Thyroid
© American Thyroid Association
© Mary Ann Liebert, Inc.
DOI: 10.1089/thy.2016.0313

Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Title: Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident

Authors: Masaharu Tsubokura, MD, PhD,[1] Shuhei Nomura, MHS,[2] Hajime Watanobe, MD, PhD,[3] Yoshitaka Nishikawa, MD,[4] Chiaki Suzuki, MD,[5] Sae Ochi, MD, PhD, MPH,[6] Claire Leppold, MSc,[7] Hirokatsu Kinoshita, MD, PhD, [1] Shigeaki Kato, PhD,[8] Yasutoshi Saito, MD, PhD[1]

Affiliations:

1. Department of Internal Medicine, Hirata Central Hospital, Hirata, Fukushima, Japan
2. Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, Norfolk Place, London, United Kingdom
3. Wako Fukushikai, Wako, Saitama, Japan
4. Department of Health Informatics, Graduate School of Medicine and Public Health, Kyoto University, Kyoto, Japan
5. Department of Otolaryngology-Head & Neck Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan
6. Department of Internal Medicine, Soma Central Hospital, Soma, Fukushima, Japan
7. Department of Research, Minamisoma Municipal General Hospital, Minamisoma, Fukushima, Japan
8. Research Center, Jyoban Hospital, Iwaki, Fukushima, Japan

Corresponding author: Masaharu Tsubokura, MD, PhD

Department of Internal Medicine, Hirata Central Hospital

Shimizu-uchi 4, Kami-Yomogida, Hirata-Mura, Ishikawa-Gun, Fukushima 963-8202, Japan.

E-mail: tsubokura-tky@umin.ac.jp, Tel: +81-247-57-5012, Fax: +81-247-57-5006

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Running title: Iodine status among children in Fukushima

Word count: 3,303 words

Keywords: iodine deficiency, thyroid cancer, radiation exposure, dietary intake

Abstract

Background

Iodine deficiency is an important modifier of the risk of thyroid cancer following irradiation; however, little information is available on the prevalence of iodine deficiency in Fukushima and its surroundings after the Fukushima Daiichi nuclear power plant accident that occurred in March, 2011.

Methods

To assess urinary iodine concentrations (UIC) and the prevalence of iodine deficiency and to elucidate any associations between demographic characteristics and UIC levels among children and adolescents aged 18 or younger at the time of the accident in Fukushima Prefecture and its surroundings, we evaluated the data on voluntary UIC testing conducted by Hirata Central Hospital, Fukushima.

Results

A total of 4410 children and adolescents with a median age of 10 years at examination underwent UIC testing between October 2012 and October 2015. Calculated for all the participants, the median level of UIC was 204 μg/L with a range of 25–21,100 μg/L. There were 133 (3.0%), 732 (16.6%) and 1472 (33.4%) participants with UIC levels of <50 μg/L, <100 μg/L, or ≥300 μg/L, respectively. Based on the WHO criteria for nutritional iodine status, no participants were severely iodine deficient (<20 μg/L), but 16.6 % of the population were mildly (50-100 μg/L) or moderately (20-50 μg/L) iodine deficient. While no significant difference in UIC was noted between those who did and did not increase dietary iodine intake after the accident ($p=0.93$), there were significant differences by year ($p<0.01$), school level ($p<0.001$), and residential area at the time of the accident ($p<0.001$), respectively.

Conclusions

Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

This study demonstrates that the children and adolescents examined had a sufficient amount of iodine during the period of 1.5-4.5 years after the nuclear accident. In addition to the differences in the scale and the countermeasures undertaken between the Fukushima and Chernobyl accidents, differences in dietary iodine intake might have played an additional role in resulting in the reportedly different radiation doses to the thyroid between the two nuclear accidents.

Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Introduction

Thyroid cancer following irradiation especially during infancy or childhood is a clearly defined clinical entity (1, 2). Radiation-related thyroid cancer has been seen following therapeutic radiation (e.g. treatments of pediatric cancer (3)), or following secondary environmental radiation from nuclear fallout such as the atomic bombings of Hiroshima and Nagasaki (4), the Marshall Islands nuclear testing (5, 6), and the Chernobyl nuclear accident (7, 8).

Within these examples, thyroid cancer following nuclear accidents has become a particularly important public health issue. According to UNSCEAR, the 1986 Chernobyl accident has resulted in over 6000 cases of thyroid cancer in the three countries of Belarus, Ukraine and Russia alone, and it is predicted that new cases will continue to develop (9). Thyroid cancer is the only radiation-related cancer effect officially identified by the UN after the Chernobyl nuclear accident (10).

With respect to thyroid cancer following irradiation in the wake of a nuclear accident, age at the time of the accident and radiation exposure dose are known as major risk factors. However, iodine deficiency can be another important modifier of the risk of thyroid cancer (8, 11), since iodine deficiency facilitates the uptake of radioactive iodine by the thyroid, leading to increased radiation doses (12). While poor control of contaminated food products such as milk led to high levels of thyroid radiation exposure after the Chernobyl accident (13), radio-contaminated districts were inland and faced chronic iodine deficiency (14), which has been identified as an additional reason for the post-Chernobyl increase in thyroid cancer in local residents.

On March 11, 2011, the Great East Japan Earthquake and tsunami led to a nuclear accident at Fukushima Daiichi nuclear power plant, resulting in widespread dispersal of radioactive substances including radioactive iodine, and unintentional radiation exposure among

Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

residents (15). The amount of radioactive iodine released after the Fukushima accident is estimated to be one-tenth (approximately 520 PBq) compared to the amount released by the Chernobyl accident (16), and direct measurements of thyroid exposure doses in children in Fukushima reported a mean dose of 4.2 mSv (17), which was far smaller than the reported levels after the Chernobyl accident with some children receiving doses as high as 4000 mSv (10). Several studies were published on the childhood thyroid cancer rate in the area following the accident from Fukushima prefectural government and Fukushima medical university (18, 19), which have implemented a thyroid ultrasound examination survey of the approximately 360,000 pediatric inhabitants who lived in Fukushima at the time of the accident in October 2011. However, there is little information on the prevalence of iodine deficiency, an important factor in the development of radioiodine-induced thyroid cancer, in Fukushima and its surroundings during the periods spanning the nuclear accident. It is generally accepted that the Japanese population has a sufficient iodine intake due to the high consumption of marine products rich in stable iodine (20). Nevertheless, the dietary patterns of Japanese children, a group susceptible to thyroid radiation exposure, have been changing in recent years due to Westernization and societal changes (21).

Measurement of urinary iodine concentrations (UIC) is a useful way to evaluate the status of dietary iodine intake and iodine deficiency (22, 23). While the median UIC is regarded as an excellent biomarker of recent exposure to iodine in populations (24), the WHO defines iodine intake as 'insufficient' for UIC levels of <100 μg/L, 'adequate or more than adequate' for 100-299 μg/L, and 'excessive' for ≥300 μg/L (25). Hirata Central Hospital, located in Hirata village, Fukushima Prefecture, 40-50 km southwest of the Fukushima Dai-ichi nuclear power plant, has conducted UIC measurements free of charge, with a main focus of evaluating schoolchildren, since October 2012 (Figure 1). The aim of the present study was two-fold: 1) to assess UIC and the prevalence of iodine deficiency in children and adolescents aged 18 or

Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

younger at the time of the nuclear accident, in Fukushima Prefecture and its surrounding areas affected by the widespread dispersal of radioactive iodine; and 2) to elucidate any associations between demographic characteristics of the participants and UIC levels.

Materials and methods

Data setting and UIC measurement

This study retrospectively assessed the results of all children and adolescents aged 18 or younger who underwent UIC testing at Hirata Central Hospital, from 2012 to 2015. Data extracted from screening records included age of participant at examinations, sex, their address prior to the accident, whether the address had changed or not following the accident, UIC levels, and dietary behavior for iodine intake inquired in the questionnaire (see below). For participants who underwent the UIC testing on multiple occasions during this period, only the data from the first testing were subjected to analysis. The UIC was determined in the spot urine by the Sandell-Kolthoff reaction utilizing the kit produced by Hitachi Chemical Co., Ltd. (Tokyo, Japan). All urine samples were assayed in duplicate. The sensitivity of the assay was 25 μg/L, and both the inter- and intra-assay coefficients of variation were less than 10 %.

Since October 2012, Hirata Central Hospital has offered voluntary UIC measurements and thyroid ultrasound examinations free of charge for residents of Fukushima and its surrounding areas who were under age 18 at the time of the accident in March 2011. Local municipalities including Miharu-machi (machi means town in Japanese), located in the Naka-Dori region of Fukushima Prefecture, and Daigo-machi, Ibaraki Prefecture, have facilitated yearly thyroid ultrasound examinations and UIC testing for all primary and secondary school students in these towns. Their geographical locations, relative to the nuclear power plant, are shown in Figure 1. This screening program is publicized online, in general magazines, and newspapers.

Questionnaire about dietary intake of iodine

On the occasion of the UIC testing, to assess potential changes of dietary habits, all participants were questioned about their dietary intake of iodine. All participants answered a yes-or-no question about whether they proactively started to consume foods rich in iodine after the accident.

Analysis

In order to assess any effects of age, sex, pre-accident residential area, and post-accident dietary behavior on UIC levels, we performed the analyses outlined below.

1. Median UICs were compared between those who proactively increased their dietary iodine intake after the accident and those who did not, by a nonparametric Wilcoxon rank-sum test.
2. For those that reported no proactive increases in their iodine intake after the accident, differences in UIC by sex, year of test (2012, 2013, 2014, 2015, defined as the government's financial year that runs from April 1 to March 31), school level [pre-school (ages ≤6), primary school (6–12), secondary school (12–15), and high school (15–18)], residential address at the time of the accident (outside of Fukushima Prefecture, Hama-Dori, Naka-Dori, and Aizu), were assessed using the Wilcoxon rank-sum test for sex, and the Kruskal-Wallis test for year of test, age bracket and residential address at the time of the accident.
3. The WHO defines iodine deficiency at the population level as 'mild' for UIC levels of 50–100 μg/L, 'moderate' for 20–50 μg/L and 'severe' for <20 μg/L (26). For the purpose of analyzing the associations between iodine deficiency and characteristics of the participants, it would be preferable to divide the participants with UIC levels of <100 μg/L into three groups.

Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

However, only a small number of participants were found to have 'moderate' or 'severe' iodine deficiency (see results), which would have diminished the statistical power of analyses. Thus, we classified the participants into two dichotomous groups: <100 μg/L or ≥100 μg/L. Then, a multiple logistic regression model was constructed to identify factors associated with UIC levels of <100 μg/L. To minimize potentially unobserved cofounding effects of evacuation on iodine intake via changed lifestyles in evacuation sites, those reporting post-accident address changes were excluded from the logistic regression.

All analyses were carried out with STATA/MP version 13.1. P values of <0.05 were considered as significant.

Ethics

This study was approved by the Hirata Central Hospital Internal Review Board (20160316-2). Informed consent was received from all subjects or their guardians participating in this study.

Results

From October 2012 to October 2015, a total of 4410 children and adolescents aged 18 or younger at the time of the accident underwent UIC testing. The age range of participants was 1–18 years old (median, 10 yrs), and 2139 (48.5%) of them were female (Table 1). The numbers of primary and secondary school students in Miharu and Daigo were 1423 and 1155, respectively. The total number of primary and secondary school students were 1379 in Miharu for fiscal year 2013 and 1113 in Daigo for fiscal year 2014, and 1221 (88.5%) and 1118 (99.6%) of these participated in this UIC testing in the corresponding fiscal years, respectively.

Figure 2 displays the distribution of UIC levels in individual participants. The levels ranged between 25–21,100 μg/L, with a median of 204 μg/L. Fifty percent (n=2206) fell within the normal range (100–299 μg/L) as per the WHO definition, and there were 133 (3.0%), 732 (16.6%) and 1472 (33.4%) participants with UIC levels of <50 μg/L, <100 μg/L, or ≥300 μg/L, respectively. No participants were below the threshold of severe iodine deficiency (<20 μg/L).

Analysis 1

In answer to our questionnaire of whether the participants increased iodine intake, 617 (14.0%) reported a proactive increase after the accident (Table 1). There were significant differences across the years of examinations in the proportions of participants who proactively increased iodine intake (p<0.001), with the largest value being observed in 2012 (40.3%), after which it decreased year after year (7.7%–20.1%). Among those who reported proactive increases in dietary iodine after the accident, few had been living outside of Fukushima at the time of the accident (6.0%), and comparatively large proportions had been living in Fukushima's Hama-Dori and Naka-Dori+Aizu regions (18.8% and 17.7%, respectively: p<0.001). As there was a small number of test participants from the Aizu region (n=13), we combined the data from the Naka-Dori and Aizu regions for analyses. There were no statistically significant differences in age and sex between those who did and did not proactively increase iodine intake after the accident. Furthermore, there was no significant difference in UIC levels between those who did and did not proactively increase iodine intake after the accident (median: 202.5 vs. 213.0, p=0.93).

Analysis 2

In the group reporting no post-accident increase in dietary iodine, we found no significant differences in UIC levels by sex. However, there were significant differences by year (p<0.01), school level (p<0.001), and residential area at the time of the accident (p<0.001),

Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

respectively (Table 2).

Analysis 3

Table 3 presents the results of the logistic regression analysis. The covariates included in the final model are school-model (categorical: pre-school (reference), primary school, secondary school, and high school), sex (binary: male (reference) and female), and pre-disaster residential area (categorical: outside of Fukushima (reference), Hama-Dori, and Naka-Dori+Aizu). Compared to primary school students, there was a significantly higher proportion of UIC levels below 100 μg/L in pre-school and secondary school students (OR: 1.92, 95% CI: 1.45–2.53, $p<0.001$; and OR: 1.45, 95% CI: 1.16–1.81, $p<0.01$). Furthermore, compared to those living outside of Fukushima, residency in Hama-Dori was associated with a significantly higher proportion of UIC levels below 100 μg/L (OR: 1.50, 95% CI: 1.04–2.17, $p<0.05$).

Discussion

In the present study, we found that the children and adolescents in Fukushima and its neighboring areas had been taking sufficient amounts of dietary iodine during the period of 1.5-4.5 years after the Fukushima nuclear power plant accident. The median level of UIC among all of the participants was 204 μg/L, well above the lower end of adequate iodine intake as per the WHO recommendations (100 μg/L).

The UIC was <100 μg/L in only 16.6 % of the participants, and there were no subjects with an UIC <20 μg/L. The WHO recommends that the proportion of individuals with an UIC <50 μg/L should be less than 20 % in a given population (26), and in the present study the proportion of participants falling under this subcategory was as low as 3.0 %. Overall, there were extremely few participants found to be severely iodine deficient, and most of our

Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

participants can be regarded as having ingested sufficient amounts of iodine with their daily diets during the years spanning 2012-2015. The findings in the present study are comparable with the results of urinary iodine screening reported in previous studies involving Japanese schoolchildren (25, 27).

Furthermore, this study found no statistically significant differences in UIC between those who did and did not increase their dietary iodine intake after the accident. The present study revealed that 14.0% of the participants increased their dietary intake of iodine after the accident. While the reason for this behavior is not clear, radiation-related fear may have played a role, similar to what has been reported after the Chernobyl accident (28). However, we assume that fear of radiation diminished year after year, since the proportion of participants reporting proactive increases of iodine intake decreased year after year. Our previous study found that a higher proportion (23.1 %) of children and adolescents in Fukushima increased their intake of seaweeds during the period of 20-30 months after the accident compared to this study, which may be an observation suggesting a declining fear for radiation over time (29). Collectively, the present findings indicating a lack of significant changes in UIC irrespective of the altered dietary behaviors after the accident may suggests that the participants in this study had already ingested sufficient amounts of iodine before the nuclear accident.

However, caution should be used in interpreting the UIC data by year of examination, group, and residential areas in this study. While no significant sex-dependent differences in UIC were found in Analysis 2, there were significant differences with respect to year, school level, and residential area at the time of the accident. Results of the multivariate analysis (Analysis 3) indicate that, compared to primary school students, pre-school and secondary school students were at a higher risk of iodine deficiency (<100 μg/L) (Table 3). The same trend could be seen in the residents of the Hama-Dori region in Fukushima, compared to the residents outside of Fukushima (Table 3). While the reason for these trends is unclear, there are some potential factors. For the variable of year, it is worth noting that this study began and ended in October, meaning that we had only such data that were obtained between October through January for years 2012 and 2015, due to the data organization based on the Japanese fiscal year which runs from April to March. This might have caused seasonal confounding with respect to the variable of year, resulting in the observed significant differences in Analysis 2; however, these differences across the years of examination disappeared when tested by multivariate analyses (Analysis 3). The finding of a lower UIC in Hama-Dori, the coastal region of Fukushima, may be caused by the post-accident changes in dietary iodine supply, due to restrictions placed on fishing. Most of the data from outside of Fukushima came from residents of Daigo, Ibaraki Prefecture, where a radiation leak accident occurred in 2013 (30). It is possible that this nuclear accident urged the population in Daigo to increase their iodine intake for prevention purposes for several years, which may have resulted in the significant differences in UIC between the residential areas examined. This may have led to the overestimation of odds ratios in the Hama-Dori and Naka-Dori+Aizu districts. The observed differences in UIC between the various age brackets and regions might reflect differences in ingredients used for school meals, and/or differing food customs by region and age. Less than school-age children are the most susceptible group to radioactive iodine exposure, and therefore the lower UIC levels detected in this subgroup may merit further investigations including nutritional surveys.

The present findings alone do not allow us to conclude that children and adolescents in Fukushima and its surrounding areas were not iodine deficient as a whole during the periods spanning both the pre-accident and early post-accident periods after the release of radioactive iodine from the damaged nuclear power plant. Given the post-accident restrictions placed on planting and shipping farmed and fished products, it is likely that there were changes in

Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

societal dietary habits (31, 32), and therefore it may be incorrect to assume that post-accident UIC levels represent pre-accident levels. During the period of social disruption that occurred immediately after the nuclear accident, there was a loss of crucial supplies such as electricity, gas and water, and many evacuees may have been forced to change their lifestyles including sole reliance on foods rationed out at evacuation centers, a factor beyond their control (33). Further research should place more attention on possible changes in dietary habits before and after the accident, and on dietary patterns of evacuees.

Direct measurements of thyroid radiation exposure after the Fukushima nuclear accident were reported to be overwhelmingly smaller than those after the Chernobyl accident (17). While this difference may be eplained by various factors, one is the reported difference in the released amount of radioiodine between Chernobyl and Fukushima, with the latter being one-tenth that of the former (16). Another factor may be the rapid evacuation and restrictions placed on the shipping and circulation of contaminated food products implemented by the Japanese government, which may have helped to substantially mitigate radiation exposure to the thyroid (34). In addition to these two reasons, the present study suggests that the overall sufficient intake of stable iodine in Fukushima residents may have prevented the thyroid from being exposed to radioactive iodine.

This study may provide several useful implications that reach above and beyond the role of radiation exposure on thyroid cancer in after the Fukushima accident. First, while most participants were found to have a sufficient intake of iodine, a minor proportion of them fell within the category of mild (50-100 µg/L) or moderate (20-50 µg/L) iodine deficiency. In comparison to the group with sufficient iodine levels, the slightly deficient group may have a higher risk to develop thyroid cancer. Even so, in the previous reports of the WHO and UN on the environmental radiation in Fukushima, the role of dietary iodine intake was not taken into account in dose estimations of thyroid radiation exposure in affected residents (35, 36).

Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

In order to have a better understanding of the actual radioiodine doses to the thyroid after the nuclear accident, it would be preferable to incorporate the stable iodine intake into analyses. The results of the present study may hopefully be a basis for future investigations addressing this aspect. Second, in marked contrast to iodine deficiency, excess iodine intake may also raise the risk of thyroid cancer, unrelated to radiation exposure (37). While the WHO defines UIC levels of 300 μg/L or more as excessive (24), 33.4% of the participants in this study were found to have very high levels of UIC with 300 μg/L or more. When assessing the risk of thyroid cancer in young individuals exposed to the Fukushima accident, it may be necessary to consider the possible effect of excessive iodine intake on thyroid cancer risk as well, rather than limiting the focus on radiation exposure.

Limitations

There are several limitations to this study. First, the urinary iodine screening was conducted on a voluntary basis, and thus the data obtained may not be representative of all areas of Fukushima Prefecture. Second, the UIC measurement is known as a test prone to a large day-to-day variation in a given individual (38).

Conclusion

In the present study, we found subtle but statistically significant differences in the UIC among the participants with respect to the year of examination following the Fukushima accident, subject age, and residential area. As a whole, the children and adolescents examined in this study had ingested sufficient amounts. In addition to the differences in the scale of the accident and countermeasures undertaken between Fukushima and Chernobyl, differences in dietary iodine intake might have played an additional role for the reportedly different radiation doses to the thyroid between the two nuclear accidents.

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Acknowledgments

We would like to thank Fumihiko Sagawa (Director of Healthcare Corporation Seireikai), Masahiko Nihei, Yu Sakuma at Hirata Central Hospital, Megumi Murakami, and Miki Abe at the Hirata Radiation Research Center. Also, we are greatly appreciative for the staff working for the municipalities, especially those of Miharu Town and Daigo Town. The study could not have taken place without their assistance. We additionally thank all people who made donations for the administration of the thyroid screening program at Hirata Central Hospital, especially Cataloghouse inc..

Contributorship statement

All the authors were responsible for the study concept and design. MT, HW, YN and CS acquired the data, which was analyzed and interpreted by all the authors. MT, SN, HW, CL, SO and SK drafted the manuscript, which was critically revised for important intellectual content by all the authors. SN performed the statistical analyses. YS served as the study supervisors and provided administrative and technical support. All the authors have approved the final draft of the manuscript.

Competing interests

Nothing to declare

Funding

None

Date sharing statement

All data underlying the findings in our study will not be available to other researchers due to the lack of informed consent.

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

References

1. Schneider AB, Sarne DH 2005 Long-term risks for thyroid cancer and other neoplasms after exposure to radiation. Nat Clin Pract Endocrinol Metab **1**:82-91.
2. Ron E, Lubin JH, Shore RE, Mabuchi K, Modan B, Pottern LM, Schneider AB, Tucker MA, Boice JD, Jr. 1995 Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies. Radiat Res **141**:259-277.
3. Tucker MA, Jones PH, Boice JD, Jr., Robison LL, Stone BJ, Stovall M, Jenkin RD, Lubin JH, Baum ES, Siegel SE, et al. 1991 Therapeutic radiation at a young age is linked to secondary thyroid cancer. The Late Effects Study Group. Cancer Res **51**:2885-2888.
4. Parker LN, Belsky JL, Yamamoto T, Kawamoto S, Keehn RJ 1974 Thyroid carcinoma after exposure to atomic radiation. A continuing survey of a fixed population, Hiroshima and Nagasaki, 1958-1971. Ann Intern Med **80**:600-604.
5. Hamilton TE, van Belle G, LoGerfo JP 1987 Thyroid neoplasia in Marshall Islanders exposed to nuclear fallout. JAMA **258**:629-635.
6. Takahashi T, Schoemaker MJ, Trott KR, Simon SL, Fujimori K, Nakashima N, Fukao A, Saito H 2003 The relationship of thyroid cancer with radiation exposure from nuclear weapon testing in the Marshall Islands. J Epidemiol **13**:99-107.
7. Kazakov VS, Demidchik EP, Astakhova LN 1992 Thyroid cancer after Chernobyl. Nature **359**:21.
8. Cardis E, Kesminiene A, Ivanov V, Malakhova I, Shibata Y, Khrouch V, Drozdovitch V, Maceika E, Zvonova I, Vlassov O, Bouville A, Goulko G, Hoshi M, Abrosimov A, Anoshko J, Astakhova L, Chekin S, Demidchik E, Galanti R, Ito M, Korobova E, Lushnikov E, Maksioutov M, Masyakin V, Nerovnia A, Parshin V, Parshkov E, Piliptsevich N, Pinchera A, Polyakov S, Shabeka N, Suonio E, Tenet V, Tsyb A, Yamashita S, Williams D 2005 Risk of thyroid cancer after exposure to 131I in childhood. J Natl Cancer Inst **97**:724-732.
9. Moysich KB, Menezes RJ, Michalek AM 2002 Chernobyl-related ionising radiation exposure and cancer risk: an epidemiological review. Lancet Oncol **3**:269-279.
10. UNSCEAR 2008 Annex D: Health effects due to radiation from the Chernobyl accident UNSCEAR 2008 Report to the General Assembly, with scientific annexes. Vol 1. United Nations Publications, New York.
11. Gembicki M, Stozharov AN, Arinchin AN, Moschik KV, Petrenko S, Khmara IM, Baverstock KF 1997 Iodine deficiency in Belarusian children as a possible factor stimulating the irradiation of the thyroid gland during the Chernobyl catastrophe. Environ Health Perspect **105 Suppl 6**:1487-1490.
12. Shakhtarin VV, Tsyb AF, Stepanenko VF, Orlov MY, Kopecky KJ, Davis S 2003 Iodine deficiency, radiation dose, and the risk of thyroid cancer among children and adolescents in the Bryansk region of Russia following the Chernobyl power station accident. Int J Epidemiol **32**:584-591.
13. UNSCEAR 1988 Annex D: Exposures from the Chernobyl accident UNSCEAR 1988 report: sources, effects and risks of ionizing radiation. Vol. United Nations, New York.
14. Ashizawa K, Shibata Y, Yamashita S, Namba H, Hoshi M, Yokoyama N, Izumi

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

M, Nagataki S 1997 Prevalence of goiter and urinary iodine excretion levels in children around Chernobyl. J Clin Endocrinol Metab **82**:3430-3433.

15. Hasegawa A, Tanigawa K, Ohtsuru A, Yabe H, Maeda M, Shigemura J, Ohira T, Tominaga T, Akashi M, Hirohashi N, Ishikawa T, Kamiya K, Shibuya K, Yamashita S, Chhem RK 2015 Health effects of radiation and other health problems in the aftermath of nuclear accidents, with an emphasis on Fukushima. Lancet **386**:479-488.

16. Steinhauser G, Brandl A, Johnson TE 2014 Comparison of the Chernobyl and Fukushima nuclear accidents: a review of the environmental impacts. Sci Total Environ **470-471**:800-817.

17. Tokonami S, Hosoda M, Akiba S, Sorimachi A, Kashiwakura I, Balonov M 2012 Thyroid doses for evacuees from the Fukushima nuclear accident. Sci Rep **2**:507.

18. Suzuki S, Suzuki S, Fukushima T, Midorikawa S, Shimura H, Matsuzuka T, Ishikawa T, Takahashi H, Ohtsuru A, Sakai A, Hosoya M, Yasumura S, Nollet KE, Ohira T, Ohto H, Abe M, Kamiya K, Yamashita S 2016 Comprehensive Survey Results of Childhood Thyroid Ultrasound Examinations in Fukushima in the First Four Years After the Fukushima Daiichi Nuclear Power Plant Accident. Thyroid **26**:843-851.

19. Suzuki S, Yamashita S, Fukushima T, Nakano K, Midorikawa S, Ohtsuru A, Yasumura S, Hosoya M, Kamiya K, Shimura H, Suzuki S, Nakamura I, Abe M 2016 The protocol and preliminary baseline survey results of the thyroid ultrasound examination in Fukushima [Rapid Communication]. Endocr J **63**:315-321.

20. Katagiri R, Asakura K, Uechi K, Masayasu S, Sasaki S 2015 Adequacy of iodine intake in three different Japanese adult dietary patterns: a nationwide study. Nutr J **14**:129.

21. Katagiri R, Asakura K, Sasaki S, Hirota N, Notsu A, Miura A, Todoriki H, Fukui M, Date C 2015 Estimation of habitual iodine intake in Japanese adults using 16 d diet records over four seasons with a newly developed food composition database for iodine. Br J Nutr **114**:624-634.

22. Ristic-Medic D, Piskackova Z, Hooper L, Ruprich J, Casgrain A, Ashton K, Pavlovic M, Glibetic M 2009 Methods of assessment of iodine status in humans: a systematic review. Am J Clin Nutr **89**:2052S-2069S.

23. Zimmermann MB 2008 Methods to assess iron and iodine status. Br J Nutr **99 Suppl 3**:S2-9.

24. Zimmermann MB, Andersson M 2012 Assessment of iodine nutrition in populations: past, present, and future. Nutr Rev **70**:553-570.

25. Zimmermann MB, Hess SY, Molinari L, De Benoist B, Delange F, Braverman LE, Fujieda K, Ito Y, Jooste PL, Moosa K, Pearce EN, Pretell EA, Shishiba Y 2004 New reference values for thyroid volume by ultrasound in iodine-sufficient schoolchildren: a World Health Organization/Nutrition for Health and Development Iodine Deficiency Study Group Report. Am J Clin Nutr **79**:231-237.

26. De Benoist B, Andersson M, Egli I, Takkouche B, Allen H 2004 Iodine status worldwide: WHO global database on iodine deficiency. Department of Nutrition for Health and Development, World Health Organization Geneva.

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

27. Fuse Y, Saito N, Tsuchiya T, Shishiba Y, Irie M 2007 Smaller thyroid gland volume with high urinary iodine excretion in Japanese schoolchildren: normative reference values in an iodine-sufficient area and comparison with the WHO/ICCIDD reference. Thyroid **17**:145-155.

28. Rahu M 2003 Health effects of the Chernobyl accident: fears, rumours and the truth. Eur J Cancer **39**:295-299.

29. Watanobe H, Furutani T, Nihei M, Sakuma Y, Yanai R, Takahashi M, Sato H, Sagawa F 2014 The thyroid status of children and adolescents in Fukushima Prefecture examined during 20-30 months after the Fukushima nuclear power plant disaster: a cross-sectional, observational study. PLoS One **9**:e113804.

30. Koseki T, Hasegawa K 2014 Present status of J-PARC-after the shutdown due to the radioactive material leak accident. Proceedings of IPAC2014, Dresden, Germany:3373-3375.

31. Nishikawa Y, Tsubokura M, Kato S, Saito Y 2014 Possible Anisakiasis Associated with Fishery Resumption. Disaster Med Public Health Prep:1-2.

32. Ozaki A, Tanimoto T, Leppold C, Tsubokura M, Kato S, Tsukada M, Kami M, Ohira H 2016 A possible association between the resumption of agricultural activities and a venomous snakebite after Fukushima nuclear crisis. Oxf Med Case Reports **2016**:22-23.

33. Hasegawa A, Ohira T, Maeda M, Yasumura S, Tanigawa K 2016 Emergency Responses and Health Consequences after the Fukushima Accident; Evacuation and Relocation. Clin Oncol (R Coll Radiol) **28**:237-244.

34. Hamada N, Ogino H 2012 Food safety regulations: what we learned from the Fukushima nuclear accident. J Environ Radioact **111**:83-99.

35. UNSCEAR 2014 Annex A: Levels and effects of radiation exposure due to the nuclear accident after the 2011 great east-Japan earthquake and tsunami UNSCEAR 2013 report: sources, effects and risks of ionizing radiation. Vol. United Nations Publications, New York.

36. WHO 2013 Health risk assessment from the nuclear accident after the 2011 Great East Japan earthquake and tsunami, based on a preliminary dose estimation. World Health Organization, Geneva.

37. Zimmermann MB, Galetti V 2015 Iodine intake as a risk factor for thyroid cancer: a comprehensive review of animal and human studies. Thyroid Res **8**:8.

38. Andersen S, Pedersen KM, Pedersen IB, Laurberg P 2001 Variations in urinary iodine excretion and thyroid function. A 1-year study in healthy men. Eur J Endocrinol **144**:461-465.

Figure legends

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

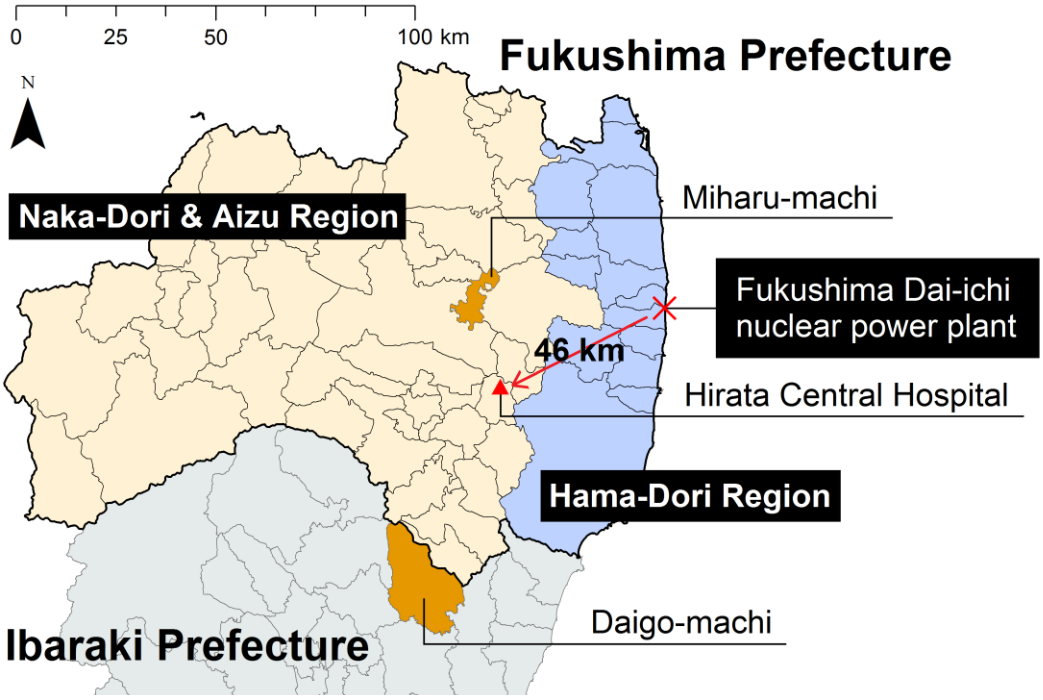

Figure 1: Location of Hirata Central Hospital in relation to the Fukushima Daiichi nuclear power plant. Miharu Town and Daigo Town, which have officially promoted urinary iodine screenings for residents, are highlighted.

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

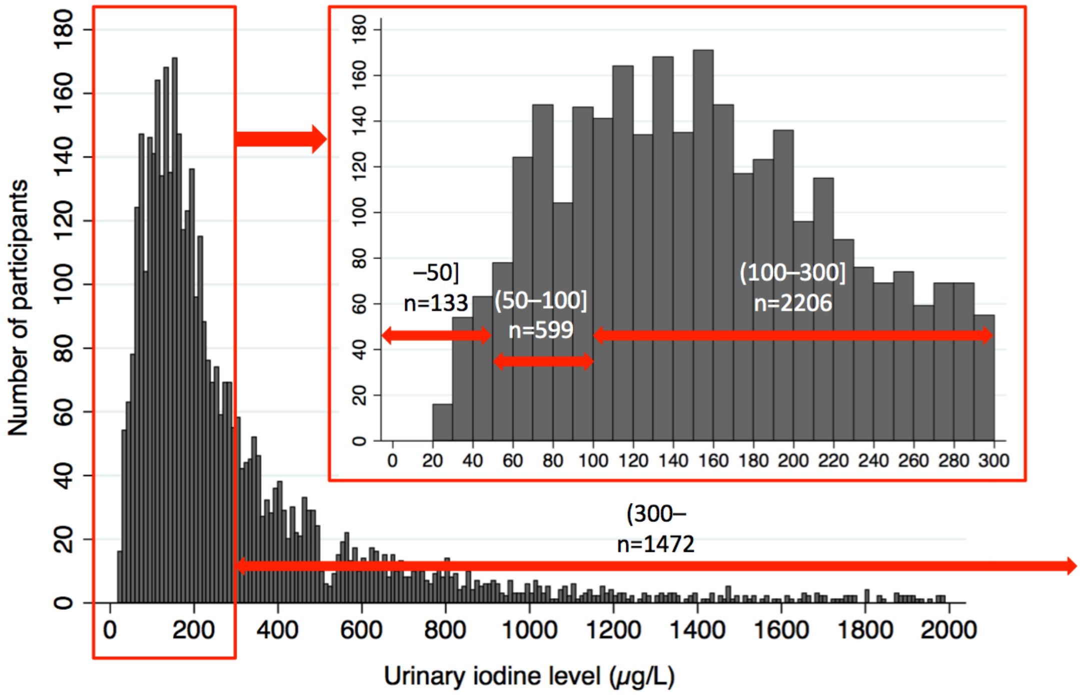

Figure 2: The results of urinary iodine screenings, and concentration distributions for all participants. No participants had severe iodine deficiency (urinary iodine concentrations <20 μg/L).

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Table 1: Demographic characteristics (n, %)

		Post-accident increase in intake of foods rich in iodine**		
	Total* (n = 4,410)	No (n = 3,793, 86.0%)	Yes (n = 617, 14.0%)	P-value for comparisons
Age (median: range)	10 (1–18)	10 (1–18)	9 (1–18)	<0.01†
Sex				0.47††
Male	2,271 (51.5)	1,945 (85.7)	326 (14.3)	
Female	2,139 (48.5)	1,848 (86.4)	291 (13.6)	
Year				<0.001††
2012	159 (3.61)	95 (59.8)	64 (40.3)	
2013	2,299 (52.1)	1,915 (83.3)	384 (16.7)	
2014	1,798 (40.8)	1,660 (92.3)	138 (7.7)	
2015	154 (3.5)	123 (79.9)	31 (20.1)	
School level				0.06††
Pre-school	671 (15.2)	569 (84.8)	102 (15.2)	
Primary school	2,432 (55.2)	2,072 (85.2)	360 (14.8)	
Secondary school	1,162 (26.4)	1,026 (88.3)	136 (11.7)	
High school	145 (3.3)	126 (86.9)	19 (13.1)	
Pre-accident residential area				<0.001††
Outside of Fukushima	1,465 (33.2)	1,377 (94.0)	88 (6.0)	
Hama-Dori	687 (15.6)	558 (81.2)	129 (18.8)	
Naka-Dori+Aizu	2,258 (51.2)	1,858 (82.3)	400 (17.7)	

* Percentage in row
** Percentage in column
† Wilcoxon rank-sum test
†† Chi-squared test

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Table 2: Urinary iodine concentrations (μg/L) in participants who did not proactively increase dietary iodine intake

	Numbers (%)	Median	Range	P-value for the median difference
Sex				0.24
Male	1,945 (51.3)	204	25–17,300	
Female	1,848 (48.7)	200	25–15,700	
Year				<0.01
2012	95 (2.5)	159	29–6,300	
2013	1,915 (50.5)	207	25–17,300	
2014	1,660 (43.8)	204	26–12,100	
2015	123 (3.2)	179	36–3,400	
School level				<0.001
Pre-school	569 (15.0)	165	25–15,700	
Primary school	2,072 (54.6)	221	25–17,300	
Secondary school	1,026 (27.1)	195	27–16,900	
High school	126 (3.3)	155	28–6,200	
Pre-accident residential area				<0.001
Outside of Fukushima	1,377 (36.3)	205	26–15,700	
Hama-Dori	558 (14.7)	180.5	25–7,300	
Naka-Dori+Aizu	1,858 (49.0)	212	25–17,300	

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Table 3: Logistic regression model for iodine deficiency (<100 µg/L)

	Odds ratio	95% CI	P-value
School level			
Pre-school	1.92	1.45–2.53	<0.001
Primary school	Ref.		
Secondary school	1.45	1.16–1.81	<0.01
High school	1.65	0.95–2.88	0.08
Sex			
Male	Ref.		
Female	1.16	0.96–1.41	0.13
Pre-accident residential area			
Outside of Fukushima	Ref.		
Hama-Dori	1.50	1.04–2.17	<0.05
Naka-Dori+Aizu	0.89	0.72–1.09	0.26

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Title: Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident

Authors: Masaharu Tsubokura, MD, PhD,[1] Shuhei Nomura, MHS,[2] Hajime Watanobe, MD, PhD,[3] Yoshitaka Nishikawa, MD,[4] Chiaki Suzuki, MD,[5] Sae Ochi, MD, PhD, MPH,[6] Claire Leppold, MSc,[7] Hirokatsu Kinoshita, MD, PhD, [1] Shigeaki Kato, PhD,[8] Yasutoshi Saito, MD, PhD[1]

Affiliations:

9. Department of Internal Medicine, Hirata Central Hospital, Hirata, Fukushima, Japan
10. Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, Norfolk Place, London, United Kingdom
11. Wako Fukushikai, Wako, Saitama, Japan
12. Department of Health Informatics, Graduate School of Medicine and Public Health, Kyoto University, Kyoto, Japan
13. Department of Otolaryngology-Head & Neck Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan
14. Department of Internal Medicine, Soma Central Hospital, Soma, Fukushima, Japan
15. Department of Research, Minamisoma Municipal General Hospital, Minamisoma, Fukushima, Japan
16. Research Center, Jyoban Hospital, Iwaki, Fukushima, Japan

Corresponding author: Masaharu Tsubokura, MD, PhD

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Department of Internal Medicine, Hirata Central Hospital

Shimizu-uchi 4, Kami-Yomogida, Hirata-Mura, Ishikawa-Gun, Fukushima 963-8202, Japan.

E-mail: tsubokura-tky@umin.ac.jp, Tel: +81-247-57-5012, Fax: +81-247-57-5006

Running title: Iodine status among children in Fukushima

Word count: 3,303 words

Keywords: iodine deficiency, thyroid cancer, radiation exposure, dietary intake

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Abstract

Background

Iodine deficiency is an important modifier of the risk of thyroid cancer following irradiation; however, little information is available on a prevalence of iodine deficiency in Fukushima and its surroundings after the Fukushima Daiichi nuclear power plant accident that occurred in March, 2011.

Methods

To assess urinary iodine concentrations (UIC) and a prevalence of iodine deficiency and to elucidate any associations between demographic characteristics and UIC levels among children and adolescents aged 18 or younger at the time of the accident in Fukushima Prefecture and its surroundings, we evaluated the data on voluntary UIC testing conducted by Hirata Central Hospital, Fukushima.

Results

A total of 4,410 children and adolescents with the median age of 10 years at examinations underwent UIC testing from October 2012 to October 2015. Calculated for all the participants, the median level of UIC was 204 μg/L with the range of 25–21,100 μg/L. There were 133 (3.0%), 732 (16.6%) and 1,472 (33.4%) participants with UIC levels of <50 μg/L, <100 μg/L, or ≥300 μg/L, respectively. Based on the WHO criteria for nutritional iodine status, no participants were severely iodine deficient (<20 μg/L), but 16.6 % of the population were mildly (50-100 μg/L) or moderately (20-50 μg/L) iodine deficient. While no significant difference in UIC was noted between those who did and did not increase dietary iodine intake after the accident ($p=0.93$), there were significant differences by year ($p<0.01$), school level ($p<0.001$), and residential area at the time of the accident ($p<0.001$), respectively.

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Conclusions

This study demonstrated that the children and adolescents examined had ingested sufficient amount of iodine as a whole during the period of 1.5-4.5 years after the nuclear accident. In addition to the differences in the scale of accident and countermeasures undertaken between Fukushima and Chernobyl, differences in dietary iodine intake might have played an additional role in engendering the reportedly different radiation doses to the thyroid between the two nuclear accidents.

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Introduction

Thyroid cancer following irradiation especially during infancy or childhood is a clearly defined clinical entity.(1, 2) Radiation-related thyroid cancer has been seen following therapeutic radiation (eg. treatments of pediatric cancer(3)), or following secondary environmental radiation from nuclear fallout such as the atomic bombings of Hiroshima and Nagasaki,(4) the Marshall Islands nuclear testing,(5, 6) and the Chernobyl nuclear accident.(7, 8)

Within these examples, thyroid cancer following nuclear accidents has become a particularly important public health issue. According to UNSCEAR, the 1986 Chernobyl accident has resulted in over 6,000 cases of thyroid cancer in only the three countries of Belarus, Ukraine and Russia, and it is predicted that new cases will continue to develop.(9) Thyroid cancer is the only radiation-related cancer effect officially identified by the UN after the Chernobyl nuclear accident.(10)

With respect to thyroid cancer following irradiation in the wake of a nuclear accident, age at the time of the accident and radiation exposure dose are known as major risks. However, iodine deficiency can be another important modifier of the risk of thyroid cancer,(8, 11) since iodine deficiency makes it easier for the thyroid to take up radioactive iodine, leading to an increased radiation exposure doses to the thyroid.(12) After the Chernobyl accident, while poor control of contaminated food products such as milk led to high levels of thyroid radiation exposure,(13) radio-contaminated districts were inland and faced chronic iodine deficiency,(14) which has been identified as an additional reason for the post-Chernobyl increase in thyroid cancer in local residents.

On March 11, 2011, the Great East Japan Earthquake and tsunami led to a nuclear accident at Fukushima Daiichi nuclear power plant, resulting in widespread dispersal of

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

radioactive substances including radioactive iodine, and unintentional radiation exposure among residents.(15) The amount of radioactive iodine released after the Fukushima accident is estimated to be one-tenth (approximately 520 PBq) of after the Chernobyl accident,(16) and direct measurements of thyroid exposure doses in children in Fukushima reported a mean dose of 4.2 mSv,(17) which was far smaller than the reported levels after the Chernobyl accident with some children receiving doses as high as 4,000 mSv.(10) Several researches were published on the childhood thyroid cancer rate in the area following the accident from Fukushima prefectural government and Fukushima medical university,(18, 19) which have commenced a thyroid ultrasound examination survey of the approximately 360,000 pediatric inhabitants who lived in Fukushima at the time of the accident in October 2011; however, there is little information on the prevalence of iodine deficiency, an important factor in the development of radiogenic thyroid cancer, in Fukushima and its surroundings during the periods spanning the nuclear accident. It is generally accepted that Japanese are a population with sufficient iodine intake owing to their daily consumption of marine products rich in stable iodine.(20) Nevertheless, the dietary patterns of Japanese children, a group susceptible to thyroid radiation exposure, have been changing in recent years alongside Westernization and societal changes.(21)

Measurement of urinary iodine concentrations (UIC) is a useful way to evaluate the status of dietary iodine intake and iodine deficiency.(22, 23) While the median UIC is regarded as an excellent biomarker of recent exposure to iodine in populations,(24) WHO defines iodine intake as 'insufficient' for UIC levels of <100 μg/L, 'adequate or more than adequate' for 100-299 μg/L and 'excessive' for ≥300 μg/L.(25) Hirata Central Hospital, located in Hirata village, Fukushima Prefecture, 40-50km southwest of the

Fukushima Dai-ichi nuclear power plant, has conducted UIC measurements free of charge, with a main focus on targeting schoolchildren, since October, 2012 (Figure 1). The aim of the present study was two-fold: 1) to assess UIC and the prevalence of iodine deficiency in children and adolescents aged 18 or younger at the time of the nuclear accident, in Fukushima Prefecture and its surrounding areas affected by the widespread dispersal of radioactive iodine; and 2) to elucidate any associations between demographic characteristics of the participants and UIC levels.

Materials and methods

Data setting and UIC measurement

This study retrospectively assessed the results of all children and adolescents aged 18 or younger who underwent UIC testing at Hirata Central Hospital, from 2012 to 2015. Data extracted from screening records included age of participant at examinations, sex, their address prior to the accident, whether address had changed or not following the accident, UIC levels, and dietary behavior for iodine intake inquired in the questionnaire (see below). For participants who underwent the UIC testing on multiple occasions during this period, only the data from the first testing were subjected to analysis. The UIC was determined in the spot urine by the Sandell-Kolthoff reaction utilizing the kit produced by Hitachi Chemical Co., Ltd. (Tokyo, Japan). All urine samples were assayed in duplicate. The sensitivity of the assay was 25 µg/L, and both the inter- and intra-assay coefficients of variation were less than 10 %.

Since October 2012, Hirata Central Hospital has offered voluntary UIC measurements and thyroid ultrasound examinations free of charge for residents of Fukushima and its surrounding areas who were under age 18 at the time of the accident in March 2011.

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Local municipalities including Miharu-machi (means 'town' in Japanese), located in the Naka-Dori region of Fukushima Prefecture, and Daigo-machi, Ibaraki Prefecture, have facilitated yearly thyroid ultrasound examinations and UIC testing for all primary and secondary school students in these towns. Their geographical locations, relative to the nuclear power plant, are shown in Figure 1. This screening program is publicized online, in general magazines, and newspapers.

Questionnaire about dietary intake of iodine

On the occasion of the UIC testing, to assess potential changes of dietary habit all participants were inquired about their dietary intake of iodine. All participants answered a yes-or-no question about whether they proactively started to consume foods rich in iodine after the accident.

Analysis

In order to assess any effects of age, sex, pre-accident residential area, and post-accident dietary behavior on UIC levels, we performed the analyses outlined below.

1. Median UICs were compared between those who proactively increased their dietary iodine intake after the accident and those who did not, by a nonparametric Wilcoxon rank-sum test.
2. For those that reported no proactive increases in their iodine intake after the accident, differences in UIC by gender, year of test (2012, 2013, 2014, 2015, defined as the government's financial year that runs from April 1 to March 31), school level [pre-school (ages ≤6), primary school (6–12), secondary school (12–15), and high

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

school (15–18)], residential address at the time of the accident (outside of Fukushima Prefecture, Hama-Dori, Naka-Dori, and Aizu), were assessed using the Wilcoxon rank-sum test for gender, and the Kruskal-Wallis test for year of test, age bracket and residential address at the time of the accident.

3. WHO defines population iodine deficiency as 'mild' for UIC levels of 50–100 μg/L, 'moderate' for 20–50 μg/L and 'severe' for <20 μg/L.(26) For the purpose of analyzing the associations between iodine deficiency and participants' characteristics, it would be preferable to divide the participants with UIC levels of <100 μg/L into three groups. However, virtually only a small number of participants were diagnosed as 'moderate' or 'severe' iodine deficiency (see the results section), which would have diminished the statistical power of analyses. Thus, we classified the participants into two dichotomous groups: <100 μg/L or ≥100 μg/L. Then, a multiple logistic regression model was constructed to identify factors associated with UIC levels of <100 μg/L. To minimize potentially unobserved cofounding effects of evacuation on iodine intake via changed lifestyles in evacuation sites, those reporting post-accident address changes were excluded from the logistic regression.

All analyses were carried out with STATA/MP version 13.1. P values of <0.05 were considered as significant.

Ethics

This study was approved by the Hirata Central Hospital Internal Review Board (20160316-2). Informed consent was received from all subjects or their guardians participating in this study.

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Results

From October 2012 to October 2015, a total of 4,410 children and adolescents aged 18 or younger at the time of the accident underwent UIC testing. The age range of participants was 1–18 years old (median, 10 yrs), and 2,139 (48.5%) of them were female (Table 1). Of them, the numbers of primary and secondary school students in Miharu and Daigo were 1,423 and 1,155, respectively. The total number of primary and secondary school students were 1,379 in Miharu for fiscal 2013 and 1,113 in Daigo for fiscal 2014, and 1,221 (88.5%) and 1,118 (99.6%) of these participated in this UIC testing in the corresponding fiscal years, respectively.

Figure 2 displays the distribution of UIC levels in individual participants. The levels ranged between 25–21,100 μg/L, with a median of 204 μg/L. Fifty percent (n=2,206) fell within the normal range (100–299 μg/L) as per the WHO definition, and there were 133 (3.0%), 732 (16.6%) and 1,472 (33.4%) participants with UIC levels of <50 μg/L, <100 μg/L, or ≥300 μg/L, respectively. No participants were below the threshold of severe iodine deficiency (<20 μg/L).

Analysis 1

In answer to our inquiry of whether the participants increased iodine intake, 617 (14.0%) reported a proactive increase after the accident (Table 1). There were significant differences across the years of examinations in the proportions of participants who proactively increased iodine intake ($p<0.001$), with the largest value being observed in 2012 (40.3%), after which it decreased year after year (7.7%–20.1%). Among those who reported proactive increases in dietary iodine after the accident, few had been living outside of Fukushima at the time of the accident (6.0%), and

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

comparatively large proportions had been living in Fukushima's Hama-Dori and Naka-Dori+Aizu regions (18.8% and 17.7%, respectively: $p<0.001$). As there were a small number of test participants from Aizu region (n=13), we combined the data from Naka-Dori and Aizu regions for analyses. There were no statistically significant differences in age and sex between those who did and did not proactively increase iodine intake post-accident. Furthermore, there was no significant difference in UIC between those who did and did not proactively increase iodine intake after the accident (median: 202.5 vs. 213.0, $p=0.93$).

Analysis 2

In the group reporting no post-accident increase in dietary iodine, we found no significant differences in UIC levels by sex. However, there were significant differences by year ($p<0.01$), school level ($p<0.001$), and residential area at the time of the accident ($p<0.001$), respectively (Table 2).

Analysis 3

Table 3 presents the results of the logistic regression analysis. The covariates included in the final model are school-model (categorical: pre-school (reference), primary school, secondary school, and high school), sex (binary: male (reference) and female), and pre-disaster residential area (categorical: outside of Fukushima (reference), Hama-Dori, and Naka-Dori+Aizu). Compared to primary school students, there was a significantly higher proportion of UIC levels below 100 μg/L in pre-school and secondary school students (OR: 1.92, 95% CI: 1.45–2.53, $p<0.001$; and OR: 1.45, 95% CI: 1.16–1.81, $p<0.01$). Furthermore, compared to those living outside of Fukushima, residency in

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Hama-Dori was associated with a significantly higher proportion of UIC levels below 100 µg/L (OR: 1.50, 95% CI: 1.04–2.17, $p<0.05$).

Discussion

In the present study, we found that the children and adolescents in Fukushima and its neighboring areas had been taking sufficient amount of dietary iodine during the period of 1.5-4.5 years after the Fukushima nuclear power plant accident. The median level of UIC among all of the participants was 204 µg/L, well above the lower bound of adequate iodine intake as per the WHO recommendations (100 µg/L).

The UIC was <100 µg/L in only 16.6 % of the participants, and there were no subjects with their UIC being <20 µg/L. WHO recommended that the proportion of individuals with UIC <50 µg/L should be less than 20 % in a given population,(26) and in the present study the proportion of participants falling under this subcategory was as low as 3.0 %. Overall, there were extremely few participants found to be severely iodine deficient, and most of our participants can be regarded as having ingested sufficient amount of iodine from their daily diets during the years spanning 2012-2015. These findings in the present study were comparable to the results of urinary iodine screenings reported in the previous studies involving Japanese schoolchildren.(25, 27)

Furthermore, this study found no statistically significant differences in UIC between those who did and did not increase their dietary iodine intake after the accident. The present study revealed that 14.0% of the participants increased their dietary intake of iodine post-accident. While the reason for this behavior is not clear, radiation-related fear may have played a role, similar to what was reported after Chernobyl;(28) however, we assume that fear of radiation diminished year after year, since the proportion of

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

participants reporting proactive increases of iodine intake decreased year after year. Our previous study found that a higher proportion (23.1 %) of children and adolescents in Fukushima than that in the present study increased their intake of seaweeds during the period of 20-30 months after the accident, which may be an observation in favor of the declining fear for radiation over time.(29) Collectively, the present finding of the lack of significant changes in UIC irrespective of the altered dietary behaviors after the accident may indicate that the participants in this study had already ingested sufficient amount of iodine ever since before the nuclear accident broke out.

However, caution should be exercised in interpreting the UIC data by year of examination, group, and residential areas in this study. While no significant gender-related differences in UIC were found in Analysis 2, there were significant differences with respect to year, school level, and residential area at the time of the accident. Results of the multivariate analysis (Analysis 3) indicated that, compared to primary school students, pre-school and secondary school students were at a higher risk of iodine deficiency (<100 μg/L) (Table 3). The same trend could be seen in the residents of the Hama-Dori region in Fukushima, compared to the residents outside of Fukushima (Table 3). While the reason for these trends is unclear, there are some potential contributors to be considered. For the variable of year, it is worth noting that this study began and ended in October, meaning that we had only such data that were obtained from October through January for years 2012 and 2015, due to the data organization based on Japanese fiscal years which run from April to March. This might have caused seasonal confounding with respect to the variable of year, resulting in the observed significant differences in Analysis 2; however, these differences across the years of examination disappeared when tested by multivariate analyses (Analysis 3).

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

The finding of the lower UIC in Hama-Dori, the coastal region of Fukushima, may be derived from the post-accident changes in dietary iodine supply, due to restrictions placed on fishing. Most of the data from outside of Fukushima came from residents of Daigo, Ibaraki Prefecture, where there was a radiation leak accident in 2013.(30) It is possible that this nuclear leakage accident urged the population in Daigo to increase their iodine intake for prevention purposes for ensuing several years, which may have resulted in the significant differences in UIC among the residential areas examined. This constraint may have led to the overestimation of odds ratios of Hama-Dori and Naka-Dori+Aizu. The observed differences in UIC among differing age brackets and regions might have reflected differences in ingredients used for school meals, and/or differing food customs by region and age. Less than school-age children are the most susceptible group to radioactive iodine exposure, and therefore the lower UIC levels detected in this subgroup may merit further investigations including nutritional surveys.

The present findings alone do not allow us to conclude that children and adolescents in Fukushima and its surrounding areas were not iodine deficient as a whole during the periods spanning both the pre-accident and early post-accident periods after the release of radioactive iodine from the crippled nuclear power plant. Given the post-accident restrictions placed on planting and shipping farmed and fished products, it is likely that there were changes in societal dietary habits,(31, 32) and therefore it may be incorrect to assume that post-accident UIC levels represent pre-accident levels. During the period of social disruption that occurred immediately after the nuclear accident, there was a loss of crucial supplies of electricity, gas and water, and many evacuees may have been forced to change their lifestyles including sole reliance on foods rationed out at evacuation centers: a factor beyond their control.(33) Further research should place

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

more attention on possible changes in dietary habits before and after the accident, and on dietary patterns of evacuees.

Direct measurements of thyroid radiation exposure after the Fukushima nuclear accident were reported to be overwhelmingly smaller than those after the Chernobyl accident.(17) While this difference may be accounted for by various factors, one is the reported difference in the released amount of radioiodine between Chernobyl and Fukushima, with the latter being one-tenth that of the former.(16) Another factor may be the rapid evacuation and restrictions placed on the shipping and circulation of contaminated food products implemented by the Japanese government, which may have served to substantially mitigate radiation exposure to the thyroid.(34) In addition to these two primary reasons, the present study suggests another contributing factor that the overall sufficient intake of stable iodine in Fukushima residents may have prevented the thyroid from being exposed to radioactive iodine.

This study may provide several useful implications that reach above and beyond the role of radiation exposure on thyroid cancer in post-nuclear accident Fukushima. First, while most participants can be considered as having had sufficient intake of iodine, a minor proportion of them fell within the category of mild (50-100 μg/L) or moderate (20-50 μg/L) iodine deficiency. In comparison to the group with sufficient iodine levels, the slightly deficient group may have a higher risk to develop thyroid cancer. Even so, in the previous reports of the WHO and UN on the environmental radiation in Fukushima, the role of dietary iodine intake was not taken into account in dose estimations of thyroid radiation exposure in residents affected by the Fukushima accident.(35, 36) In order to have a better understanding of the actual radioiodine doses that the thyroids of Fukushima residents incurred after the nuclear accident, it would be

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

preferable to incorporate into analyses the stable iodine status in individuals. The results of the present study may hopefully be a clue to future investigations relevant to this important discipline. Second, in marked contrast to iodine deficiency, excess iodine intake may also raise the risk of thyroid cancer, unrelated to radiation exposure.(37) While WHO defines UIC levels of 300 μg/L or more as excessive,(24) part of the participants (33.4%) in the present study had very high levels of UIC with 300 μg/L or more. When assessing the risk of thyroid cancer in the young in post-nuclear accident Fukushima, it may be necessary to consider the possible effect of excess iodine intake on thyroid cancer risk as well, rather than limiting our focus to radiation exposure.

Limitation

There are several limitations to this study. First, the urinary iodine screening was conducted on a voluntary basis, and thus the data obtained may not be representative of all areas of Fukushima Prefecture. Second, the UIC measurement is known as a test prone to a large day-to-day variation in a given individual.(38)

Conclusion

In the present study, we found subtle but statistically significant differences in the UIC among the participants with respect to the year of examination following the Fukushima accident, subject age, and residential area. Even so, it was revealed that the children and adolescents examined had ingested sufficient amount of iodine as a whole. In addition to the differences in the scale of accident and countermeasures undertaken between Fukushima and Chernobyl, differences in dietary iodine intake might have played an additional role in engendering the reportedly different radiation doses to the thyroid between the two nuclear accidents.

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Acknowledgments

We would like to thank Fumihiko Sagawa (Director of Healthcare Corporation Seireikai), Masahiko Nihei, Yu Sakuma at Hirata Central Hospital, Megumi Murakami, and Miki Abe at the Hirata Radiation Research Center. Also, we are greatly appreciative for the staff working for the municipalities, especially those of Miharu Town and Daigo Town. The study could not have taken place without their assistance. We additionally thank all people who made donations for the administration of the thyroid screening program at Hirata Central Hospital, especially Cataloghouse inc..

Contributorship statement

All the authors were responsible for the study concept and design. MT, HW, YN and CS acquired the data, which was analyzed and interpreted by all the authors. MT, SN, HW, CL, SO and SK drafted the manuscript, which was critically revised for important intellectual content by all the authors. SN performed the statistical analyses. YS served as the study supervisors and provided administrative and technical support. All the authors have approved the final draft of the manuscript.

Competing interests

Nothing to declare

Funding

None

Date sharing statement

All data underlying the findings in our study will not be available to other researchers due to the lack of informed consent.

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

References

1. Schneider AB, Sarne DH 2005 Long-term risks for thyroid cancer and other neoplasms after exposure to radiation. Nat Clin Pract Endocrinol Metab **1**:82-91.

2. Ron E, Lubin JH, Shore RE, Mabuchi K, Modan B, Pottern LM, Schneider AB, Tucker MA, Boice JD, Jr. 1995 Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies. Radiat Res **141**:259-277.

3. Tucker MA, Jones PH, Boice JD, Jr., Robison LL, Stone BJ, Stovall M, Jenkin RD, Lubin JH, Baum ES, Siegel SE, et al. 1991 Therapeutic radiation at a young age is linked to secondary thyroid cancer. The Late Effects Study Group. Cancer Res **51**:2885-2888.

4. Parker LN, Belsky JL, Yamamoto T, Kawamoto S, Keehn RJ 1974 Thyroid carcinoma after exposure to atomic radiation. A continuing survey of a fixed population, Hiroshima and Nagasaki, 1958-1971. Ann Intern Med **80**:600-604.

5. Hamilton TE, van Belle G, LoGerfo JP 1987 Thyroid neoplasia in Marshall Islanders exposed to nuclear fallout. JAMA **258**:629-635.

6. Takahashi T, Schoemaker MJ, Trott KR, Simon SL, Fujimori K, Nakashima N, Fukao A, Saito H 2003 The relationship of thyroid cancer with radiation exposure from nuclear weapon testing in the Marshall Islands. J Epidemiol **13**:99-107.

7. Kazakov VS, Demidchik EP, Astakhova LN 1992 Thyroid cancer after Chernobyl. Nature **359**:21.

8. Cardis E, Kesminiene A, Ivanov V, Malakhova I, Shibata Y, Khrouch V, Drozdovitch V, Maceika E, Zvonova I, Vlassov O, Bouville A, Goulko G, Hoshi M, Abrosimov A, Anoshko J, Astakhova L, Chekin S, Demidchik E, Galanti R, Ito M, Korobova E, Lushnikov E, Maksioutov M, Masyakin V, Nerovnia A, Parshin V, Parshkov E, Piliptsevich N, Pinchera A, Polyakov S, Shabeka N, Suonio E, Tenet V, Tsyb A, Yamashita S, Williams D 2005 Risk of thyroid cancer after exposure to 131I in childhood. J Natl Cancer Inst **97**:724-732.

9. Moysich KB, Menezes RJ, Michalek AM 2002 Chernobyl-related ionising radiation exposure and cancer risk: an epidemiological review. Lancet Oncol **3**:269-279.

10. UNSCEAR 2008 Annex D: Health effects due to radiation from the Chernobyl accident UNSCEAR 2008 Report to the General Assembly, with scientific annexes. Vol 1. United Nations Publications, New York.

11. Gembicki M, Stozharov AN, Arinchin AN, Moschik KV, Petrenko S, Khmara IM, Baverstock KF 1997 Iodine deficiency in Belarusian children as a possible factor stimulating the irradiation of the thyroid gland during the Chernobyl catastrophe. Environ Health Perspect **105 Suppl 6**:1487-1490.

12. Shakhtarin VV, Tsyb AF, Stepanenko VF, Orlov MY, Kopecky KJ, Davis S 2003 Iodine deficiency, radiation dose, and the risk of thyroid cancer among children and adolescents in the Bryansk region of Russia following the Chernobyl power station accident. Int J Epidemiol **32**:584-591.

13. UNSCEAR 1988 Annex D: Exposures from the Chernobyl accident UNSCEAR 1988 report: sources, effects and risks of ionizing radiation. Vol. United Nations, New York.

14. Ashizawa K, Shibata Y, Yamashita S, Namba H, Hoshi M, Yokoyama N, Izumi

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

M, Nagataki S 1997 Prevalence of goiter and urinary iodine excretion levels in children around Chernobyl. J Clin Endocrinol Metab **82**:3430-3433.

15. Hasegawa A, Tanigawa K, Ohtsuru A, Yabe H, Maeda M, Shigemura J, Ohira T, Tominaga T, Akashi M, Hirohashi N, Ishikawa T, Kamiya K, Shibuya K, Yamashita S, Chhem RK 2015 Health effects of radiation and other health problems in the aftermath of nuclear accidents, with an emphasis on Fukushima. Lancet **386**:479-488.

16. Steinhauser G, Brandl A, Johnson TE 2014 Comparison of the Chernobyl and Fukushima nuclear accidents: a review of the environmental impacts. Sci Total Environ **470-471**:800-817.

17. Tokonami S, Hosoda M, Akiba S, Sorimachi A, Kashiwakura I, Balonov M 2012 Thyroid doses for evacuees from the Fukushima nuclear accident. Sci Rep **2**:507.

18. Suzuki S, Suzuki S, Fukushima T, Midorikawa S, Shimura H, Matsuzuka T, Ishikawa T, Takahashi H, Ohtsuru A, Sakai A, Hosoya M, Yasumura S, Nollet KE, Ohira T, Ohto H, Abe M, Kamiya K, Yamashita S 2016 Comprehensive Survey Results of Childhood Thyroid Ultrasound Examinations in Fukushima in the First Four Years After the Fukushima Daiichi Nuclear Power Plant Accident. Thyroid **26**:843-851.

19. Suzuki S, Yamashita S, Fukushima T, Nakano K, Midorikawa S, Ohtsuru A, Yasumura S, Hosoya M, Kamiya K, Shimura H, Suzuki S, Nakamura I, Abe M 2016 The protocol and preliminary baseline survey results of the thyroid ultrasound examination in Fukushima [Rapid Communication]. Endocr J **63**:315-321.

20. Katagiri R, Asakura K, Uechi K, Masayasu S, Sasaki S 2015 Adequacy of iodine intake in three different Japanese adult dietary patterns: a nationwide study. Nutr J **14**:129.

21. Katagiri R, Asakura K, Sasaki S, Hirota N, Notsu A, Miura A, Todoriki H, Fukui M, Date C 2015 Estimation of habitual iodine intake in Japanese adults using 16 d diet records over four seasons with a newly developed food composition database for iodine. Br J Nutr **114**:624-634.

22. Ristic-Medic D, Piskackova Z, Hooper L, Ruprich J, Casgrain A, Ashton K, Pavlovic M, Glibetic M 2009 Methods of assessment of iodine status in humans: a systematic review. Am J Clin Nutr **89**:2052S-2069S.

23. Zimmermann MB 2008 Methods to assess iron and iodine status. Br J Nutr **99 Suppl 3**:S2-9.

24. Zimmermann MB, Andersson M 2012 Assessment of iodine nutrition in populations: past, present, and future. Nutr Rev **70**:553-570.

25. Zimmermann MB, Hess SY, Molinari L, De Benoist B, Delange F, Braverman LE, Fujieda K, Ito Y, Jooste PL, Moosa K, Pearce EN, Pretell EA, Shishiba Y 2004 New reference values for thyroid volume by ultrasound in iodine-sufficient schoolchildren: a World Health Organization/Nutrition for Health and Development Iodine Deficiency Study Group Report. Am J Clin Nutr **79**:231-237.

26. De Benoist B, Andersson M, Egli I, Takkouche B, Allen H 2004 Iodine status worldwide: WHO global database on iodine deficiency. Department of Nutrition for Health and Development, World Health Organization Geneva.

Thyroid
Assessment of nutritional status of iodine through urinary iodine screening among local children and adolescents after the Fukushima Daiichi nuclear power plant accident (doi: 10.1089/thy.2016.0313)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

27. Fuse Y, Saito N, Tsuchiya T, Shishiba Y, Irie M 2007 Smaller thyroid gland volume with high urinary iodine excretion in Japanese schoolchildren: normative reference values in an iodine-sufficient area and comparison with the WHO/ICCIDD reference. Thyroid **17**:145-155.

28. Rahu M 2003 Health effects of the Chernobyl accident: fears, rumours and the truth. Eur J Cancer **39**:295-299.

29. Watanobe H, Furutani T, Nihei M, Sakuma Y, Yanai R, Takahashi M, Sato H, Sagawa F 2014 The thyroid status of children and adolescents in Fukushima Prefecture examined during 20-30 months after the Fukushima nuclear power plant disaster: a cross-sectional, observational study. PLoS One **9**:e113804.

30. Koseki T, Hasegawa K 2014 Present status of J-PARC-after the shutdown due to the radioactive material leak accident. Proceedings of IPAC2014, Dresden, Germany:3373-3375.

31. Nishikawa Y, Tsubokura M, Kato S, Saito Y 2014 Possible Anisakiasis Associated with Fishery Resumption. Disaster Med Public Health Prep:1-2.

32. Ozaki A, Tanimoto T, Leppold C, Tsubokura M, Kato S, Tsukada M, Kami M, Ohira H 2016 A possible association between the resumption of agricultural activities and a venomous snakebite after Fukushima nuclear crisis. Oxf Med Case Reports **2016**:22-23.

33. Hasegawa A, Ohira T, Maeda M, Yasumura S, Tanigawa K 2016 Emergency Responses and Health Consequences after the Fukushima Accident; Evacuation and Relocation. Clin Oncol (R Coll Radiol) **28**:237-244.

34. Hamada N, Ogino H 2012 Food safety regulations: what we learned from the Fukushima nuclear accident. J Environ Radioact **111**:83-99.

35. UNSCEAR 2014 Annex A: Levels and effects of radiation exposure due to the nuclear accident after the 2011 great east-Japan earthquake and tsunami UNSCEAR 2013 report: sources, effects and risks of ionizing radiation. Vol. United Nations Publications, New York.

36. WHO 2013 Health risk assessment from the nuclear accident after the 2011 Great East Japan earthquake and tsunami, based on a preliminary dose estimation. World Health Organization, Geneva.

37. Zimmermann MB, Galetti V 2015 Iodine intake as a risk factor for thyroid cancer: a comprehensive review of animal and human studies. Thyroid Res **8**:8.

38. Andersen S, Pedersen KM, Pedersen IB, Laurberg P 2001 Variations in urinary iodine excretion and thyroid function. A 1-year study in healthy men. Eur J Endocrinol **144**:461-465.