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# Benefits of thyroid screening and evidence suggesting radiation exposure as a cause of increased pediatric thyroid cancer in Fukushima Prefecture

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**Article**

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## Abstract

The Fukushima Daiichi nuclear accident released a large quantity of radioactive materials, including radioactive iodine, which can cause thyroid cancer. Following the accident, Fukushima Prefecture conducted thyroid ultrasound examinations (TUEs) among approximately 380,000 individuals aged 18 years or younger or in utero at the time of the accident. The thyroid cancer (TC) incidence detected through this program was several dozen times higher than the national average, raising concerns regarding screening effects, overdiagnosis, and whether to reduce or discontinue the program. However, the clinical benefits of TUEs remain unclear. Using data from the NPO 311Fund, which supports patients inside and outside Fukushima, we evaluated the clinical implications of screening. Compared with patients diagnosed clinically after symptomatic presentation, those identified through screening exhibited approximately one-fifth the total thyroidectomy rate, one-sixth the rate of distant metastasis, and 40% of the radioiodine therapy rate. Furthermore, a strong positive correlation was observed between regional radiation dose estimates and TC incidence ($R^2 = 0.9723$, $p = 0.014$). This correlation, combined with the increasing proportion of male cases, suggests that radiation exposure is a causal factor for the observed increase in thyroid cancer in this population.


## Introduction

Following the Fukushima Daiichi Nuclear Power Plant disaster, a large quantity of radioactive materials was dispersed across a wide area of Eastern Japan, particularly in Fukushima Prefecture. The Japanese government decided to limit systematic thyroid examinations to Fukushima Prefecture and delegated their implementation to the prefectural government. The prefectural government decided to conduct the Fukushima Prefectural Health Management Survey (FHMS) [1] to asses residents' radiation exposure levels, monitor their health status, enable early detection and treatment of diseases, and promote the health of the Prefecture’s population. Given the potential exposure of Fukushima residents to radioactive iodine, they included thyroid examinations in the FHMS. The entire FHMS process, from study design to analysis of results, was outsourced by the Fukushima Prefecture to Fukushima Medical University (FMU). No publicly funded, systematic thyroid examinations were conducted outside Fukushima Prefecture. FMU initiated thyroid ultrasound examinations (TUEs) in October 2011, seven months after the accident.

The examination program targets approximately 380,000 individuals who were aged 18 years or younger or were in utero at the time of the accident. Examinations are performed every 2 years until the age of 20 years, and every five years thereafter using ultrasound equipment. If a nodule of 5.1 mm or larger or a cyst of 20.1 mm or larger in diameter is detected, the participant proceeds to the secondary confirmatory examination. Cases diagnosed as malignant or suspicious for malignancy through fine needle aspiration cytology are reported to the FHMS Oversight Committee (OC) established by the prefecture to evaluate the results of the FHMS, and are made public simultaneously [2]. Based on the understanding that the incidence of thyroid cancer (TC) began to increase four to five years after the Chernobyl accident, the FMU designed the first round of examinations as a baseline survey to establish background incidence levels. However, at Chernobyl, ultrasound examinations were not introduced until four to five years after the accident. Contrary to expectations, the results showed that the incidence of TC in the first and second rounds was several dozen times higher than the national average [3–5]. TC has continued to be detected at a high rate in each subsequent round, through the sixth round; the seventh round of examination is currently underway.

There is some debate as to the cause of this high incidence of TC. The FMU research group and some other researchers reject substantial contribution from the radiation exposure, citing the low levels of radiation doses received by the population, the lack of a correlation between radiation exposure and TC incidence, and the short latency period. They attribute the high incidence primarily to the effects of intensive screening using highly sensitive ultrasonography [3, 6]. Researchers who have attribute the findings to overdiagnosis [5, 7] cite the low radiation exposure dose as a major argument against a radiation-induced increase in TC incidence. This interpretation has gained wide public

attention but has also been discussed in the UNSCEAR 2020/2021 report. Some members of the OC have advocated scaling back or discontinuing TUEs to minimize the risk of overdiagnosis. In contrast, researchers outside the FMU have argued that radiation exposure contributed to the increased incidence, based on the observed correlation between radiation dose and incidence rates [8–12].

Although there have been calls to reduce or discontinue TUEs in FHMS, their potential benefits have not yet been adequately evaluated. Therefore, this study aimed to investigate whether TUEs contribute to health promotion through the early detection and treatment of TC, one of the goals of FHMS, and to assess their clinical benefits to patients. In addition, although FMU reports have found no correlation between radiation exposure and TC incidence, we examined this relationship using data reported by the OC and data presented in the UNSCEAR 2020/2021 report.

## Materials and Methods

# Establishment of the 3.11 Fund for Children with Thyroid Cancer

The 3.11 Fund for Children with Thyroid Cancer (311Fund) [14] is a nonprofit organization (NPO) established in 2016 to support individuals diagnosed with TC following the Fukushima Nuclear Power Plant accident. The 311Fund collects donations from the public to provide various forms of support, including medical expenses and consultations. Eligible individuals are those who were aged 18 years or younger at the time of the accident and resided in areas where radioactive iodine dispersed, including Fukushima Prefecture and 15 other prefectures [15].

## Participants

By October 2024, the 311Fund had provide support to 167 TC patients residing in Fukushima Prefecture (311FR) and 79 patients residing outside Fukushima Prefecture (311OF). Of those, 163 patients in the 311FR and all 79 patients in the 311OF agreed to participate in this study.

Clinical characteristics and treatment histories of the 311Fund recipients were obtained from the application forms submitted by the recipients. The application form requires applicants to provide their address at the time of the accident, name, sex, date of birth, circumstances surrounding the discovery of TC, medical institution where surgery was performed, the surgeon's name, date of surgery, extent of surgery (total thyroidectomy or unilateral lobectomy), histological types of TC, and the presence of lymph node or distant metastases. If the recipient undergoes further surgery or radiotherapy due to recurrence or metastasis, a separate application form must be submitted for each treatment, detailing the date of treatment, the procedure performed, the name of the hospital, and the name of the surgeon. Each application was reviewed by a committee comprising three members (two physicians and one attorney), who determined the applicant's eligibility for financial support. After personal identifiers were removed from the application forms, the resulting information was used as research data.

## Methods

The effectiveness of thyroid screening was evaluated by comparing the clinical characteristics of patients identified through screening with those of patients who presented to general thyroid outpatient clinics. Since the clinical characteristics of 311Fund recipients were obtained from the participants' application forms, the available information was limited to what the participants could accurately obtain from their physicians. Therefore, comparisons were limited to four clinical variables: the rate of total thyroidectomy, the incidence of distant metastasis, the rate of radioactive iodine (RAI) therapy, and the recurrence rate. The screening group comprised 136 patients with papillary thyroid cancer (PTC) detected by TUEs from the 311FR group (out of 163), along with 219 patients reported by Matsumoto et al. [16]

and 213 cases reported by Shio et al. [17] from FMU. The comparison group consisted of 60 PTC patients from the 311OF group and 479 PTC cases aged 20 years or younger from three thyroid hospitals: 142 reported by Enomoto et al. [18], 110 by Ito et al. [19], and 227 by Sugino et al. [20]. All methods were performed in accordance with the Ethical Guidelines for Life Science and Medical Research Involving Human Subjects issued by the three relevant Ministries of Japan, as well as all other relevant guidelines and regulations.

# Statistical analysis

For comparisons between groups, categorical variables were compared using Fisher's exact test. A two-sided p-value < 0.05 was considered statistically significant. Simple linear regression analysis was performed to assess the association between radiation dose and TC incidence, with radiation dose as the independent variable and TC incidence as the dependent variable. All statistical analyses were performed using EZR, a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) that provides additional statistical functions commonly used in biostatistics [21].

For thyroid exposure assessment, we utilized the estimated thyroid doses for 10-year-old children by municipality from the UNSCEAR 2020/2021 report [22]. We calculated the mean dose for each of the four regions designated by Fukushima Prefecture: the evacuation zone, Nakadori, Hamadori, and Aizu. The estimated radiation doses received by residents across the 13 municipalities in the evacuation zone were calculated based on evacuation routes from points of departure to destinations. To calculate the average for these 13 municipalities, the highest value for each municipality was used.

The total number of TC cases was determined by adding 47 individuals, who had been omitted from the FHMS TUE statistics, to the regional numbers of TC cases reported through the fifth round of the FHMS TUE, as the regional data for the sixth round have not yet been published. These 47 individuals were assigned to the four regions according to the classification provided in the 24th evaluation subcommittee report [23]. The TC incidence per 100,000 people was calculated using the total number of individuals eligible for thyroid screening in each region as the denominator.

## Results

# Discrepancies in thyroid cancer case tallies within the FHMS program

FMU reported that 368 cases of thyroid malignancy or suspected malignancy were identified up to the sixth round of the FHMS TUEs (Table 1). However, the 311Fund inquired with FMU regarding an unrecorded patient who was missing from the published statistics. This inquiry prompted FMU to cross-check the FHMS TUE data with regional and national cancer registries, which subsequently revealed a structural mechanism within the program that led to the undercounting of cases. Consequently, FMU identified and reported 47 missing patients up to 2019 [24–27], but the university has not released any subsequent data since then. Furthermore, the 311Fund identified 12 additional patients omitted from the tally between January 2020 and October 2024. Because the screening program has not been revised to address these reporting gaps, the exact number of patients diagnosed from 2020 onwards remains uncertain. A total of 311 patients underwent surgery; papillary carcinoma was by far the predominant histological type of thyroid cancer (98.4%). Of the 71 cases diagnosed in the second round, 33 (46.5%) had been classified as “no detectable findings” in the first-round examination conducted approximately two years earlier. This indicates that, within this short period, 46.5% of these tumors had grown by at least 5.1 mm in diameter from a stage undetectable even by high-sensitivity ultrasonography.

The participation rate in the examination program has declined with each subsequent round, with a particularly pronounced decrease among individuals aged 20 years and over. Of the six rounds, the incidence rate is highest in the fifth and remains extremely high among those aged 20 years and over. Furthermore, the mean age at the time of the accident decreased progressively across consecutive rounds, reaching its lowest value in the sixth round. These findings suggest that the latency period may be longer in younger children, consistent with observations in Belarus following the Chernobyl accident [28].

Table 1
Overview of the thyroid cancers detected through the Fukushima Health Management Survey thyroid examinations

| **Rounds** | **1** | **2** | **3** | **4** | **5** | **6** | **Age 25-** | **Age 30-** | **Total** |
|---|---|---|---|---|---|---|---|---|---|
| **(Fiscal year)** | **(2011-13)** | **(2014-15)** | **(2016-17)** | **(2018-19)** | **(2020-22)** | **(2023-)** | **(2017-)** | **(2022-)** | |
| Malignancy or suspected | 116 | 71 | 31 | 39 | 50 | 24 | 27 | 10 | 368 |
| No previous abnormalities | | 33 | 7 | 6 | 11 | 5 | | | 62 |
| Male: Female | 39:77 | 32:39 | 13:18 | 17:22 | 13:37 | 6:18 | 4:23 | 2:8 | 126:242 |
| Average age at Accident (range) | 14.9 ± 2.6 (6–18) | 12.6 ± 3.2 (5–18) | 9.6 ± 2.9 (5–16) | 8.3 ± 2.9 (0–14) | 6.1 ± 3.2 (0–12) | 4.2 ± 3.2 (0–9) | 15.3 ± 1.7 (12–18) | 17.4 ± 0.8 (16–18) | |
| Average age at Diagnosis (range) | 17.3 ± 2.7 (8–22) | 16.9 ± 3.2 (9–23) | 16.3 ± 2.9 (12–23) | 17.0 ± 3.1 (9–24) | 17.3 ± 2.9 (12–24) | 17.2 ± 3.2 (12–23) | 25.7 ± 1.2 (24–29) | 30.0 ± 0.5 (29–31) | |
| Confirmed cancer | 102 | 56 | 29 | 34 | 46 | 19 | 20 | 5 | 311 |
| Histological types | PTC:100 PDTC:1 BN:1 | PTC:55 OTC:1 | PTC:29 | PTC:34 | PTC:45 OTC:1 | PTC:19 | PTC:19 FTC:1 | PTC:5 | PTC:306 PDTC:1, FTC:1 OTC:2, BN:1 |
| Participants | 300,472 | 270,552 | 217,922 | 183,410 | 113,959 | 69,032 | 14.195 | 4,642 | |
| Rate (%) | (81.7) | (71.0) | (64.7) | (62.3) | (45.1) | (32.6) | (7.5) | (5.3) | |
| Incidence (%) | 0.034 | 0.026 | 0.014 | 0.021 | 0.044 | 0.035 | 0.19 | 0.22 | |

Prepared from the data presented at the 60th FHMS OC (July 2026). Abbreviations; PTC: Papillary thyroid cancer, PDTC: Poorly differentiated thyroid cancer, BN: Benign nodule, OTC: Other type of thyroid cancer, FTC: Follicular thyroid cancer.

## The characteristics of the study participants in the 311FR and 311OF cohorts

Table 2 summarizes the characteristics of the study participants. Among TC patients in the 311FR, 144 individuals (88.3%) were identified through the FHMS TUEs or other thyroid screening program. In contrast, since systematic thyroid screening was not conducted outside Fukushima Prefecture, only six patients (7.6%) in the 311OF cohort were

identified through thyroid screening conducted by local or non-governmental organizations. Following diagnosis, three patients (1.8%) in the 311FR and two patients (2.5%) in the 311OF selected active surveillance [29] rather than undergoing immediate surgery. The proportion of males was significantly higher in the 311FR than in the 311OF. An increased incidence of TC among males following radiation exposure has also been reported after the Chernobyl nuclear accident. No significant difference was observed between the 311FR and 311OF in the average age at the time of the accident or at diagnosis. Regarding histopathological classification, papillary carcinoma accounted for 93.9% and 82.3% in the 311FR and 311OF, respectively, whereas follicular carcinoma accounted for 12.7% in the 311OF.

Table 2
Clinical and demographic characteristics of the 311FR and 311OF cohorts.

| **Male: Female** | **311FR(N = 163)** | **311OF(N = 79)** | **p value** |
|---|---|---|---|
| | **66: 97** | **15: 64** | **0.0008** |
| Average age at the accident ± SD | 12.2 ± 4.4 | 12.0 ± 5.0 | 0.794 |
| (median, range) | (13.0, 0–18) | (13.0, 0–18) | |
| Average age at the diagnosis ± SD | 18.9 ± 4.3 | 19.2 ± 4.6 | 0.592 |
| (median, range) | (19.0, 9–31) | (19.0, 10–30) | |
| Method of detection Thyroid screening | 144 (88.3%) | 6 (7.6%) | 2.5e-36 |
| Others | 19 (11.7%) | 73 (92.4%) | |
| Clinical treatment Surgically treated | 160 (98.2%) | 77 (97.5%) | 0.663 |
| Active surveillance | 3 (1.8%) | 2 (2.5%) | |
| Histological types PTC | 155 (95.1%) | 67 (84.8%) | |
| FTC | 5 (3.1%) | 10 (12.7%) | |
| Others | 2 (1.2%) | 2 (2.5%) | |
| Unknown | 1(0.6%) | | |

## The effectiveness of TUEs in the FHMS

To assess the clinical implications of thyroid ultrasound screening for patients with TC, we compared the clinical characteristics of patients with PTC identified through screening in the 311FR (n = 136) with those of patients with PTC in the 311OF (n = 60), whose cancers were detected outside of screening. Patients in the 311FR are considered to have been exposed to varying degrees of radioactive iodine during the accident. In contrast, although the 311OF included individuals residing in areas where radioactive iodine was dispersed during the accident, their individual exposure status remains uncertain. Furthermore, contamination levels varied considerably across these areas, and the number of individuals examined was extremely small relative to the total eligible population across the 15 prefectures. Therefore, the effects of radiation exposure cannot be adequately evaluated at this stage.

The two cohorts were stratified according to age at the time of the accident (0–14 and 15–18 years), and their clinical characteristics were compared (Table 3). Among patients aged 0–14 years at the time of the accident, the proportions undergoing total thyroidectomy, presenting with distant metastasis, and receiving radioactive iodine (RAI) therapy were significantly higher in the 311OF than in the 311FR. Notably, the odds ratio for total thyroidectomy was particularly high in the 311OF. Among patients aged 15–18 years, these proportions were also higher in the 311OF; though the differences were not statistically significant except for the rate of total thyroidectomy. These findings suggest that

patients in the 311OF, whose thyroid cancers were generally detected following symptomatic presentation, tended to have more advanced disease at diagnosis compared with the 311FR cohort, which underwent regular screening. Furthermore, the differences in clinical characteristics between the two cohorts appeared to be more pronounced among patients who were younger at the time of the accident.

Table 3
Comparison between the 311FR and 311OF cohorts with papillary thyroid cancer, stratified by age at the time of the accident.

| | **Age at the accident: 0–14** | | | **Age at the accident: 15–18** | | | **All subjects** | | |
|---|---|---|---|---|---|---|---|---|---|
| | **311FR n = 92 (%)** | **311OF n = 35 (%)** | **Odds ratio 311FR = 1 (95% CI) p value** | **311FR n = 44 (%)** | **311OF n = 25 (%)** | **Odds ratio 311FR = 1 (95% CI) p value** | **311FR N = 136 (%)** | **311OF N = 60 (%)** | **Odds ratio 311FR = 1 (95% CI) p value** |
| Sex, male | 45 (48.9) | 5 (14.3) | 0.176 (0.05–0.51) 0.0004 | 14 (31.8) | 4 (16) | 0.413 (0.09–1.57) 0.253 | 59 (43.4) | 9 (15) | 0.232 (0.09–0.53) 0.00009 |
| Total Thyroidectomy | 10 (10.9) | 23 (65.7) | 15.212 (5.48–45.93) 2e-9 | 4 (9.1) | 11 (44) | 7.583 (1.87–38.17) 0.0016 | 14 (10.3) | 34 (56.7) | 11.203 (5.06–26.10) 2.02e-11 |
| Unilateral lobectomy | 82 (89.1) | 12 (34.3) | 0.066 (0.022–0.182) 2e-9 | 40 (90.9) | 14 (56) | 0.132 (0.026–0.534) 0.0016 | 122 (89.7) | 26 (43.3) | 0.089 (0.038–0.198) 2.02e-11 |
| Distant metastasis | 3 (3.3) | 6 (17.1) | 6.031 (1.20-39.53) 0.0132 | 1 (2.3) | 4 (16) | 7.937 (0.73-411.48) 0.0543 | 4 (2.9) | 10 (16.7) | 6.526 (1.78–29.85) 0.0013 |
| RAI therapy | 15 (16.3) | 16 (45.7) | 4.263 (1.66–11.19) 0.0011 | 4 (9.1) | 6 (24) | 3.101 (0.65–16.81) 0.152 | 19 (14.0) | 22 (36.7) | 3.538 (1.64–8.75) 0.0005 |
| Recurrence | 16 (17.4) | 5 (14.3) | 0.793 (0.218–2.54) 0.793 | 4 (9.1) | 3 (12) | 1.357 (0.12–8.84) 0.698 | 20 (14.7) | 8 (13.3) | 0.893 (0.32–2.29) 1 |

The proportion of males was higher in the 311FR than in the 311OF. This difference was statistically significant in the 0–14 age group but not in the 15–18 age group. Previous studies have reported a greater increase in the incidence of TC among boys following the Chernobyl accident and among younger males exposed to the atomic bombings [30–32].

When the two age groups were combined, the differences in the clinical characteristics between the 311FR and 311OF became more apparent. No statistically significant difference in the recurrence rate was observed between the two cohorts in either the individual age groups or the combined population.

Because the 311OF included substantially fewer patients with PTC than the 311FR, we examined whether the potential benefits of screening could also be demonstrated by comparison with patients who presented to thyroid outpatient clinics. For this analysis, we included patients aged 20 years or younger with PTC and no history of radiation exposure who were treated at three thyroid hospitals as reported in previous studies [18–20] (three hospitals). In addition, using data reported from the FMU [16, 17], we examined whether the benefits of screening observed in the 311FR were also evident in FMU patients (Fig. 1).

Cases detected through thyroid screening were the 311FR and FMU cases, while routine clinical cases were the 311OF and three hospital cases. The rates of total thyroidectomy and distant metastasis were similar between the 311FR and FMU cases and between the 311OF and three hospital cases. Compared with the clinically detected group, the screening-detected group had approximately one-fifth the rate of total thyroidectomy and one-sixth the rate of distant metastasis.

The rate of RAI therapy in the three hospitals cohort was less than half that of 311OF cohort. One possible explanation is that most patients in the three-hospital cohorts were diagnosed before the Fukushima Daiichi Nuclear Power Plant disaster. According to the cancer treatment guidelines published by the Japan Association of Endocrine Surgeons and the Japanese Society of Thyroid Surgery [33], at that time, only a limited number of hospitals had facilities capable of providing RAI therapy. In addition, some hospitals, including those reported by Ito et al. [19], deliberately avoided RAI therapy because of concerns about the radiation exposure risks for younger patients [34]. Thus, the low rate of RAI therapy performed in the three hospitals cohort may reflect this situation. Following the nuclear disaster, the number of facilities offering RAI therapy increased. Therefore, a comparison of RAI therapy rates between the 311FR and 311OF cohorts is now feasible. The rate in the 311FR was approximately 40% of that in the 311OF. According to Matsumoto, the rate of RAI therapy in FMU was 1.8% (Fig. 2). However, at the 2023 Annual Meeting of the Japanese Thyroid Association, Suzuki S. reported in an oral presentation that 16 of 217 patients who underwent surgery received RAI therapy, corresponding to a rate of 7.3% [35]. Nevertheless, this rate remained substantially lower than that in the 311OF. Taken together, the findings regarding the potential benefits of TUEs were consistent across comparisons using data from the 311Fund and analyses incorporating data from external thyroid hospitals and FMU.

Regarding recurrence rates, the rate in the three-hospital cohort was more than twice that in the FMU cohort. This finding is consistent with the potential benefits of thyroid ultrasound screening. However, the follow-up period was substantially longer in the three hospitals cohort (up to 40 years) than in the FMU cohort (around 10 years). Therefore, the possibility that the recurrence rate in the FMU cohort may increase with longer follow-up cannot be excluded. A comparison of recurrence rates between the two cohorts within the 311Fund revealed no statistically significant difference. This may be attributable to the small number of patients in the 311OF and the relatively short follow-up period, which may have limited the statistical power to detect differences in recurrence rates. Further investigation with larger patient populations and longer follow-up periods are needed to clarify differences in recurrence rates between the two cohorts.

## Correlation between radiation dose and thyroid cancer incidence

FMU does not publish region-specific data on patients aged 20 years or older. Furthermore, from the third round onwards, FMU stopped reporting the number of TC cases by municipality and instead reported numbers by using four regional categories. Therefore, we analyzed the correlation between regional radiation dose and TC incidence using data from the first through fifth examination rounds, together with data on the 47 individuals who had been excluded from the original tally [23] (Table 4). Regional radiation dose estimates were obtained from the UNSCEAR 2020/2021 report [22]. A strong positive correlation was observed between radiation dose and TC incidence ($R^2 = 0.9723$, $p = 0.014$; Fig. 2).

Table 4. Estimated thyroid absorbed doses in 10-year-old children and numbers of thyroid cancer cases in four regions of Fukushima Prefecture

| District (Number of municipalities) | Average 10-year-old thyroid dose (mGy) (median, range) | Target population | Number of patients in rounds 1–5 | Missed count from FHMS Tally | Total patients | Incidence per 100,000 |
|---|---|---|---|---|---|---|
| Aizu (17) | 1.62 (1.3, 1.0-3.2) | 51,758 | 31 | 4 | 35 | 67.62 |
| Nakadori (26) | 3.67 (2.5, 1.4–13) | 207,189 | 163 | 22 | 185 | 89.29 |
| Hamadori (3) | 6.60 (6.9, 4.2–8.7) | 72,857 | 67 | 7 | 74 | 101.57 |
| Evacuation areas (13) | 9.02 (9.30, 2.3–22) | 49,457 | 45 | 14 | 59 | 119.30 |
| Total (59) | | 381,261 | 306 | 47 | 353 | 92.6 |

Figure 2.

## Discussion

Fukushima Prefecture initiated FHMS, which includes TUEs, to facilitate early detection of thyroid diseases enable timely treatment, and protect the health of residents. As shown in Fig. 1, compared with the 311OF cohort and patients treated at the three hospitals, the 311FR and FMU cohorts had approximately one-fifth the rate of total thyroidectomy and one-sixth the rate of distant metastasis. Total thyroidectomy is associated with complications including postoperative hypoparathyroidism and postoperative laryngeal nerve palsy [36]. In addition, patients who undergo total thyroidectomy must take thyroid hormone medication for life. Therefore, reducing the rate of total thyroidectomy provides substantial benefits to patients. Distant metastasis is associated with a poorer prognosis and may necessitate RAI therapy. RAI therapy carries potential risks including secondary malignancies [37, 38], salivary gland dysfunction [39] and infertility [40]. Reducing these risks to approximately one-third is also a major benefit for patients. Furthermore, previous studies have reported higher long-term survival rates among patients with thyroid cancer (TC) detected through screening than among those diagnosed clinically after symptom onset [41, 42]. The SHAMISEN Consortium [43] and IARC [44] recommend that post-nuclear accident thyroid screening should only be implemented when the benefits outweigh the harms. In Fukushima Prefecture, the findings of the present study suggest that TUEs may offer important clinical benefits. Furthermore, a questionnaire survey conducted by the 311 Fund among its recipients found that more than 90% of patients with TC and all of their family members supported the continuation of TUEs [45].

The definition of overdiagnosis is the diagnosis of disease that would not cause symptoms or death during a person's lifetime if left untreated. It is therefore more likely to occur in slow-growing cancers and in older individuals. Among the cancers identified through TUEs in the FHMS, some cases showed rapid growth (Table 1). Moreover, because the patients are children and adolescents, determining whether overdiagnosis has occurred will require considerable follow-up. Meanwhile, many reports on TC overdiagnosis concern patients aged 20 years and over [46, 47]. Therefore, findings from these studies cannot be directly extrapolated to children and adolescents in Fukushima Prefecture. In addition, Suzuki S. [48], who performed most TC surgeries at FMU, also argued against overdiagnosis. He cited the findings that more than 70% of surgical cases showed lymph node metastasis and over 40% showed extrathyroidal extension. However, he attributed the increased detection of TC primarily to the use of highly sensitive ultrasonography and considered radiation exposure to be an unlikely explanation.

The primary aim of screening is the early detection of disease, enabling timely intervention when necessary. The findings of this study suggest that the TUE program within the FHMS may achieve this objective. Because TUEs use highly sensitive ultrasonography to detect nodules measuring 5.1 mm or larger, the number of newly detected TC cases would be expected to decrease in subsequent screening rounds as previously existing detectable lesions are identified in the initial round, provided that few new lesions develop. However, as shown in Table 1, the higher detection rate observed in the fifth screening round than in the first four rounds appears inconsistent with this expected screening effect.

If the use of highly sensitive ultrasonography were to result in overdiagnosis or a screening effect a substantially increased the detection of otherwise clinically occult TC, one might expect the sex distribution of screen-detected TC cases to resemble that of sporadic TC, with higher detection rates among women than men. Ahn et al. [49], in their report on the effects of thyroid cancer screening in South Korea, demonstrated a similar pattern: the male-to-female incidence ratio remained consistent with that typically observed in sporadic TC. Although most participants in the study were aged 20 years or older, the incidence rates per 100,000 population for men and women during 2008–2010, when screening substantially increased TC detection rates, were 12.1 and 107.3, respectively. Thus, the incidence rate among women was approximately nine times that among men, indicating a marked female predominance. There are also reports that TC was not detected through screening in children born after radioactive iodine had decayed following the Chernobyl accident [50–52]. These findings suggest that the implementation of TUEs in children does not necessarily lead to overdiagnosis or a screening effect. In Japan, measures to reduce the risk of overdiagnosis were introduced at an early stage [53]. Clinical Guidelines on the Management of Thyroid Tumors, published by the Japan Association of Endocrine Surgery [54] recommend specific criteria for fine-needle aspiration cytology to minimize the risk of overdiagnosis associated with screening.

The main arguments against attributing the high incidence of TC in Fukushima Prefecture to radiation exposure are that the estimated radiation doses were low, no dose-response relationship has been observed, and the latency period of less than four years was shorter than that generally reported after the Chernobyl disaster [55]. However, the estimated radiation doses in the UNSCEAR 2020/2021 report have been criticized as underestimates [56, 57], and several studies have reported association between radiation dose and TC incidence [8–12]. Furthermore, the report of the FHMS OC summarizes findings from a case-control study that reported an association between radiation dose and TC incidence [58].

The argument that a latency period of less than four years is too short compared with that observed after the Chernobyl disaster warrants reconsideration. As shown in Table 1, in some cases no abnormalities were detectable by highly sensitive ultrasonography initially, but nodules measuring 5.1 mm or larger were detected within two years. It is also important to note that ultrasound screening was not introduced in Chernobyl until four to five years after the accident. Furthermore, some reports suggest that the minimum latency period for TC may be less than one year [59].

Finally, a clear correlation between estimated radiation doses and TC incidence was observed, even when using the dose estimates reported in the UNSCEAR 2020/2021 report (Fig. 3).

## Conclusion

Based on the available data to us, our findings suggest that thyroid ultrasound examinations in Fukushima Prefecture provide clinical benefits to patients. Analyses of data published by the OC suggest that the increased incidence of TC among children and adolescents in Fukushima Prefecture cannot be fully explained by overdiagnosis or the screening effect alone. Furthermore, the correlation between radiation dose and thyroid cancer incidence, together with the increasing proportion of male cases, raises the possibility that radiation exposure may have contributed to the increased incidence of TC.

# Data availability

All data reported in this study were included in the manuscript.

Should you have any further inquiries, please contact the corresponding author.

## Abbreviations

**311Fund**: 3.11 Fund for Children with Thyroid Cancer
**FHMS**: Fukushima Prefecture Health Management Survey

## Declarations

**Author contributions**

H.S. and Y.Y. conducted conceptualization, wrote the main manuscript text and prepared figures 1,2 and Tables 1–4. All authors reviewed the manuscript.

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**Informed Consent Statement:** We obtained informed consent from all participants in this study, and in the case of children, from their parents.

This study was approved by the Ethics Committee of the ‘311 Fund for Children with Thyroid Cancer’ in December 2024.

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## Figures

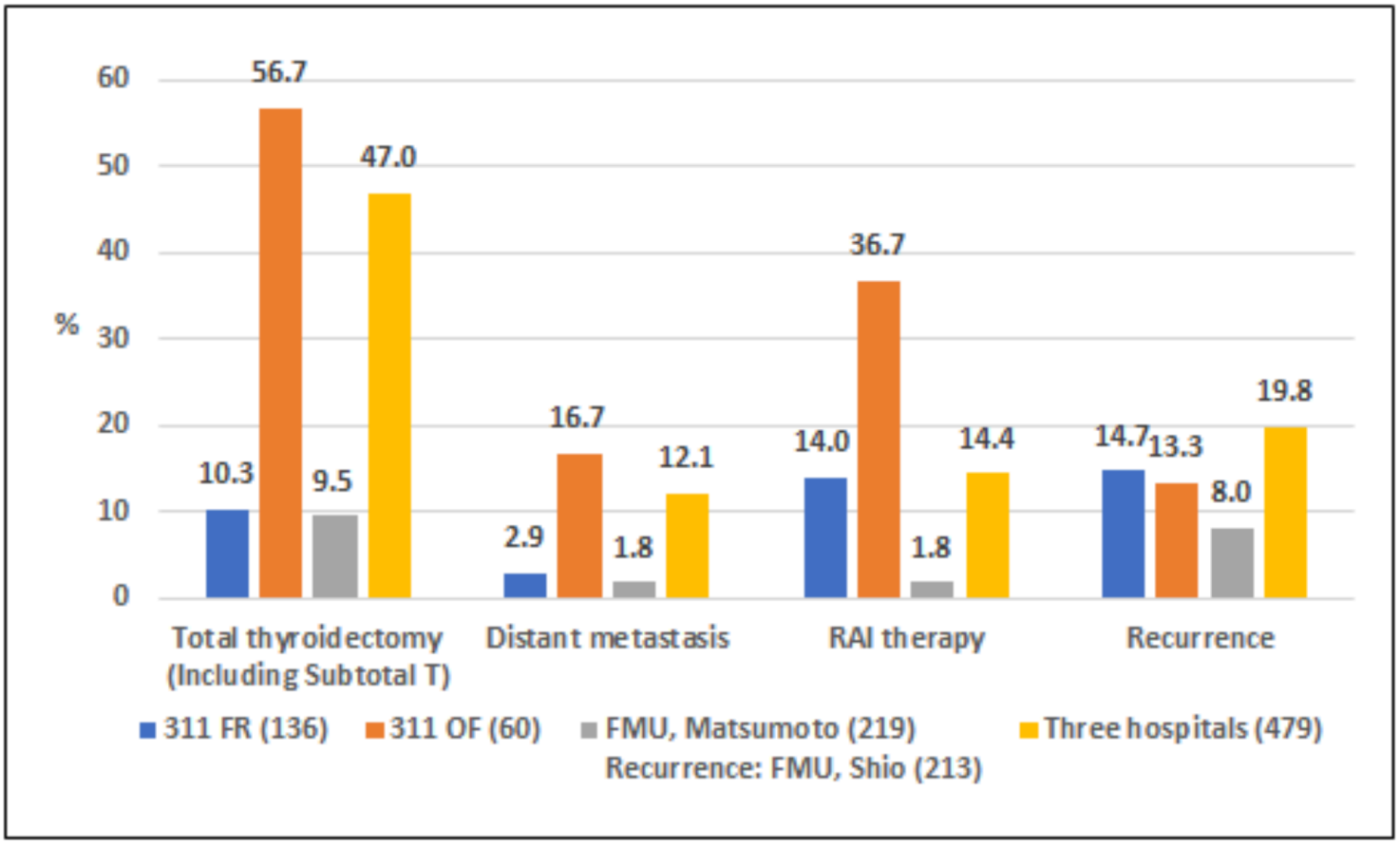



**Figure 1**

Comparison of the clinical characteristics and treatment outcomes with thyroid cancer detected through screening and those diagnosed in routine clinical practice.

Number of cases reported by the three thyroid hospitals; Enomoto Y. et al. [18], 142 cases; Ito Y, et al. [19], 110 cases; Sugino K, et al. [20], 227 cases (total, 479 cases).

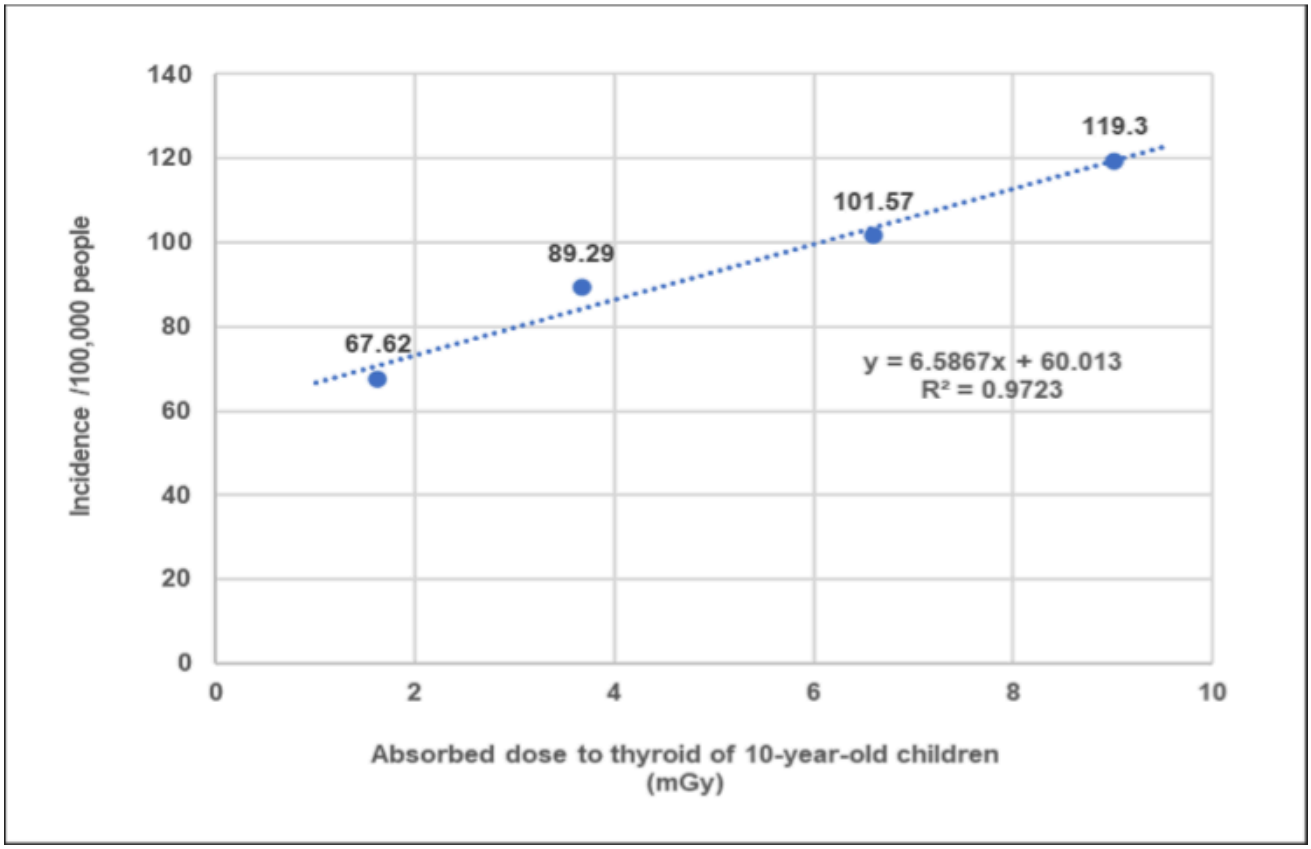



**Figure 2**

Correlation between estimated radiation dose and thyroid cancer incidence in Fukushima Prefecture.