides deposited on the ground, and internal irradiation primarily due to an intake of 131-iodine [16] which can occur via several routes. During the first days, contamination was due mainly to inhalation and ingestion of contaminated water or raw food. Some days later, contamination was due to ingestion of contaminated milk or dairy products, as well as of leafy vegetables [12,15,17]. In France, most of the thyroid doses came from internal irradiation, because the thyroid dose due to external irradiation was very weak at only 0.1 mSv for the first year [12,18].

In the present study we focused on potential thyroid contamination due to food intake during the 2 months following the accident. We aimed to evaluate the relationship between specific dietary reports from April to June 1986 – in particular concerning consumption of fresh milk, fresh dairy products and leafy vegetables – and thyroid cancer risk. We have taken into account the differences in radioactive fallout received by these food items according to the region in which they were produced.

2. Methods

2.1. Study population

Study population and methods have been reported previously [19,20]. In brief, the study was conducted with subjects diagnosed with DTC between January 1st 2002 and December 31st 2006 who were aged younger than 35 years. Subjects who were older than 15 at the time of the Chernobyl accident were excluded. Cases resided in the eastern part of France (Alsace, Champagne-Ardennes, Corse, Franche-Comté, Lorraine, Rhône-Alpes, or Provence-Alpes-Côte d'Azur) at the time of the diagnosis.

Controls were randomly selected from the general population using the landline telephone directory. Each control was individually matched to a single case of the same sex, year of birth (within 1 year), and region of residence during the year in which the thyroid cancer

The initial case–control study included 805 participants with DTC, matched with 876 controls. Because this study focused on dietary consumption during the 2 months following the Chernobyl accident in April 1986, 100 cases and 82 controls were not included in the present analysis because they had not yet been born (43 cases and 52 controls), were still in utero (15 cases and 9 controls), or were not in metropolitan France (42 cases and 21 controls) at the time of the Chernobyl accident (Table 1). Hence this study included 747 DTC cases and 815 controls.

The study was approved by the French Data Protection Authority (agreement no. 051120, April 5th 2005). Written informed consent was obtained from all participants.

2.2. Data collection

Between July 2005 and October 2010, a trained investigator interviewed the cases and control participants using a structured questionnaire. The same interviewer systematically interviewed all participants in the same strata (i.e. same sex, age, and region). The questionnaire included items on ethnicity, anthropometry, personal and family history of thyroid disease and cancer, places of residence, educational level, smoking status, alcohol consumption, gynecological and reproductive factors, medical x-ray exposure, and diet at the time of the diagnosis or the referent year and the 2 months after the Chernobyl accident.

2.3. Consumption of potentially contaminated foods

Part of the questionnaire focused exclusively on reporting consumption of food items known to be at risk of contamination by 131-iodine as a result of nuclear fallout during the 2 months following the Chernobyl accident (from April 26th to June 30th 1986). Questionnaires were sent by mail to study subjects about 2 weeks before interviews. Hence subjects, especially those who were too young to remember their food consumption, could ask their mother or family to help them to fill the dietary questionnaire.

The consumption report questions investigated frequency and quantity of consumption of fresh cows' milk, products derived from fresh cows' milk, fresh goat or sheep milk and products derived therefrom, and leafy vegetables. Frequency was classified as daily, weekly or monthly, and consumption of fresh dairy products, milk and leafy vegetable was converted into g/day.

Because in 1986 most milk, dairy products and leafy vegetables consumed in eastern France, as in other westernized countries, were bought in supermarkets or hypermarkets by consumers unaware of their origins (which are moreover extremely variable from one day to another), we excluded food items bought in supermarkets or hypermarkets. Nevertheless, some in the population, both in the countryside and in urban areas, still prefer fresh products of known origin (in most cases, near to their area of residence), from local markets, local farms, or from their own vegetable garden. In local markets, milk and vegetables frequently come from the neighbors and their origin is more frequently known by consumers. Fig. 1 illustrates the mean levels of radioactive deposits on agricultural areas which have been calculated for each French *département* from 131-iodine measurements in samples of cows' milk and leafy vegetables across France during the 2 months following the accident [12,18].

2.4. Statistical analysis

The data were analyzed using conditional logistic regression using SAS, version 9.3(SAS Institute, Inc., Cary, North Carolina, USA). Odds ratios were stratified for age, sex, and region of residence, and were adjusted for level of education, height, body mass index (BMI), ethnic group, smoking status, number of pregnancies (for women), and age class at the time of the Chernobyl accident (April 1986). All statistical tests were 2-sided, and a significance level of 0.05 was adopted.

These adjustment criteria were chosen either because they have already been highlighted in previous studies as risk factors for DTC (height, BMI, ethnic group, smoking status, number of pregnancies) or because these factors could influence the results (educational level and age class at the time of the Chernobyl accident). Most of these factors have also been studied separately. The quantitative factors, such as quantities of vegetables or dairy products, were divided into quartiles according to the distribution of the consumption values among controls (for consumptions > 0). For categorical variables, tests for trend were calculated by fitting models with a variable using the ranks of categorization as the values of the variable (e.g. 0, 1, or 2 for a variable in three categories).

3. Results

3.1. Characteristics of cases and controls

Among cases, papillary carcinoma was the most frequent histological type (720 cases; 89.4%); 73 cases presented with a follicular carcinoma and two cases with an oncocytic variant. Among all these cases, 136 (16.9%) had non-aggressive microcarcinomas (< 10 mm without tumor extension and only unifocal tumor). In ten cases (1.2%) the histological type was not available (Table 1).

3.2. Consumption of fresh dairy products or fresh milk

Consumption of fresh dairy products (i.e. the sum of the quantities of fresh milk from cows, goats or sheep and milk byproducts of local and known origin) was reported by 30.2% of the subjects. Fresh dairy product consumption, assessed in "never"/"ever" categories and by quartiles of quantities, are reported in Table 2. This reported consumption was not statistically associated with DTC risk, even when including only women, or excluding microcarcinomas, or including only papillary cancers.

To examine the effect of the difference in the intensity of the radioactive fallout across the four areas defined in Fig. 1, we tested the association between consumption of fresh dairy products and DTC separately for subjects from areas 1, 2 and 3 + 4. The association between fresh milk and dairy product consumption and DTC remained not statistically significant (data not shown).

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Lastly, to examine the robustness of the lack of association through different confounding factors (urban/non-urban area, smoking/non-smoking status, educational level, ethnicity, BMI < 22 or 22, age class at the time of the Chernobyl accident, and for women nulliparity), we tested the cases and controls for interaction between these variables and consumption of fresh dairy products. One statistically significant interaction has been found for smoking status (P = 0.03): among smokers, the consumption of fresh milk or dairy products was associated with a decreased risk of DTC (OR = 07, 95% CI: 0.5–0.9). The other interactions tested were not significant (data not shown).

3.3. Leafy vegetable consumption

Local leafy vegetable consumption was reported by 71.3% of the subjects, and assessed in "never"/"ever" categories and by quartile of quantities detailed in Table 3. Local leafy vegetable consumption was significantly associated with a higher risk of DTC, whatever the evaluation modality. For all subjects: OR "ever" versus "never" was = 1.3 (95%CI: 1.0-1.7) and OR "never" versus 4th quartile was = 1.7 (95%CI: 1.2-2.4). This association was still statistically significant when including only women, excluding microcarcinomas, or including only papillary cancers.

To examine the effect of the difference in the intensity of the radioactive fallout across the four areas defined in Fig. 1, we similarly tested the association between leafy vegetable consumption and DTC separately for subjects from areas 1, 2 and 3 + 4. The association between leafy vegetable consumption and DTC risk was not stronger in more contaminated areas than in the others (Table 4).

Lastly, the robustness of the association between leafy vegetable consumption and DTC was tested according to the same confounding factors (urban/non-urban area, smoking status, educational level, ethnicity, BMI < 22 or 22, age class at the time of the Chernobyl accident and, for women, nulliparity), statistically significant interaction between DTC risk and leafy vegetable consumption was found only for subjects with BMI < 22 (*P* interaction = 0.05). The association remained statistically significant only for the following subgroups: nulliparous women, non-smokers, subjects with higher educational levels, subjects aged 4–7 and 8–11 years at the time of the Chernobyl accident, and for nulliparous women (data not shown).

4. Discussion

This case–control study focused on the consumption of food potentially contaminated by the Chernobyl fallout during the 2 months following the accident and its potential link with DTC risk. We observed a slightly significant increased risk of DTC associated with the reporting of a higher consumption of leafy vegetables: OR for the fourth quartile versus never consumed = 1.7 (95% CI: 1.2-2.4). This association remains significant in only two age subgroups (4–7 and 8–11 years); no significant association was evident for subjects aged < 4 or > 12. An explanation could be that children < 4 years old may not have had a diversified diet, and rarely ate leafy vegetables. Moreover, this association was not stronger in areas more contaminated by Chernobyl fallout that in the others (Fig. 1). In contrast, no significant association has been evidenced for consumption of fresh milk or dairy products

and DTC risk. But it should be stressed that only 30% of the study subjects (205 cases and 257 controls) reported any consumption of fresh milk or fresh dairy products, while 70% of them reported consumption of leafy vegetables. Interestingly, according to Renaud et al. [18], leafy vegetables were the food most contaminated by radioactive fallout shortly after the Chernobyl accident (from May to June 1986); they estimated that leafy vegetables were ten times more contaminated than milk [18].

In areas close to Chernobyl, fresh milk consumption at the time of the accident was reported as a risk factor for developing cancer [21,22]. However, the levels of contamination received by those pastures were considerably higher than those in France.

The milk from sheep and goats was the most contaminated type of dairy product [12], but only a small proportion of subjects (65 cases and 77 controls) reported consumption of these types of milk/milk products.

The main limitation of this study comes from memory bias or uncertainties in dietary reports because questionnaires were taken more than 20 years ago after the Chernobyl accident. Bias or uncertainties may also have occurred due to misunderstanding of questions (e.g. only foods from local and known origin should have been taken into account, not foods from supermarkets). Another limitation comes from the lack of items in our diet questionnaire about consumption of other potentially contaminated foods such as fresh fruits, cereals, mushrooms, game meat [18]. But the most important limitation of our analysis is the lack of detailed data on radioactive fallout. Indeed, we used average deposits per *département* which is a quite large administrative unit. Within each *département*, fallout deposits were extremely heterogeneous, depending mostly on local rainfall during the days following the Chernobyl accident. Much more accurate estimations at the level of a municipality have been produced by the IRSN (Institut de Radio-protection et de Sureté Nucléaire), but these have not been disclosed. Such data are nevertheless needed in order to estimate individual thyroid doses, which would be the correct way to approach the question of a potential role of the Chernobyl accident in the incidence of thyroid cancer in the eastern part of France.

Our study has also several strengths, including the large sample size, the homogenous age range of subjects, as well as the consistency between the time at diagnosis (9–35 years) and at the age at the time of the Chernobyl accident (0–15 years). Moreover, in order to uncover a potential bias in dietary reports, an investigation to identify a potential specific link between irradiation risk perception and dietary reports – for instance, subjects who believe that thyroid cancers are due to Chernobyl fallout might over-declare their consumption of potentially contaminated food – has been performed and no such bias has been observed among cases or controls [23].

5. Conclusion

This study focused on the consumption of potentially contaminated food in the 2-month period following the Chernobyl accident. Other potential sources of contamination were not investigated. Our main result is the documentation of a slightly significant increased risk of DTC related to the consumption of leafy vegetables. However, because there was

no relationship between DTC risk increase potentially associated with the consumption of locally produced vegetables and the level of local *département* contamination, our study provides no clear evidence to suggest a causal role of the Chernobyl accident through consumption of potentially contaminated food in DTC. However, the present analysis lacks power, especially for less contaminated areas, because few people were living in these latter areas (because the study focused on the eastern part of France) and consumption of fresh milk and fresh dairy products was seldom reported in the dietary questionnaires.

Our results thus need to be confirmed using much more geographically detailed fallout deposit data at municipality level, and such data are not yet available.

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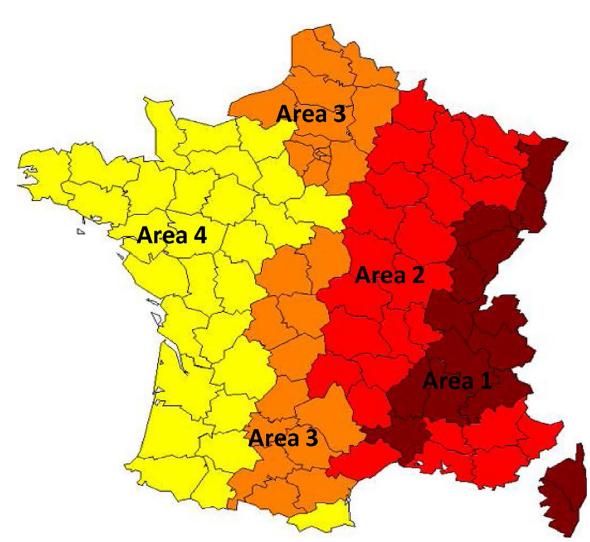


Fig. 1.

Mean deposits of 131I in France after the accident at Chernobyl (source IPSN – estimates for May 1986) (in Bq/m²). 131I deposits in Bq/m²: area 1 (brown) = from 30,000 to 60,000; area 2 (red) = from 15,000 to 30,000; area 3 (orange) = from 7500 to 15,000; and area 4 (yellow) 7500. Estimations based on concentrations measured in cow's milk and leafy vegetables (Renaud et al., 1997).

Table 1

Characteristics of the cases and controls.

	Cases (n = 805)	%	Controls (n = 876)	%
Histological type				
Papillary (microcarcinomas ^a)	720 (134)	89.4		
Follicular (microcarcinomas ^a)	73 (1)	9.1		
Oncocytic	2	0.3		
Unknown (microcarcinomas ^a)	10(1)	1.2		
Sex				
male	172	21.4	197	22.5
female	633	78.6	679	77.5
Age category at diagnosis or at the	e referent year			
< 16	18	2.2	18	2.1
16–20	57	7.1	64	7.3
21–25	170	21.1	183	20.9
26–30	265	32.9	290	33.1
31–35	295	36.7	321	36.6
Age category at the time of Cherne	obyl accident (april	26, 198	6)	
not born yet	43	5.3	52	5.9
in utero	15	1.9	9	1.0
0 – 3	100	12.4	108	12.3
4–7	161	20	171	19.5
8-11	235	29.2	251	28.7
12–15	251	31.2	285	32.5
Residential area between April and	1 June 1986			
Zone 1	305	37.9	379	43.3
Zone 2	331	41.1	330	37.7
Zone 3	44	5.5	47	5.4
Zone 4	44	5.5	37	4.2
Other country	42	5.2	21	2.4
Missing data	2	0.3	1	0.1

^aMicrocarcinomas were defined as tumor < 10 mm, without extension and only unifocal tumor. Zones 1 to 4 are reported in Fig. 1.

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Odds Ratios of thyroid cancer risk according to categories of fresh milk or dairy products consumption between April and June 1986, Eastern France,

	All cancer	cer				Women only	n only				Exclud	Excluding microcarcinoma	arcinor	na		Papilla	Papillary cancer			
	Ca (705)	Co (794)	OR	OR 95% CI	p trend	Ca (633)	Co (679)	OR	95% CI	p trend	Ca (669)	Co (727)	OR	95% CI	p trend	Ca (720)	Co (780)	OR	95% CI	p trend
Never	500	537	ref			387	421	ref			403	438	Ref			442	474	ref		
Ever	205	257	0.9	0.7 - 1.1	0.22	166	197	0.9	0.7 - 1.2	0.43	174	214	6.0	0.7 - 1.1	0.29	188	229	0.9	0.7 - 1.2	0.45
Quartiles (g/day)	(g/day)																			
-	500	537	Ref			387	421	Ref			403	438	Ref			442	474	Ref		
< 35.71 46	46	57	0.9	0.6 - 1.4		41	43	1.1	0.6 - 1.8		39	51	6.0	0.5 - 1.4		40	48	1.0	0.6 - 1.5	
35.71– 250	57	06	0.8	0.5 - 1.1		43	69	0.7	0.4 - 1.1		48	72	0.8	0.5 - 1.2		52	83	0.8	0.5 - 1.2	
250- 335.71	38	57	0.7	0.4 - 1.1		30	48	0.6	0.4 - 1.1		35	48	0.8	0.4 - 1.3		37	50	0.7	0.4 - 1.3	
> 335.71 64	64	53	1.2	0.8-1.8	0.41	52	37	1.4	0.8 - 2.3	0.71	52	43	1.1	0.7 - 1.8	0.68	59	48	1.2	0.8 - 1.9	0.57

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Table 3

Odds Ratios of thyroid cancer risk according to categories of leafy vegetables consumption between April and June 1986, Eastern France, 2002–2006.

	All cancers	cers				Women only	6 mm				Excludi	Excluding microcarcinomas	carcinol	nas		Papillaı	Papillary cancers			
	Ca (705)	Co (794)	OR	95% CI	p trend	Ca (633)	Co (679)	OR	95% CI	p trend	Ca (669)	Co (727)	OR	95% CI	p trend	Ca (720)	Co (780)	OR	95% CI	p trend
Never	187	242	ref			149	188	ref			162	195	ref			162	208	ref		
Ever	518	552	1.3	1.0 - 1.7	0.02	404	430	1.3	1.0 - 1.7	0.09	415	457	1.2	0.9 - 0.1.6	0.29	468	495	1.4	1.0 - 1.8	0.04
Quartiles (g/day)	(g/day)																			
0	187	242	ref			149	188	ref			162	195	ref			162	208	ref		
< 25.33	126	168	1.1	0.8 - 1.5		102	131	1.0	0.7 - 1.6		109	138	1.0	0.7 - 1.5		113	146	1.1	0.8 - 1.5	
25.33- 38.57	110	138	1.1	0.8 - 1.5		85	109	1.0	0.7 - 1.5		85	116	0.9	0.6 - 1.3		102	125	1.1	0.8 - 1.6	
38.57– 64.29	142	124	1.7	1.2 - 2.4		104	66	1.5	1.0 - 2.1		108	103	1.4	1.0 - 2.0		127	112	1.7	1.2 - 2.4	
> 64.29	140	122	1.7	1.2 - 2.4	< 0.01	113	91	1.8	1.3 - 2.7	< 0.01	113	100	1.5	1.1 - 2.2	< 0.01	126	112	1.7	$\frac{1.2}{2.4}$	< 0.01

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Table 4

Odds Ratios of thyroid cancer risk according to categories of radioactive fallout across France and of leafy vegetables consumption between April and June 1986, Eastern France, 2002–2006.

	Quartiles (g/day)	Ca	Со	OR	95% CI
	0	187	242	ref	
Zones 3 & 4	< 25.33	13	11	1.6	0.7–4.0
	25.33-38.57	6	19	0.5	0.2–1.4
	38.57-64.29	13	14	1.3	0.6–3.1
	> 64.29	11	7	2.5	0.9–7.0
Zone 2	< 25.33	60	75	1.2	0.7 - 1.8
	25.33-38.57	55	60	1.1	0.7–1.8
	38.57-64.29	56	43	1.6	1.0-2.7
	> 64.29	63	44	2.1	1.3–3.3
Zone 1	< 25.33	53	82	0.8	0.5-1.3
	25.33-38.57	49	59	1.1	0.7–1.8
	38.57-64.29	73	67	1.5	0.9–2.5
	> 64.29	66	71	1.6	1.0-2.5

OR are stratified by sex, age and region of origin and adjusted for educational level, ethnicity, smoking status, size, number of pregnancies (for women), age classes at the time of Chernobyl accident.

Zone 1: 30 000 to 60 000 Bq/m^2 ; zone 2: 15 000 Bq/m^2 ; zone 3 and 4: < 15 000 Bq/m^2 . Ca, cases; Co, controls, OR, Odds ratio; 95%CI, confidence interval.