Seaweed intake and Thyroid cancer risk

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Background

Background (1)

- Iodine is an essential micronutrient that is oxidized to produce iodine-containing thyroid hormones.
- Iodine deficiency has long been a recognized global public health problem, however, there was not much emphasis on the possible "consequences" of iodine excess.
- The sources of excess iodine can be from
    - iodized salt, ~~drinking water~~, ~~milk rich in iodine~~, seaweeds, and dietary supplements.
- Iodine excess can cause subclinical or overt thyroid dysfunction, and even thyroid (papillary) cancer.

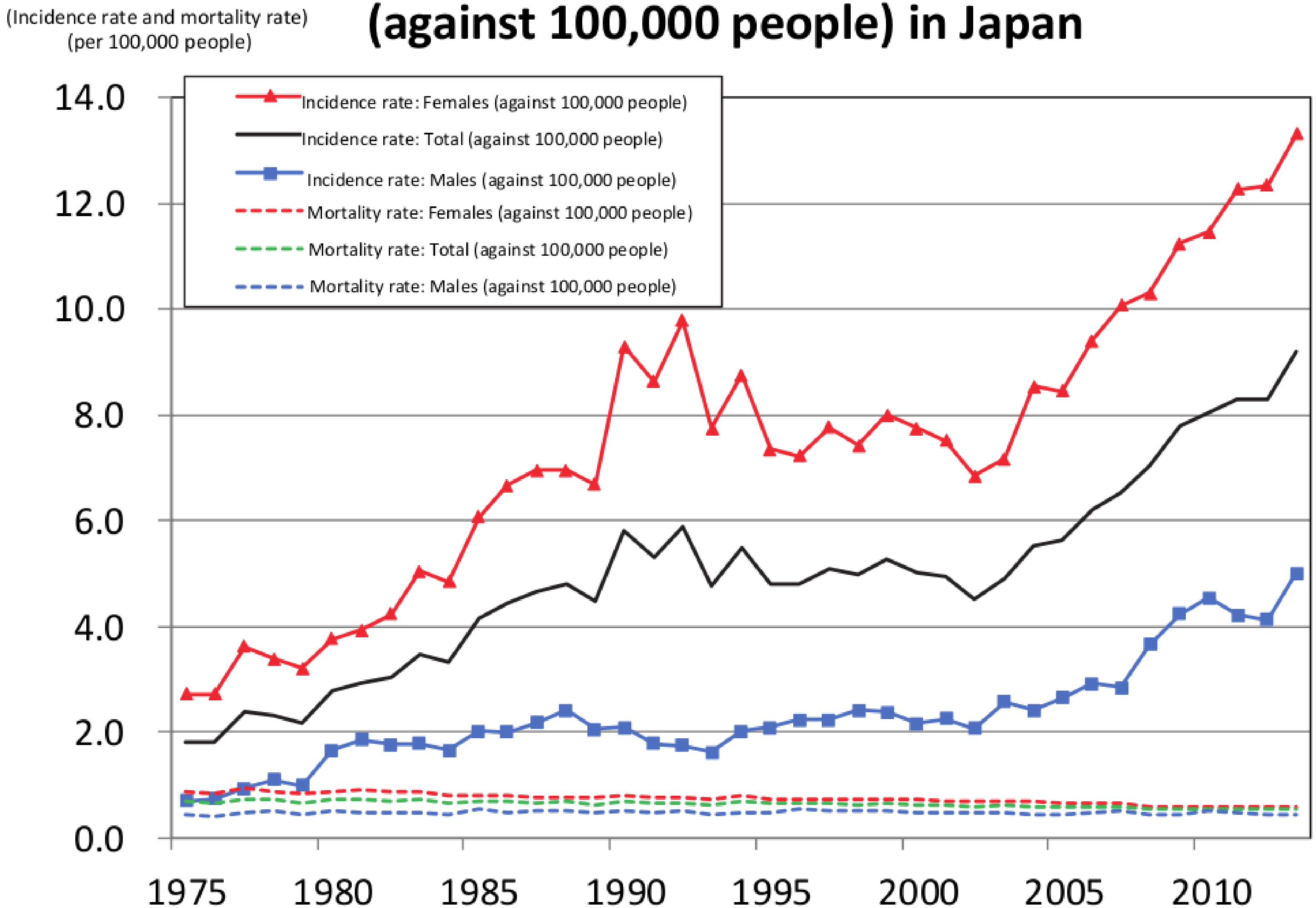
Background (2)

- Thyroid cancer might have already become the third leading cancer diagnosis in the United States in women.
- Age-adjusted incidence rate in Japan (2016, per 100,000 person-years):
  - 5.7 in men
  - 16.7 in women
- However, the numbers may include substantial portions of "incidentally-detected" cases through health/cancer screenings.
- The only mostly accepted risk factor for thyroid cancer is radiation exposure.

Basic Information on Thyroid

Incidence Rates of Thyroid Cancer: Japan

Annual changes in age-adjusted incidence rates and mortality rates (against 100,000 people) in Japan



(Source: "Cancer Registration and Statistics," Cancer Information Service, National Cancer Center Japan))

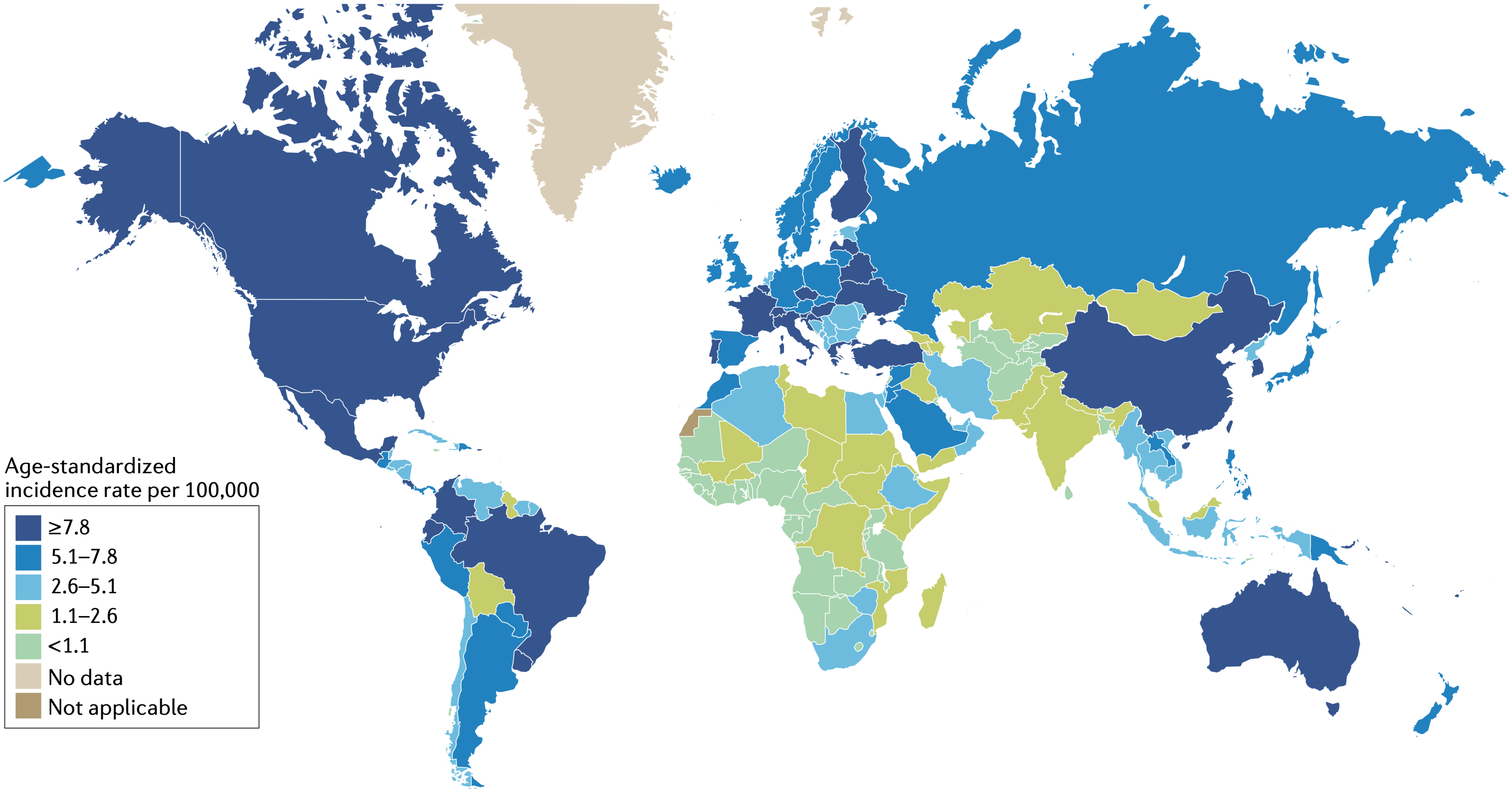


Fig. 1 | **Global estimated age-standardized incidence rates of thyroid cancer in 2018.** Thyroid cancer incidence is higher in high-income countries compared with low-income and middle-income countries. Global variability in the incidence of thyroid cancer has been attributed to multiple causes such as differences in diagnostic practices, health-care systems, environmental exposures and individual risk factors. Data are from REF.[131].

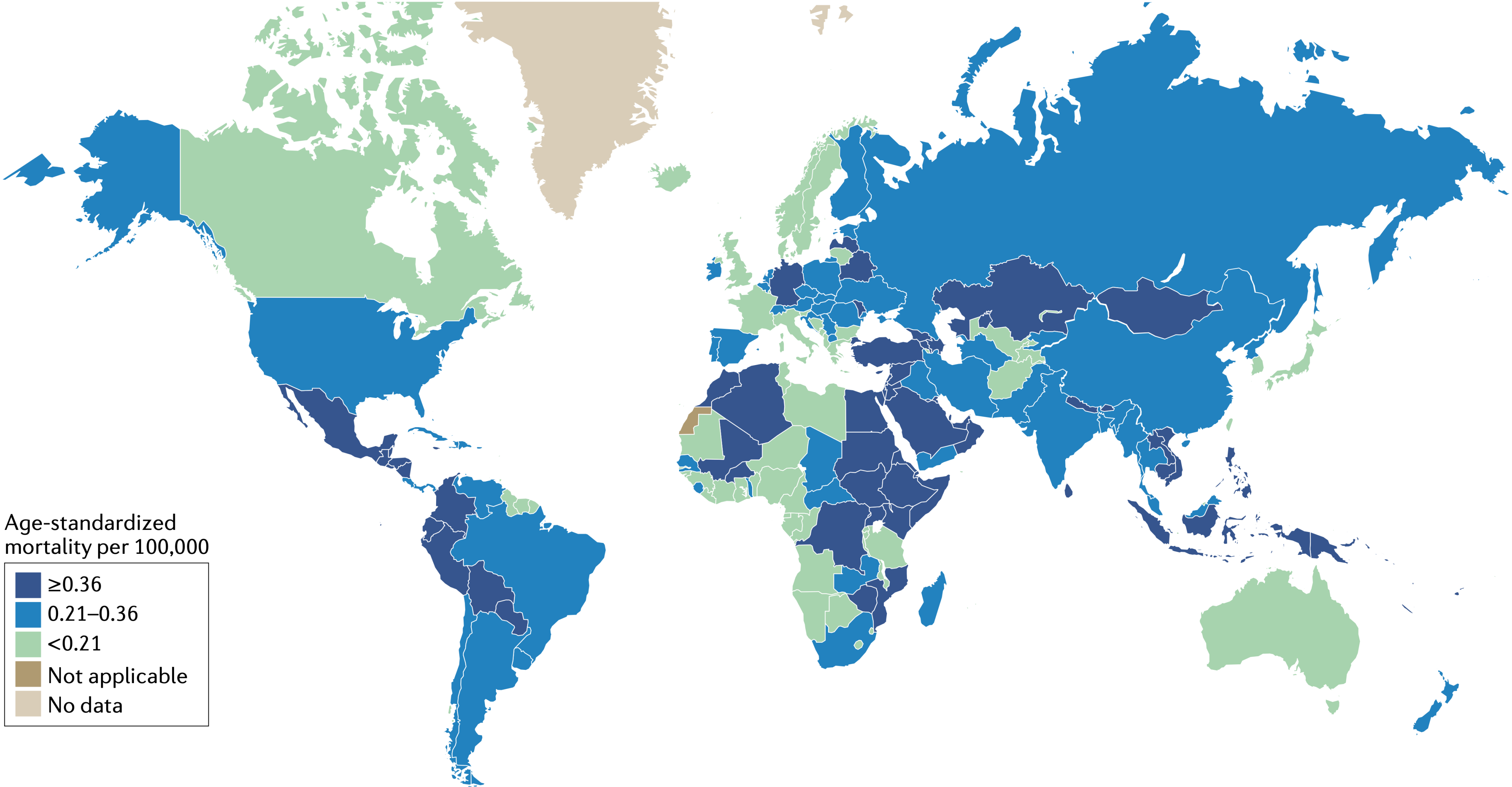


Fig. 2 | **Global estimated age-standardized mortality of thyroid cancer in 2018.** Mortality related to thyroid cancer varies by region. For the most part, high-income countries have seen a decline in mortality, while middle-income countries experience higher mortality rates related to thyroid cancer. Data are from REF.[131].

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CLINICAL REVIEW

WILEY

Relationship between iodine levels and papillary thyroid carcinoma: A systematic review and meta-analysis

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Abstract

Background: Iodine excess has been suggested as an exogenous risk factor of papillary thyroid cancer (PTC). We performed a systematic review and meta-analysis to assess the relationship between iodine exposure measured in various forms and PTC prevalence.

Methods: We searched MEDLINE, Embase, and the Cochrane Library for case-control studies on iodine and PTC published up to December 2015. Exposure to iodine was compared between PTC and control groups.

Results: From the 16 selected studies, the odds ratio (OR) for the overall effect size between high iodine exposure and PTC risk was 1.418 (95% confidence interval [CI] 1.054-1.909). Based on 7 studies conducted in high iodinated regions, a positive association between iodine exposure and PTC was observed (OR 2.200; 95% CI 1.389-3.483).

Conclusion: This study demonstrated a higher exposure to iodine in patients with PTC compared with controls, especially for patients from high iodinated regions.

TABLE 2 Summary of risk estimates according to iodine measurement methods of included studies

Variables	No. of studies	Summary OR (95% CI)[a]	*P* value	*P* heterogeneity	I^2, %	Publication bias Egger's
All studies	16	**1.418 (1.054-1.909)**	**<.001**	<.001	90.38	0.612
Measurement methods						
Urinary iodine	2	4.272 (0.760-23.999)	.099	<.001	95.49	
Dietary iodine	6	0.842 (0.608-1.177)	.314	.003	72.03	
Salt iodination	5	1.881 (0.883-4.008)	.102	<.001	90.93	
Regional variation in iodine levels	3	1.295 (0.853-1.966)	.226	<.001	87.30	
Regional variation						
High iodinated region	7	**2.200 (1.389-3.483)**	**.001**	<.001	88.58	
Low iodinated region	3	0.715 (0.269-1.729)	.457	<.001	89.44	
Eligible controls						
Healthy controls	7	1.428 (0.803-2.538)	.225	<.001	92.51	
FTC controls	9	1.385 (0.967-1.984)	.076	<.001	88.98	

Abbreviations: CI, confidence interval; FTC, follicular thyroid carcinoma; OR, odds ratio.
[a]The summary ORs (95% CI) in each meta-analysis were estimated by the random effect model.

- This meta-analysis evaluated iodine level measured by several methods and we can see there is no evidence for increased thyroid cancer risk in any kind of measurements.
- Another problem in this study is that they only included subjects in the highest and the lowest exposure groups.

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REVIEW ARTICLE

Check for updates

Impact of seaweed intake on health

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Abstract

Seaweeds contain minerals, vitamins, soluble dietary fibers, and flavonoids, which are regarded as preventive agents against lifestyle-related diseases. Seaweeds are consumed commonly in East Asian countries including Japan. Thus, intake of seaweeds might contribute to Japanese longevity via prevention of lifestyle-related diseases. Recently, two large Japanese cohort studies have reported the association of seaweed intake with reduced risk of cardiovascular diseases. On the other hand, seaweeds also contain iodine and heavy metals such as arsenic species, which are considered to have adverse effects on health. We here reviewed studies of the association between seaweed intake and mortality from or incidence of cancer and cardiovascular diseases, and their risk factors such as blood pressure or serum lipids. We also summarized the adverse effects of iodine and arsenic species in seaweeds. Although seaweeds have not been widely consumed in Western countries, dietary diversification and an increased proportion of immigrants from East Asia may increase seaweed consumption in those countries. Further epidemiological studies including observational and interventional studies are necessary to clarify the effects of seaweeds on disease and health.

Seaweed consumption and the risk of thyroid cancer in women: the Japan Public Health Center-based Prospective Study

Takehiro Michikawa[a,b], Manami Inoue[a], Taichi Shimazu[a], Norie Sawada[a], Motoki Iwasaki[a], Shizuka Sasazuki[a], Taiki Yamaji[a], Shoichiro Tsugane[a] and for the Japan Public Health Center-based Prospective Study Group

Iodine is a suspected risk factor for thyroid cancer. Seaweed accounts for about 80% of Japanese people's iodine intake. We examined the association between seaweed consumption and the risk of thyroid cancer in Japanese women. Women participating in the Japan Public Health Center-based Prospective Study (*n*=52 679; age: 40–69 years) were followed up for a mean of 14.5 years; 134 new thyroid cancer cases, including 113 papillary carcinoma cases, were identified. Seaweed consumption was assessed using a food-frequency questionnaire and divided into three categories: 2 days/week or less (reference); 3–4 days/week; and almost daily. The Cox proportional hazards model was applied to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Seaweed consumption was clearly associated with an increased risk of papillary carcinoma (HR for almost daily consumption compared with 2 days/week or less=1.71; 95% CI: 1.01–2.90; trend *P*=0.04). After stratification for menopausal status, an increased risk was observed in postmenopausal women (papillary carcinoma HR for almost daily consumption compared with 2 days/week or less=3.81, 95% CI: 1.67–8.68; trend *P*<0.01), but not in premenopausal women (HR=0.91, 95% CI: 0.44–1.91; trend *P*=0.76). This study identified a positive association between seaweed consumption and the risk of thyroid cancer (especially for papillary carcinoma) in postmenopausal women. *European Journal of Cancer Prevention* 21:254–260

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Keywords: cohort study, Japanese, papillary carcinoma, seaweed, thyroid cancer

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Prospective study of seaweed consumption and thyroid cancer incidence in women: the Japan collaborative cohort study

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Excess intake of iodine is a suspected risk factor for thyroid cancer. Previous epidemiological research from Japan reported that daily intake of seaweed was associated with a four-fold higher risk in postmenopausal women, whereas others reported a null association. A major source of iodine intake in Japan is from edible seaweeds, and it is reported to be among the highest in the world. We examined the association between seaweed intake frequency and the risk of thyroid cancer in women in the Japan Collaborative Cohort Study followed from 1988 to 2009. Seaweed intake, together with other lifestyle-related information was collected using a self-administered questionnaire at baseline. Seaweed intake frequency was categorized as follows: 1–2 times/week or less, 3–4 times/week, and almost daily. Hazard ratios and the 95% confidence intervals of thyroid cancer incidence according to seaweed intake frequency were estimated using Cox proportional hazards regression. During 447 876 person-years of follow-up ($n = 35\ 687$), 94 new cases of thyroid cancer were identified. The crude incidence rate was 20.9 per 100 000 person-years. The hazard ratio of thyroid cancer in women who consumed seaweed daily compared with women who ate it 1–2 times/week or less was 1.15 (95% confidence interval: 0.69–1.90, *P* for trend = 0.59). Further analyses did not indicate any association between seaweed intake and the risk of thyroid cancer on statistically adjusting for potential confounding variables as well as on stratification by menopausal status. The present study did not find an association between seaweed intake and thyroid cancer incidence in premenopausal or in postmenopausal women. *European Journal of Cancer Prevention* 00:000–000

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Keywords: prospective study, seaweed consumption, thyroid cancer

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Objective

With greater numbers of participants as well as cases that can be identified through ACC database, we propose to assess the maximum association between seaweed intake and the risk of thyroid cancer in ACC for both men and women, through a revised statistical approach.

Methods

Methods

- Descriptive analysis - show numbers and distributions of:
  - cases and total participants
  - seaweed intake
  - Other variables that could related to both exposure and the outcome
- Bayesian surival analysis will be conducted in each joining cohort to estimate an maximum effect size of the relationship.
- Random effect meta-analysis - to evaluate the pooled maximum effect.

Methods
- Bayesian survival analysis

- We already know that incidence increases over time
  - the hazard ratio could change over time (not proportonal)
- It is no longer appropriate to use the Cox proportional hazard model anymore
- Weibull model in the accelerated failure time (AFT) model form is one option.
  - produce an acceleration factor for comparing seaweed consumers to non-consumers about who is faster/slower to develop thyroid cancer during a given time period.

Methods
- Maximum seaweed effect

$$\mu_i = \beta_E \sum_{j=0}^{E_i - 1} \delta_j + \text{other covariates}$$

$$\delta \sim \text{Dirichlet}(\alpha)$$

- Instead of coding the seaweed consumption groups as dummy variables, they should be entered as ordered categorical predictors
  β_E is the maximum seaweed effect
  δ_j is the fractions (proportions) for each level of seaweed consumption

Methods - example

- If in A study, the data about seaweed consumption is collected as 5 different levels:
  'never', '1–2 times/month', '1–2 times/week', '3–4 times/week', and 'daily or almost daily' (JACC study).
- The effect changes from
  level 0 (never) to level 1 (1-2 times/month) is a proportion δ_0 of the maximum effect β_E
  level 1 (1-2 times/month) to level 2 (1–2 times/week) is a proportion δ_1 of the maximum effect β_E
  $\ldots$
  level 3 to level 4 is a proportion δ_4 of β_E
- Four fractions $\delta_0, \delta_1, \ldots, \delta_4$, they sum upto 1 $\sum_{j=0}^{4} = 1$

Methods - combining the β_Es

- These β_Es are the maximum effects of seaweed on the risk of thyroid cancer.

- Therefore the pooled effect could be estimated, if there are K studies in the ACC join our working group:
    - The observed $\widehat{\beta_{Ek}}, i = 1, \ldots, K$ is an estimate of the "real" effect β_{Ek} of study k
    - These "real" effects β_{Ek} themselves follow a distribution centered with the pooled effect μ, and variance τ^2 - the between-study heterogeneity.

$$\widehat{\beta_{Ek}} \sim N(\beta_{Ek}, \sigma_k^2)$$
$$\beta_{Ek} \sim N(\mu, \tau^2)$$

Thanks

link to visit this webslide:
https://wangcc.me/ACC_seaweed/

Looking forward to seeing your data.