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BRIEF REPORT

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Burden of cancer attributable to consumption of highly salted food in Japan in 2015

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Abstract: Salt consumption is high in most parts of the world, particularly among populations in Asia-Pacific region, including Japan. The recent portion of global deaths attributable to excess salt was largest among dietary exposures. We estimated the cancer in 2015 attributable to highly salted food in the Japanese population. Consumption of highly salted food in grams per day was available by sex and age group for 2005 from the Japanese National Health and Nutrition Survey. The optimal consumption of highly salted food for this study was assumed to be 0 g/day. Population attributable fractions (PAFs) for stomach cancer, which is positively associated with highly salted food intake in Japan, were estimated for respective sex and age groups according to a standard formula, and aggregated to obtain the PAF among total cancer incidence and mortality. In both sexes, 2.4% of cancer incidence and 2.2% of cancer mortality in 2015 were due to intake of highly salted food. Annually at least 22,000 total cancer cases in Japan could have been prevented by avoiding highly salted food.

***Keywords*:** cancer, highly salted food, population attributable fraction, Japan

Introduction

Cancer and cardiovascular disease are the leading causes of death in many parts of the world. High sodium consumption and salt-preserved foods are considered major dietary risk factors of cardiovascular diseases caused by high blood pressure (*1*) and some cancers (*2*). The World Health Organization (WHO) recommends keeping salt intake to less than 5 g/day to prevent these non-communicable diseases (NCDs) (*3*). The East Sub-Saharan African region is reported to have the lowest intake, with an average of 5 grams of salt per day (*4*). Most people in the world consume too much salt. Intake is highest in high income Asia-Pacific countries, including Japan, at an average of approximately 12 g/day as measured by 24-hour urinary excretion, and in Central Asia, at 13 grams of salt per day, in 2010 (*4*). The World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) reaffirmed in 2018 that salt-preserved foods increase risk for cancers of the stomach with a positive dose-response relationship (*2*). The latest estimate by the International Agency for Research on Cancer (IARC) describes stomach cancer as the fifth-most common cancer worldwide, with around 1,033,701 new cases globally in 2018 (*5*). Salt consumption in the Japanese population decreased by 1g at most in the 10 years between 2005 and 2015 (*6*). Despite global and domestic efforts, 2015 intake levels were still far from the WHO recommendation. At least 50% of salt in the diet appears to come from commercially processed foods with salt (*e.g.* salted-preserved fish or salted pickled vegetables). This remains the case even after salty seasonings such as soy sauce and miso - major sources of personal preference-based discretional sodium among Japanese - are excluded (*7*).

The fundamental etiology of stomach cancer by highly salted food intake is suggested to be as follows (*2*): high salt levels alter the viscosity of the mucous protecting the stomach, and intake of highly salted food may stimulate the colonization of H. *pylori*, the greatest known risk factor for stomach cancer. Highly salted food is not essential for optimal health in stomach cancer.

Here, we estimated the fraction of cancer incidence and mortality in 2015 attributable to highly salted food in the Japanese population.

Materials and Methods

Cancers associated with highly salted food

The WCRF/AICR reaffirmed that salt-preserved food increases risk for cancers of the stomach with a positive dose-response relationship (*2*). We therefore included these target cancers in the present evaluation; specifically, those with sufficient evidence for a positive association with highly salted food, and with available relative risk estimates in Japan, including stomach cancer.

Theoretical minimum risk exposure level

For this study, the optimal consumption of highly salted food in Japan was set at 0 g/day. The latent period - the interval period between "exposure" to highly salted food and the increase in risk of cancers of the stomach - is unknown. Based on previous epidemiological studies of exposure, we assumed a latent period of 10 years, and accordingly calculated the 2015 fraction of avoidable cancers using an estimate of highly salted food intake in 2005.

Prevalence of highly salted food consumption

The data on highly salted food consumption were derived from the Japanese National Health and Nutrition Survey (JNHNS) from 2005 (*8*). For this purpose, we used the 3-year mean of individual data for the years 2004-2006 provided by the Ministry of Health, Labour, and Welfare, Japan, with permission. Highly salted foods include pickled salty vegetables and salt-preserved fish. The survey presents mean consumption and its standard deviation by sex and age group. Table 1 shows the consumption of highly salted food per day by sex and age group for the Japanese population in 2005.

Table 1. Sex- and age-group-specific average consumption of highly salted food in Japan in 2005

Age at exposure (2005)	Highly salted food consumption (g/day)	
	Men	Women
0 - 4	7.2	7.8
5 - 9	10.0	10.5
10 - 14	13.5	16.1
15 - 19	20.3	20.4
20 - 24	21.8	20.4
25 - 29	25.5	19.6
30 - 34	26.7	20.4
35 - 39	27.2	20.5
40 - 44	30.9	23.5
45 - 49	36.9	29.6
50 - 54	38.9	32.4
55 - 59	43.6	37.8
60 - 64	49.0	39.8
65 - 69	49.1	44.8
70 - 74	50.7	43.3
≥ 75	46.8	41.6
Total	33.5	29.6

Cancer incidence and mortality in Japan in 2015

Cancer incidence data in 2015 were estimated using the annual estimate of cancer incidence in 2013 by the Monitoring of Cancer Incidence in Japan project (*9*). We used an age and period spline model. This type of model is used for short-term projection of cancer incidence in Japan (*10*). The sex- and age-specific incidence data for target cancers were coded in accordance with the International Statistical Classification of Diseases and Related Health Problems, 10th edition (ICD-10), using the morphology code of the International Classification of Disease for Oncology, 3rd edition (ICD-O-3).

The data on cancer mortality statistics from 2015 were based on the vital statistics of Japan (*11*). We obtained sex- and age-specific mortality data by cause of death from available data sources from the Health, Labour, and Welfare Statistics Association (*12*), using 4-digit ICD-10 codes to classify the cause of death.

Estimation of relative risk

The relative risk (RR) of stomach cancer in relation to highly salted food consumption was obtained from a meta-analysis of eight cohort studies (91% weight of combined results was sourced from four studies in Japan) conducted by the WCRF (*13*). This 2018 meta-analysis reported an RR of 1.09 (95% confidence interval: 1.05-1.13) per 20 g/day. We derived the increase in risk of stomach cancer for 1 g/day of highly salted food and average RR for the whole population based on the average highly salted food consumption, with an assumed log-linear relationship between highly salted food consumption and stomach cancer risk of:

$$Risk = exp^{[\ln(\text{risk per gram of highly-salted food intake}) \times \text{average exposure level}]}$$

Estimation of population attributable fractions (PAFs)

For stomach cancer, PAF was calculated for each sex and age group according to the standard formula (*14*):

$$\text{PAF} = \frac{(Risk - 1)}{Risk}$$

The number of attributable cancers was then totaled across all sex and age categories in order to show the percentage of the total number of all incidence and mortality of cancer in Japan in 2015.

Results and Discussion

The consumption of highly salted food among Japanese

people in 2005 is shown in Table 1. On average, across age categories, consumption was 33.5 g/day and 29.6 g/day for men and women, respectively. Consumption increased by age category up to 65-74 years for men (approximately 50 g/day) and women (approximately 45 g/day).

Tables 2 and 3 show the estimated number of incidence and mortality of stomach cancer in 2015 attributed to excessive consumption of highly salted food in 2005. Consumption of highly salted food was attributed to 17.7% of stomach cancer incidence for men and 15.4% for women. A similar trend was seen for stomach cancer mortality (18.1% for men, 15.8% for women). Likewise, consumption of highly salted food was attributed to 3.0% of total cancer incidence for men and 1.6% for women, and to 2.5% of total cancer mortality for men and 1.7% for women. Accordingly, in both sexes, 2.4% of cancer incidence and 2.2% of cancer mortality in 2015 were due to excessive intake of highly salted food. These results were not changed when the latent period was assumed to be 15 years (exposure mean calculated based on the 2000 National survey).

Our study suggests that 2.4% (22 thousand) of total cancer incidence and 2.2% (8 thousand) of cancer mortality in 2015 could have been prevented by avoiding highly salted food. Three PAFs of cancer were reported, based on inadequate salt intake, a reasonable optimal intake of ≤ 6 g/day (*15,16*), and a strict optimal

Table 2. Numbers and proportion of cancer cases in 2015 attributable to highly salted food consumption (> 0 g intake of highly salted food consumption)

Age at exposure (2005)	Age at outcome (2015)	Stomach cancer			Total cancers	
		PAF	Obs. cases	Attrib. cases	Obs. cases	Attrib. cases
Men						
0 - 4	10 - 14	0.03	1	0	410	0
5 - 9	15 - 19	0.04	3	0	519	0
10 - 14	20 - 24	0.06	13	1	682	1
15 - 19	25 - 29	0.08	36	3	974	3
20 - 24	30 - 34	0.09	88	8	1,595	8
25 - 29	35 - 39	0.10	231	24	2,962	24
30 - 34	40 - 44	0.11	682	74	6,281	74
35 - 39	45 - 49	0.11	1,476	163	10,557	163
40 - 44	50 - 54	0.12	2,867	357	17,827	357
45 - 49	55 - 59	0.15	4,937	726	29,272	726
50 - 54	60 - 64	0.15	9,056	1,398	53,238	1,398
55 - 59	65 - 69	0.17	15,599	2,672	91,095	2,672
60 - 64	70 - 74	0.19	16,743	3,189	96,962	3,189
65 - 69	75 - 79	0.19	16,081	3,065	93,375	3,065
70 - 74	80 - 84	0.20	13,054	2,560	77,034	2,560
≥ 75	≥ 85	0.18	11,015	2,010	65,753	2,010
Total		0.18	91,883	16,249	549,241	16,249
% of incident cases				17.7		3.0
Women						
0 - 4	10 - 14	0.03	1	0	351	0
5 - 9	15 - 19	0.04	6	0	531	0
10 - 14	20 - 24	0.07	18	1	914	1
15 - 19	25 - 29	0.08	48	4	1,791	4
20 - 24	30 - 34	0.08	120	10	3,780	10
25 - 29	35 - 39	0.08	277	22	7,759	22
30 - 34	40 - 44	0.08	605	51	14,970	51
35 - 39	45 - 49	0.08	912	77	19,397	77
40 - 44	50 - 54	0.10	1,300	125	22,922	125
45 - 49	55 - 59	0.12	1,853	222	26,467	222
50 - 54	60 - 64	0.13	3,104	404	36,091	404
55 - 59	65 - 69	0.15	5,182	778	50,521	778
60 - 64	70 - 74	0.16	5,834	920	49,841	920
65 - 69	75 - 79	0.18	6,358	1,117	49,967	1,117
70 - 74	80 - 84	0.17	6,704	1,142	50,482	1,142
≥ 75	≥ 85	0.16	9,881	1,623	72,222	1,623
Total		0.15	42,203	6,497	408,572	6,497
% of incident cases				15.4		1.6
Both sexes			134,087	22,746	957,813	22,746
% of incident cases				17.0		2.4

Abbreviations: Attrib. = Attributable; Obs. = observed; PAF = population attributable fraction.

Table 3. Numbers and proportion of cancer mortality in 2015 attributable to highly salted food consumption (> 0 g intake of highly salted food consumption)

Age at exposure (2005)	Age at outcome (2015)	Stomach cancer			Total cancers	
		PAF	Obs. deaths	Attrib. deaths	Obs. deaths	Attrib. deaths
Men						
0 - 4	10 - 14	0.03	0	0	52	0
5 - 9	15 - 19	0.04	0	0	86	0
10 - 14	20 - 24	0.06	8	0	112	0
15 - 19	25 - 29	0.08	19	2	153	2
20 - 24	30 - 34	0.09	30	3	260	3
25 - 29	35 - 39	0.10	66	7	521	7
30 - 34	40 - 44	0.11	141	15	1,225	15
35 - 39	45 - 49	0.11	256	28	2,035	28
40 - 44	50 - 54	0.12	524	65	3,923	65
45 - 49	55 - 59	0.15	992	146	7,622	146
50 - 54	60 - 64	0.15	2,199	339	16,179	339
55 - 59	65 - 69	0.17	4,108	704	29,367	704
60 - 64	70 - 74	0.19	4,939	941	34,860	941
65 - 69	75 - 79	0.19	5,504	1,049	37,820	1,049
70 - 74	80 - 84	0.20	5,710	1,120	40,650	1,120
≥ 75	≥ 85	0.18	6,312	1,152	44,515	1,152
Total		0.18	30,809	5,571	219,508	5,571
% of cancer deaths				18.1		2.5
Women						
0 - 4	10 - 14	0.03	0	0	55	0
5 - 9	15 - 19	0.04	3	0	61	0
10 - 14	20 - 24	0.07	5	0	64	0
15 - 19	25 - 29	0.08	13	1	170	1
20 - 24	30 - 34	0.08	52	4	394	4
25 - 29	35 - 39	0.08	75	6	763	6
30 - 34	40 - 44	0.08	141	12	1,623	12
35 - 39	45 - 49	0.08	211	18	2,484	18
40 - 44	50 - 54	0.10	279	27	3,841	27
45 - 49	55 - 59	0.12	436	52	5,501	52
50 - 54	60 - 64	0.13	803	105	9,146	105
55 - 59	65 - 69	0.15	1,352	203	14,322	203
60 - 64	70 - 74	0.16	1,617	255	16,783	255
65 - 69	75 - 79	0.18	1,991	350	20,329	350
70 - 74	80 - 84	0.17	2,739	467	25,876	467
≥ 75	≥ 85	0.16	6,153	1,011	49,345	1,011
Total		0.16	15,870	2,510	150,838	2,510
% of cancer deaths				15.8		1.7
Both sexes			46,679	8,081	370,346	8,081
% of cancer deaths				17.3		2.2

Abbreviations: Attrib. = Attributable; Obs. = observed; PAF = population attributable fraction.

intake of ≤ 0.5 g/day (*17*). These were a PAF of 1.6% of cancer incidence in 2005 for Japanese (*15*), 0.5% of cancer incidence in 2010 for the UK (*16*), and 14,000 cancers cases (4%) among 335,000 deaths of total cancer in 2007 for Japanese (*17*). The difference in consumption of highly salted foods, such as pickled vegetables, and stomach cancer incidence between Japanese or Asian countries and Western countries suggests the presence of a burden gap between Japan and Western countries (*7,18*). Exposure prevalence in the present study was estimated based on the intake of highly salted food rather than of salt, from the suggestion that the intake of highly salt-concentrated preserved foods confers a greater risk of stomach cancer than that of whole salt (*19*). Similarly, the 2018 WCRF report summary for stomach cancer was updated to describe exposure to highly salted food, from salt intake in the preceding 2007 report (*13*). A further strength of our present study is that exposures (mean intake) were calculated for individual survey-derived age classes, compared to a representative mean for all ages based on household surveys in the previous 1990 estimation. This improvement was permitted by a change in data collection methods in the 1995 JNHNS, and revealed higher mean intake for older age classes, with higher stomach cancer incidence and mortality (*8*).

This study has some potential limitations. In a meta-analysis of salt-preserved foods and digestive cancers,

only a single large study from Japan showed positive associations between intake of salt-preserved fish or salt-preserved fish roe and risk of colorectal cancer (*19*). Therefore, the PAF of highly salted food was calculated for stomach cancer only, which may have led to an underestimation of risk. Also, we used an RR of 1.09 per 20 g increment in this estimation based on a meta-analysis for salted vegetables in the WCRF 2018 report (*2*), because this meta-analysis included nearly all the published Japanese studies and clearly defined the exposure. A meta-analysis by Kim *et al.* of pickled vegetables and stomach cancer in Japanese and Korean populations reported an RR of 1.28. That study included observational case-control and cohort studies for highest *vs.* lowest intake in quantitative amounts or combined frequency (*20*). The WCRF 2018 report included another meta-analysis of stomach cancer estimates, with an RR of 1.70 for unspecified highly salted food, including salty confectionary and foods deep boiled in soy sauce (*tsukudani*) (*2*). PAFs of highly salted food for cancers may be slightly larger than the present results if other detailed food items were used for mean exposure calculation. Carcinogenesis by highly salted food intake may be confounded by other factors, such as H. *pylori* infection. Given that stomach cancer has a multifactorial etiology, a multivariate estimation of PAF would provide a better estimation of the burden.

Allowing for these limitations, these estimates have major implications for Japan's national health policy for cancer prevention and control strategies. In a previous study of the burden of non-communicable disease death, including death due to cardiovascular disease and cancers, assessed for dietary factors in Japan, the burden for cardiovascular disease attributable to salt intake was larger than that for cancer, with corresponding numbers of 19,000 and 14,500, respectively (*17*). In the global burden of death attributable to behavioral, environmental, occupational, and metabolic risk factors, the major portion for diet risks, and the portion due to excess salt was largest among dietary exposures such as fruit or vegetables (*21*). The current Japanese salt intake level is highest in the world. Policymakers and public health agencies must invest in and implement interventions to reduce salt intake and diets with highly salted foods to control the burden of non-communicable diseases in Japan, including cancers.

Conclusion

Our analysis provides evidence for the current burden of cancer attributable to intake of highly salted foods. In 2015, at least 22,000 cancer cases in Japan could have been prevented by avoiding highly salted foods. The results of this study may provide useful evidence to reduce the cancer burden in Japan.

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