External Radiation Dose, Obesity, and Risk of Childhood Thyroid Cancer After the Fukushima Daiichi Nuclear Power Plant Accident: The Fukushima Health Management Survey

MS# EDE18-0307

Original Research Article

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Keywords: Childhood, Disaster, Epidemiology, Population-based, Prospective study, Radiation, Thyroid gland

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Running title: External radiation dose, obesity, and risk of thyroid cancer

Sources of financial support: This work was supported by the National Health Fund for Children and Adults Affected by the Nuclear Incident for design and conduct of the study.

Conflicts of interest: There is no conflict of interest.

A statement on availability of data and code for replication: No additional data are available.

ABSTRACT

Background: The 2011 Great East Japan Earthquake led to a nuclear accident at Fukushima Daiichi Nuclear Power Plant. This study examined the associations of radiation dose and lifestyle factors with incidence of thyroid cancer in Fukushima.

Methods: We applied a prospective study design with 300,473 participants aged 18 years or younger who underwent thyroid examinations from October 2011. Follow-up surveys were conducted through June 2017, and 245,530 participants (123,480 men and 122,050 women, 82% follow-up) received follow-up examinations. Fukushima Prefecture was divided into five areas based on individual external radiation dose. The relative risks and 95% confidence intervals (CIs) for thyroid cancer in all areas, with area of lowest radiation dose as a control reference, were calculated using Poisson regression models adjusted for age. The risks of overweight and obesity were also calculated.

Results: The incidence rates per 100,000 for Groups A (highest-dose), B, C, D, and E (lowest-dose) were 13.5, 19.2, 17.3, 9.0, and 8.3, respectively. Compared with Group E, the age-adjusted risks (95% CIs) for Groups A, B, C, and D were 1.62 (0.59–4.47), 2.32 (0.86–6.24), 2.21 (0.82–5.94), and 1.02 (0.36–2.86), respectively. Obesity was positively associated with thyroid cancer incidence; the age- and sex-adjusted risk of thyroid cancer was 2.26 (1.03-4.95) for obese individuals compared with that for non-obese.

Conclusions: Regional differences in radiation dose were not associated with an increased risk of thyroid cancer among children in Fukushima within 4–6 years after the nuclear power plant accident. Obesity may be an important factor in a further follow-up study in Fukushima.

Keyword: Childhood, Disaster, Epidemiology, Population-based, Prospective study, Radiation, Thyroid gland

INTRODUCTION

The Great East Japan Earthquake, registering 9.0 on the Richter scale, occurred on March 11, 2011. From the day of the disaster, the Fukushima Daiichi Nuclear Power Plant, located in the central eastern coast area in Fukushima Prefecture, released radioactive elements owing to a nuclear accident caused by the earthquake and the subsequent tsunami that struck the plant. Many residents living in the areas surrounding the nuclear power plant were forced to evacuate their homes and change their lifestyles.[1]

Previous studies reported that one of the main adverse health effects of radiation is a substantial rise in thyroid cancer among exposed young people,[2] and numerous cases of thyroid cancer among younger children were reported after the accident at the Chernobyl Nuclear Power Plant in 1986.[2] Although the internal exposure to ^{131}I among children in Fukushima, even in areas with the highest contamination, was much smaller than those in Chernobyl, Fukushima Prefecture started to examine the thyroid gland by ultrasonography among residents aged 18 years or younger 6 months after the accident to detect the long-term effects of low-dose radiation exposure on thyroid cancer incidence and to reduce anxiety among residents in Fukushima.[3]

We reported that regional and individual differences in external radiation doses were not associated with thyroid cancer prevalence among children in the 4 years after the accident.[4–6] However, follow-up surveys should be conducted for a prolonged period before any conclusions are drawn; the previous studies conducted cross-sectional analyses only. Furthermore, although several risk factors for thyroid cancer, such as obesity and diet, have been reported among adults, few studies have reported risk factors among children. Because children in the evacuation area were forced to change their lifestyles after the accident,[7] it was

necessary to examine the association between lifestyle factors and the incidence of thyroid cancer among children in Fukushima Prefecture.

We therefore sought to examine the association between radiation dose and the risk of thyroid cancer detected by ultrasonography among residents of Fukushima in a prospective study. We also investigated the associations of lifestyle factors with thyroid cancer, using data collected from about 300,000 residents aged 18 years or younger obtained from the Fukushima Health Management Survey.

METHODS

Study Population and Design

The subjects were inhabitants of Fukushima Prefecture, with a target population of 367,685, who were aged between 0 and 18 years on March 11, 2011. The first thyroid examinations were conducted from October 2011 through April 2015 as part of the Fukushima Health Management Survey.[3] Through April 2015, 300,473 subjects (82%), including evacuees currently living in other prefectures, were examined.

Follow-up examinations were conducted among subjects who agreed to participate in the survey from April 2014 through June 2017, and the follow-up survey was also conducted countrywide. As a result, 245,530 participants (123,480 men and 122,050 women; 82% follow-up) received follow-up examinations (Figure 1), with average follow-up periods of 2.1 years from the baseline examination and 4.0 years from the nuclear power plant accident. The Ethics Committee of Fukushima Medical University approved this study (#1318 and 1294). Written informed consent was obtained from the parents of all surveyed children.

Thyroid Ultrasound Screening Programme

Ultrasonography was used for thyroid gland examinations; the detailed protocol is reported elsewhere.[3,5,8,9] Thyroid volume, nodules, cysts, and other findings, such as congenital defects and ectopic thymus, were recorded. Secondary confirmatory examinations were recommended when the ultrasonography findings met the following criteria: nodules ≥5.1 mm or cysts ≥20.1 mm; or immediate need for confirmatory examination for clinical reasons. In the follow-up survey, secondary confirmatory examinations were recommended for 2,049 participants, of whom 1,670 (82%) completed the examinations through June 2017. At baseline and follow-up, height in stocking feet and weight in light clothing were measured or self-reported (n=237,230), and the body mass index (BMI) was calculated as weight (kg)/height $(m)^2$.

The secondary confirmatory examinations included further ultrasonography, blood tests, urinalysis, and fine-needle aspiration cytology if needed. According to the Japan Association of Breast and Thyroid Sonology guidelines,[10] fine-needle aspiration cytology is recommended for nodules >5 mm in diameter if thyroid carcinoma is strongly suspected, nodules >10 mm in diameter if carcinoma is suspected, and all nodules >20 mm in diameter.[5] These guidelines were followed to avoid unnecessary fine-needle aspiration cytology, especially for nodules >5 mm but <10 mm. Of 1,670 participants, 214 (13%) underwent fine-needle aspiration cytology. Among them, 70 participants had nodules classified as suspicious or malignant, with 50 participants receiving surgical treatment. Finally, 50 participants were diagnosed with thyroid carcinoma.

Estimation of External Radiation Dose

The Basic Survey of the Fukushima Health Management Survey for estimation of radiation dose (methods detailed elsewhere[11,12]) was launched around 4 months after the nuclear power plant accident. To examine the association between radiation dose and the risk of thyroid cancer, we used the basic survey data (individual external radiation doses based on personal behaviours) because of the limited availability of information on internal exposure to ^{131}I. In the basic survey, self-administered questionnaires were prepared to collect information from all residents (about 2.06 million) in Fukushima Prefecture on residence, places visited, length of time spent indoors and outdoors, and travelling time during the period from March 11 to July 11, 2011, because most people who were living in the evacuation area moved from their original locations after the accident and such moves were different from person to person. Individual external doses were estimated by digitising these behavioural data and comparing them against computations of daily gamma ray dose rate maps drawn after the accident. Of all residents, 566,773 (27%) responded to the questionnaire through June 30, 2017, and individual dose estimates were completed for around 97% of them (552,298).[13] Although some were estimated for periods of <4 months due to the absence of data on behaviour in the returned questionnaires, most of the individual doses were estimated for the 4 months (March 11 to July 11, 2011). The distribution of individual external doses of the respondents for the first 4 months (excluding radiation workers) was highly right-skewed: <1 mSv, 62%; <2 mSv, 94%; and <5 mSv, 99.8%. We used the distribution data for 59 municipalities in these analyses. All of the population screened for thyroid examination is included in population for external dose assessment. Although the response rate to the questionnaire to estimate external doses in this study was different among municipalities, we confirmed that the estimated external doses were representative of the dose distribution for the whole population of each

municipality.[12] Data on estimated individual radiation doses were available for 113,150 of 245,530 participants. As mentioned above, some of them were estimated for periods of <4 months, and we deleted them (n = 4,170). As a result, 108,980 individual dose data were used for analysis.

Statistical Analysis

In the present study, we considered thyroid cancer to be thyroid cancer as detected by fine-needle aspiration cytology (70 cases). We calculated the proportion of residents who received an external radiation exposure of ≥1 mSv in each municipality in Fukushima (59 municipalities) based on the data for estimated individual radiation doses, and then classified the 59 municipalities into quintiles according to the order of the proportion, as shown in Figure 2. First, we compared the means or prevalences of baseline variables of interest between participants with and without thyroid cancer. Because 1,033 participants did not live in Fukushima Prefecture on March 11, 2011, and information on municipality of residence was lacking for 2,665 participants, we excluded these participants, and the remaining 241,832 participants were included in the final analysis. It should be noted that the excluded population included one thyroid cancer case. Time at risk (time to event or time to censoring) was calculated from the date of the baseline examination to the date of the second-round examination. The relative risks (RRs) and 95% confidence intervals (CIs) for thyroid cancer in all areas, with the area of lowest radiation dose as a control reference, were calculated using Poisson regression models adjusted for age and sex. The age- and sex-adjusted RRs and 95% CIs for thyroid cancer incidence according to obesity and individual external radiation dose were also calculated.

Because BMI was closely associated with age at the time of survey, overweight and obesity were defined as age- and sex-specific BMI higher than the 85% (overweight) and 95% (obesity) percentiles of all Japanese in their age as the criteria given by the Japanese society for pediatric endocrinology and the Japanese association for human auxology, [14] which was recommended to evaluate Japanese children and adolescents. We calculated the age- and sex-adjusted RR (95% CI) of thyroid cancer for overweight and obesity, compared with non-obese individuals.

Moreover, as a sensitivity analysis, we conducted the same analysis limited to nodules 10 mm or more in diameter for thyroid cancer (n = 34), because the proportion of fine-needle aspiration cytology varied when the diameter of the nodules was between 5 and 10 mm. Furthermore, we analysed the association between the incidence of thyroid cancer and quintiles of radiation doses using the proportion of residents who received an external radiation exposure of ≥2 mSv in each municipality in Fukushima.

Because internal exposure was closely associated with the incidence of thyroid cancer among children after the Chernobyl Nuclear Power Plant accident,[2] we further used internal thyroid doses to 1-year-old children as estimated by Kim et al.[15] The adjusted RRs and 95% CIs for thyroid cancer incidence according to internal thyroid dose were also calculated. A total of 59 municipalities in Fukushima were divided into three groups according to the 90th percentile values of internal thyroid dose to 1-year-old children: Group I (3 municipalities: 30 mSv), Group II (8 municipalities: 10–20 mSv), and Group III (48 municipalities: <10 mSv).[15]

SAS, version 9.4 (SAS Institute, Cary, NC, USA), was used for all analyses.

RESULTS

The means (SD) and prevalences of characteristics of participants with and without thyroid cancer are presented in Table 1. The mean values of age and BMI and the prevalence of obesity tended to be higher among participants with cancer than among those without cancer. The age- and sex-adjusted RRs and 95% CIs for thyroid cancer according to the external radiation doses are presented in Table 2. The incidence rates per 100,000 for Group A, B, C, D, and E were 13.5, 19.2, 17.3, 9.0, and 8.3. Compared with the lowest-dose area (Group E), the age- and sex-adjusted RRs (95% CIs) for Groups A, B, C and D were 1.62 (0.59 to 4.46), 2.32 (0.86 to 6.24), 2.20 (0.82 to 5.93) and 1.02 (0.36 to 2.86), respectively. When we further analysed the association between the incidence of thyroid cancer and quintiles of radiation doses, using the proportion of residents who received an external radiation exposure of ≥2 mSv in each municipality in Fukushima, the associations were essentially unchanged. Compared with the lowest-dose area (the proportion of exposed external radiation of 2 mSv or more <0.05%), the age- and sex-adjusted RRs (95% CIs) for groups of the highest (proportion of 2 mSv or more >12.2%), high middle (12.2%> proportion of 2 mSv or more ≥8.8%), middle (8.8%> proportion of 2 mSv or more ≥0.25%), and low middle (0.25%> proportion of 2 mSv or more ≥0.05%) were 1.27 (0.42 to 3.85), 1.92 (0.65 to 5.67), 1.68 (0.57 to 4.94), and 0.81 (0.27 to 2.46), respectively.

Age was positively associated with the incidence of thyroid cancer, but there was no association between sex and the incidence of thyroid cancer. Obesity was positively associated with the incidence of thyroid cancer, and the age- and sex-adjusted RR (95% CI) of thyroid cancer was 2.26 (1.03 to 4.95, p <0.05) for obese individuals compared with that for non-obese (Table 3). Furthermore, the adjusted RR was unchanged after adjustment for external radiation doses.

Data on the individual external radiation dose were available for 36 cases. Of the participants with thyroid cancer, 31 (0.03%) had an external radiation dose <2 mSv and 5 (0.05%) had a dose ≥2 mSv among 108,980 participants with external radiation dose data. When we analysed the relationship between thyroid cancer and individual external radiation dose, the age- and sex-adjusted RR and 95% CI for thyroid cancer with individual external radiation doses ≥2 mSv, with an external dose <2 mSv as a reference, was 2.09 (0.81 to 5.40; $p = 0.13$).

As shown in eTable 1, the association between the external radiation dose and the incidence of thyroid cancer was attenuated when we limited the analysis to thyroid cancers with diameter >10 mm. Compared with the lowest-dose area (Group E), the age- and sex-adjusted RRs (95% CIs) for Groups A, B, C, and D were 0.91 (0.22 to 3.80), 1.30 (0.32 to 5.19), 2.24 (0.63 to 8.03), and 1.19 (0.32 to 4.41), respectively. On the other hand, the association between obesity and the incidence of thyroid cancer was almost unchanged, and the age- and sex-adjusted RR (95% CI) of thyroid cancer was 2.59 (0.91 to 7.40; $p = 0.08$) for obese individuals compared with that for non-obese.

The age- and sex-adjusted RRs and 95% CIs for thyroid cancer according to the internal thyroid doses are presented in eTable 2. The incidence rates per 100,000 for groups I (30 mSv), II (10–20 mSv), and III (<10 mSv) were 9.6, 18.8, and 13.7, respectively. Compared with the lowest-dose area (Group III), the age- and sex-adjusted RRs (95% CIs) for groups I and II were 0.63 (0.31 to 1.27) and 1.50 (0.71 to 3.16), respectively. There were no cancer cases in Group I with the highest external radiation exposure area (Group A).

DISCUSSION

The main finding of this longitudinal study was that regional and individual differences in external radiation dose were not associated with the incidence of thyroid cancer among children in the 4 to 6 years after the Fukushima Daiichi Nuclear Power Plant accident resulting from the Great East Japan Earthquake. On the other hand, obesity was positively associated with the incidence of thyroid cancer among the children, regardless of whether they lived close to or far from the nuclear power plant. Since children in the evacuation area tended to be overweight after the accident, we need to pay attention not only to radiation but also to overweight/obesity when monitoring for future thyroid cancers in Fukushima Prefecture.

Previous epidemiological studies reported associations between external and/or internal radiation doses and the risk of thyroid cancer among children.[16–20] An obvious increase in the incidence of childhood thyroid cancer in Belarus and Ukraine, especially in highly exposed areas, was reported after the Chernobyl Nuclear Power Plant accident.[16] Since the dose of radiation in Fukushima was much lower than that in the Chernobyl accident,[11] regional differences in external radiation dose might not be associated with the incidence of thyroid cancer in this study. Furthermore, although age was inversely associated with the incidence of radiation-related thyroid cancer in Chernobyl,[18] there was a positive association between age and the incidence of thyroid cancer in the present study. Excessive cases of thyroid cancer among younger children, especially those aged between 0 and 4 years, were reported after the Chernobyl accident.[21] However, the patients in whom thyroid cancer was detected in the present study tended to be older: the number of cases was zero (0.0%) for children 0 to 4 years old, 11 (0.01%) for those 5 to 9 years old, 36 (0.05%) for those 10 to 14 years old, and 23 (0.12%) for those 15 to 18 years old.

Conversely, we previously reported the associations between radiation doses and the prevalence of thyroid cancer using the data of the first thyroid examinations, and compared with the lowest dose area (Group E), the age- and sex-adjusted odds ratios (95% CIs) for Groups A, B, C, and D were 0.95 (0.48–1.88), 1.44 (0.75–2.75), 1.05 (0.53–2.09), and 1.08 (0.58–2.01), respectively.[6] In the present study, although there were no dose-dependent associations between radiation dose and the risk of thyroid cancer, the adjusted RRs in groups A–C were between 1.6 and 2.3, and low statistical power may have led to statistical non-significance. However, the increased RRs in groups A–C may be explained by the differences in rate of fine-needle aspiration cytology, regardless of low statistical power. As shown in Table 2, the rates of fine-needle aspiration cytology in groups A–C were higher (Group A: 16.3%, Group B: 14.7%, and Group C: 11.4%) than Group E (7.1%), while the rates of needing confirmatory testing were not so different among the groups. The reasons of the differences in the rates of fine-needle aspiration cytology among the groups are not fully elucidated. However, the participants in the areas of higher radiation dose might tend to undergo fine-needle aspiration cytology due to anxiety of radiation effects. Indeed, the increased RRs in groups A and B were not observed when the diameter of the nodules was limited to 10.0 mm or more in the present study, and this may support our hypothesis.

In Chernobyl, the increase in thyroid cancer among children after the accident was caused mainly by internal exposure to ^{131}I radiation from intake of contaminated food, such as milk and other dairy products.[22] On the other hand, although only the external radiation dose was evaluated in the present study, it was reported that radiation doses to the thyroid were much lower in Fukushima than in Chernobyl, even if internal doses from both caesium and iodine were included.[23–26] The dose assessment of internal exposure due to caesium conducted

among 184,205 residents in Fukushima by using a whole body counter showed that 99.99% received <1 mSv, with the maximum dose being 3 mSv.[26] A study analysed the huge data set of the post-Fukushima food monitoring campaign and estimated the doses to the general public in a worst-case scenario by using a conservative dose model.[27] The results showed that the internal exposure levels due to iodine, even for infants and young children, did not reach 50 mSv in the worst-case scenario, which is a maximum dose as thyroid equivalent dose for exposure from ingestion of contaminated food and beverages confirmed by the Nuclear Safety Committee in Japan.[27] Kim E, et al. estimated that the highest internal thyroid doses were expected to affect residents of Futaba town, Iitate village, and Iwaki city, and their doses were estimated to be mostly below 30 mSv.[15] In the present study, we further calculated the adjusted RRs of thyroid cancer for the three municipalities with the highest doses compared with the lowest-dose area, and there were no dose-dependent associations between internal thyroid doses and incidence of thyroid cancer. Therefore, the thyroid cancer cases observed after the Fukushima nuclear power plant accident were unlikely to be linked to the release of radioiodine from the accident, but were rather caused by a screening effect[28,29] or other confounding factors.

Overweight/obesity is one of the plausible lifestyle-related risk factors for thyroid cancer. A meta-analysis of 21 observational studies showed that obesity was associated with an increased risk of thyroid cancer other than medullary thyroid cancer, regardless of age, sex, and ethnicity.[30] In the present study, the postoperative pathological diagnosis revealed that most cases (99%) were papillary thyroid carcinoma[29]; therefore, the results of the present study are in line with those of previous studies. On the other hand, few studies have found an association between obesity and thyroid cancer among children.[31] The Copenhagen School

Health Records Register, in a prospective study among 7- to 13-year-old children, reported that higher BMI during childhood was associated with an increased risk of thyroid cancer in later life (median follow-up, 38.6 years).[31] Our results added the further finding that obesity might be associated with an increased risk of thyroid cancer among children at an earlier age than expected.

The BMI of boys and girls in Fukushima who were aged 3 to 4 years at the time of the accident increased more 19 months after the accident than did the BMI of children in unaffected prefectures (Yamagata, Akita, and Aomori).[32] Further, the prevalence of overweight among primary school boys 6 to 11 years of age and girls 6 to 10 years of age in Fukushima increased from before to after the accident. Moreover, the increment of overweight/obese people was influenced by evacuation after the accident, regardless of age and sex.[7,33] Therefore, the Fukushima nuclear power plant accident may have led to an increased risk of thyroid cancer due, in part, to weight gain.

The strength of the present study is that we analysed risk factors for thyroid cancer based on a large number of residents, including both evacuees and non-evacuees after the accident, in a prospective study. Ultrasonography was used for examination of the thyroid gland in all participants in both the baseline and follow-up surveys.

Some potential limitations of this study should, however, be considered. First, low-exposure doses, especially compared with those at Chernobyl, and small inter-regional differences in doses within Fukushima made it difficult to obtain precise estimates of effects. Second, we did not examine life style factors other than BMI, such as dietary iodine intake. Previous epidemiological studies reported that some dietary factors, including iodine-rich foods and goitrogens, were associated with an increased risk of thyroid cancer.[34,35] Because

food frequency questionnaires for iodine-rich foods were administered in the follow-up surveys in the Fukushima Health Management Survey, the association between dietary factors and risk of thyroid cancer should be analysed in the future. Third, the response rate to the questionnaire to estimate external doses in this study was low, which may have affected the results, although the estimated external doses were representative of the dose distribution for the whole population of each area.[12] Furthermore, because external doses were estimated using self-administered questionnaire, some uncertainties in replies of the participants were possible due to faulty memories of their behaviours. This may have led to misclassification in the groups of external doses. Fourth, because the sensitivity of thyroid examination by ultrasonography is unknown, the thyroid cancers observed in the present study were likely a mixture of prevalent and incident cases. This may have led to an underestimation of the association between radiation dose and the risk of thyroid cancer. Fifth, although obesity was associated with the incidence of thyroid cancer in the present study, it is not clear whether obesity is a causal factor or a marker of other confounding factors, such as diet and hormonal factors, including growth hormone and thyroid-stimulating hormone,[36] among children. Finally, the mean duration from accident to diagnosis was about 4 years, which may be too short to detect all radiation-related thyroid cancers, although the incidence of thyroid cancer in children and adolescents increased 4 years after the Chernobyl NPP accident.[16] Therefore, longer follow-up surveys should be conducted for several years before any conclusions can be drawn.

In conclusion, although there were no associations of regional and individual differences in external radiation doses with the incidence of thyroid cancer among children in Fukushima within 4 to 6 years of the nuclear power plant accident, lifestyle factors, such as

obesity, may be an important factor in a further follow-up study. The further long-term follow-up survey should help clarify the effects of low-dose radiation exposure on the incidence of thyroid cancer in Fukushima.

ACKNOWLEDGMENTS

The authors thank the staff of the Fukushima Health Management Survey for their important contributions.

FUNDING/SUPPORT

This survey was supported by the National Health Fund for Children and Adults Affected by the Nuclear Incident for design and conduct of the study. The findings and conclusions of this article are solely the responsibility of the authors and do not represent the official views of the Fukushima Prefecture government.

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Figure legends

Figure 1. Flow chart of the selection of participants in the present study of the association between external radiation dose and incidence of thyroid cancer. The Fukushima Health Management Survey.

Figure 2. Geographic details of the highest-dose, high-middle-dose, middle-dose, low-middle-dose, and lowest-dose areas according to the first 4-month external radiation doses estimated by the Fukushima Health Management Survey. [6]

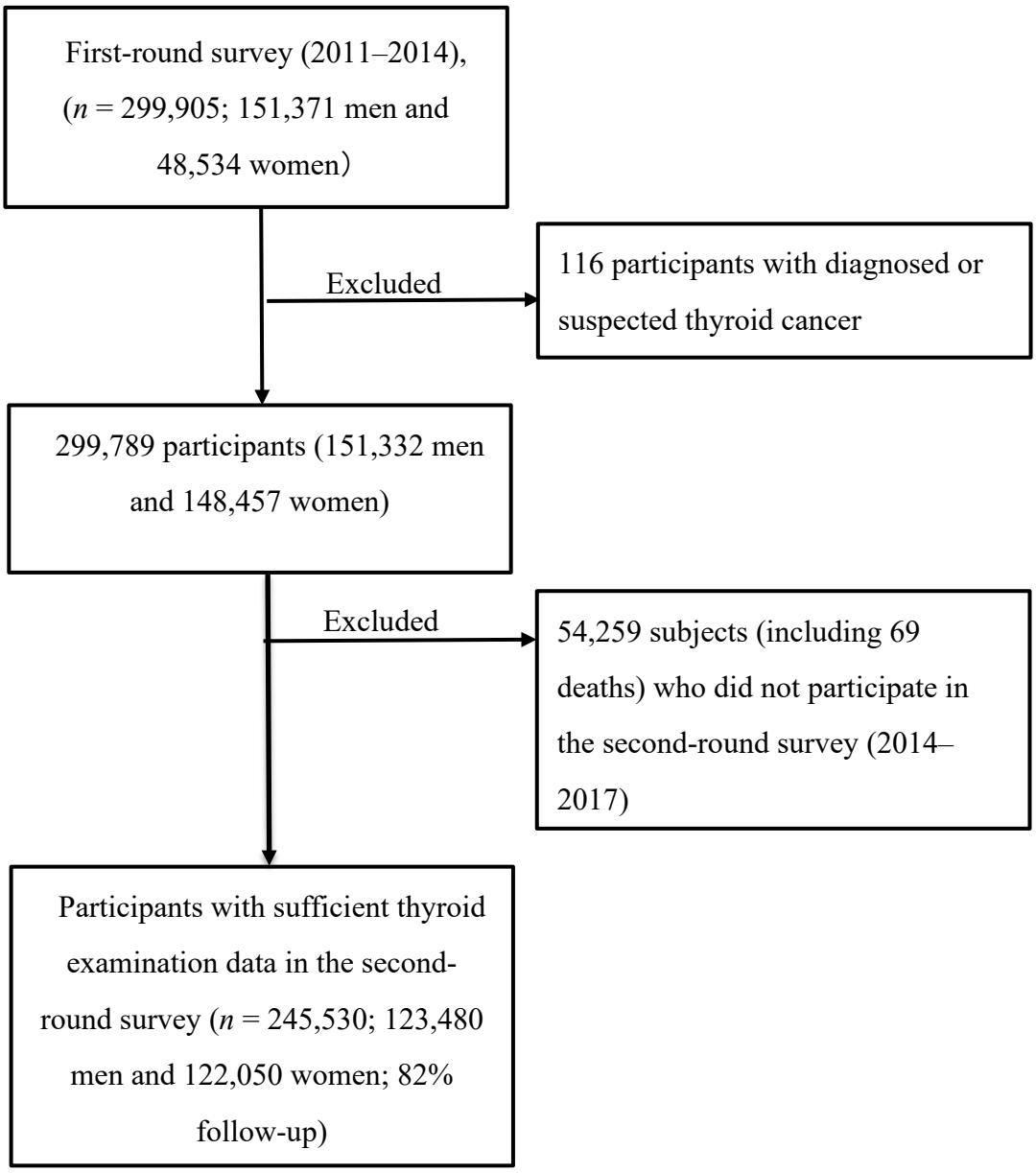
First-round survey (2011–2014), (n = 299,905; 151,371 men and 48,534 women)
Excluded
116 participants with diagnosed or suspected thyroid cancer
299,789 participants (151,332 men and 148,457 women)
Excluded
54,259 subjects (including 69 deaths) who did not participate in the second-round survey (2014–2017)
Participants with sufficient thyroid examination data in the second-round survey (n = 245,530; 123,480 men and 122,050 women; 82% follow-up)

Fig 1

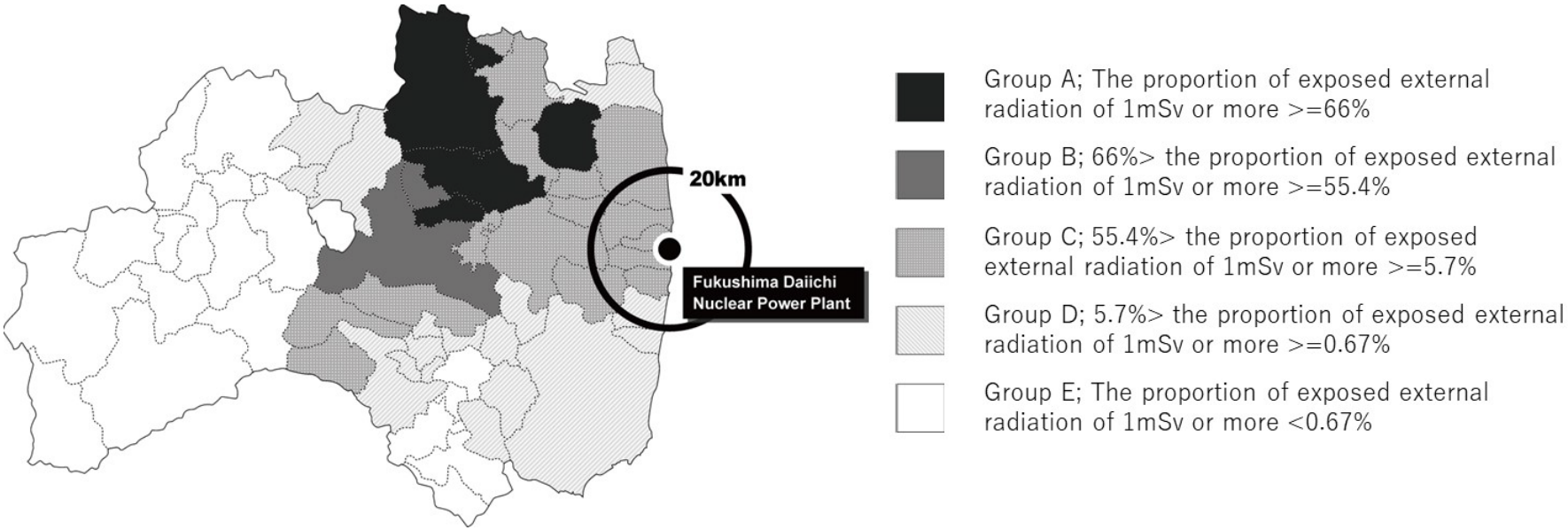
20km
Fukushima Daiichi
Nuclear Power Plant
Group A; The proportion of exposed external radiation of 1mSv or more >=66%
Group B; 66%> the proportion of exposed external radiation of 1mSv or more >=55.4%
Group C; 55.4%> the proportion of exposed external radiation of 1mSv or more >=5.7%
Group D; 5.7%> the proportion of exposed external radiation of 1mSv or more >=0.67%
Group E; The proportion of exposed external radiation of 1mSv or more <0.67%

Fig 2

Table 1. Mean (SD) or prevalence of characteristics of participants with and without thyroid cancer, Fukushima Health Management Survey, 2011–2015

Characteristic	Incident thyroid cancer (n = 70)		No thyroid cancer (n = 245,460)	
Age at NPP accident, yr	12.6	(3.3)	8.0	(4.6)
Age at NPP accident <5 yr, %	0.0		25.9	
5 yr ≤ age at NPP accident < 10 yr, %	15.7		34.7	
10 yr ≤ age at NPP accident < 15 yr, %	51.4		31.8	
Age at NPP accident ≥ 15 yr, %	32.9		7.7	
Age at baseline thyroid examination, yr	14.3	(3.3)	9.9	(4.6)
Age at follow-up thyroid examination, yr	16.6	(3.3)	12.0	(4.6)
Sex (women), %	55.7		49.7	
Height at baseline, cm	155.5	(13.4)	134.8	(24.9)
Weight at baseline, kg	50.1	(14.7)	34.9	(16.6)
Body mass index, kg/m^2	20.3	(3.8)	17.9	(3.5)
Age- and sex-specific obesity, %	10.6		6.2	
External radiation dose*, mSv	1.10	(0.59)	0.92	(0.68)
External radiation dose* (≥ 1 mSv), %	58		42	

*n = 36 for incident thyroid cancer and n = 113,114 for no thyroid cancer.

NPP, Fukushima Daiichi Nuclear Power Plant.

Table 2. Adjusted relative risks (RRs) and 95% confidence intervals (CIs) for thyroid cancer according to location group by first 4-month external radiation doses estimated by the Fukushima Health Management Survey, 2011–2017

Variable	Group A	Group B	Group C	Group D	Group E
No. at risk	52,693	44,743	44,875	67,893	31,628
Sex (women), %	49.7	49.4	50.3	49.7	49.8
Age at NPP accident, yr	8.3	8.0	8.2	7.9	7.6
Age at baseline thyroid examination, yr	9.7	9.9	9.5	10.2	10.4
Age at follow-up thyroid examination, yr	11.8	12.0	11.8	12.3	12.3
Participants needing confirmatory testing, n (%)	441 (0.84)	349 (0.78)	437 (0.97)	535 (0.79)	255 (0.81)
Participants completed confirmatory testing, n (%)	369 (84)	279 (80)	367 (84)	440 (82)	196 (77)
Participants underwent FNAC, n (%)*	60 (16.3)	41 (14.7)	42 (11.4)	31 (7.0)	14 (7.1)
Person-years	111,067	93,740	103,941	144,637	60,409
No. of cases	15	18	18	13	5
Incidence rate per 100,000	13.5	19.2	17.3	9.0	8.3
Age- and sex-adjusted RR	1.62	2.32	2.20	1.02	Reference
(95% CI)	(0.59–4.46)	(0.86–6.24)	(0.82–5.93)	(0.36–2.86)	
Multivariable-adjusted** RR	1.68	2.40	2.16	1.05	Reference
(95% CI)	(0.61–4.62)	(0.89–6.48)	(0.80–5.82)	(0.37–2.95)	

* Participants underwent FNAC/ Participants completed confirmatory testing. **Adjusted for age, sex, and obesity (normal-weight, overweight, obesity). NPP, Fukushima Daiichi Nuclear Power Plant. FNAC, fine-needle aspiration cytology

Table 3. Adjusted relative risks (RRs) and 95% confidence intervals (CIs) of thyroid cancer according to overweight/obese group

	Non-overweight/obesity	Overweight	Obesity
No. at risk	200,146	22,392	14,626
Women, %	50.9	44.5	42.0
Age at NPP accident, yr	8.2	7.2	6.9
Age at baseline thyroid examination, yr	10.1	9.1	8.7
Age at follow-up thyroid examination, yr	12.2	11.3	10.9
Participants needing confirmatory testing, n (%)	1,697 (0.84)	184 (0.81)	134 (0.90)
Participants completed confirmatory testing, n (%)	1,375 (81)	158 (86)	111 (83)
Participants underwent FNAC, n (%)*	163 (11.9)	11 (7.0)	10 (9.0)
Person-years	424,337	47,641	31,269
No. of cases	56	3	7
Incidence rate per 100,000 people	13.2	6.3	22.4
Age- and sex-adjusted RR (95% CI)	Reference	0.58 (0.18-1.85)	2.26 (1.03-4.95)
Multivariable-adjusted** RR	Reference	0.63 (0.20-2.01)	2.20 (1.00-4.85)

* Participants underwent FNAC/ Participants completed confirmatory testing. **Adjusted for age, sex, and location group by first 4-month external radiation doses. NPP, Fukushima Daiichi Nuclear Power Plant. FNAC, fine-needle aspiration cytology

eTable 1. Adjusted relative risks (RRs) and 95% confidence intervals (CIs) of thyroid cancer according to location group by first 4-month external radiation doses estimated by The Fukushima Health Management Survey, stratified by tumor size, 2011-2017.

	Group A	Group B	Group C	Group D	Group E
Tumor size:10mm and over					
Person-years	111,067	93,740	103,941	144,637	60,409
No. of cases	5	6	11	9	3
Incidence rate per 100,000 people	4.5	6.4	10.6	6.2	5.0
Age-adjusted RR	0.91	1.30	2.24	1.19	Reference
(95% CI)	(0.22-3.80)	(0.32-5.19)	(0.63-8.03)	(0.32-4.41)	
Mutivariable-adjusted* RR	0.92	1.31	2.22	1.20	Reference
(95% CI)	(0.22-3.84)	(0.33-5.25)	(0.62-7.95)	(0.32-4.44)	
Tumor size:9.9mm and less					
Person-years	111,067	93,740	103,941	144,637	60,409
No. of cases	10	12	7	4	2
Incidence rate per 100,000 people	9.0	12.8	6.7	2.8	3.3
Age- and sex-adjusted RR	2.68	3.83	2.14	0.77	Reference
(95% CI)	(0.59-12.3)	(0.86-17.1)	(0.44-10.3)	(0.14-4.23)	
Mutivariable-adjusted** RR	2.85	4.08	2.08	0.82	Reference
(95% CI)	(0.62-13.1)	(0.91-18.3)	(0.43-9.99)	(0.15-4.48)	

* Participants underwent FNAC/ Participants completed confirmatory testing. **Adjusted for age, sex, and obesity (normal-weight, overweight, obesity). NPP, Fukushima Daiichi Nuclear Power Plant. FNAC, fine-needle aspiration cytology

eTable 2. Adjusted relative risks (RRs) and 95% confidence intervals (CIs) of thyroid cancer according to location group by 90th percentile values of internal thyroid doses to 1-year-old children, estimated by Kim E, et al.[15)]

	Group I (30mSv)	Group II (10-20mSv)	Group III (<10mSv)
No. at risk	42,183	16,880	182,769
Women, %	50	50	50–
Age at NPP accident, yr	8.1	8.3	8.0
Age at baseline thyroid examination, yr	10.4	9.2	9.9
Age at follow-up thyroid examination, yr	12.7	11.8	12.0
Participants needing confirmatory testing, n (%)	350 (0.83)	178 (1.05)	1,489 (0.81)
Participants completed confirmatory testing, n (%)	285 (81)	152 (85)	1,214 (82)
Participants underwent FNAC, n (%)*	23 (8.1)	21 (13.8)	144 (11.9)
Person-years	93,202	42,479	378,112
No. of cases	9	8	52
Incidence rate per 100,000 people	9.7	18.8	13.8
Age- and sex-adjusted RR (95% CI)	0.63 (0.31-1.27)	1.50 (0.71-3.16)	Reference
Multivariable-adjusted** RR	0.63 (0.31-1.28)	1.37 (0.64-2.94)	Reference

* Participants underwent FNAC/ Participants completed confirmatory testing. **Adjusted for age, sex, and obesity (normal-weight, overweight, obesity). NPP, Fukushima Daiichi Nuclear Power Plant. FNAC, fine-needle aspiration cytology