Burden of cancer attributable to insufficient vegetable, fruit and dietary fiber consumption in Japan in 2015

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Abstract: Consumption of vegetables, fruit and dietary fiber is closely associated with cancer incidence and mortality in the population, especially under conditions of insufficient consumption. We estimated the fraction of cancer incidence and mortality in 2015 attributable to insufficient consumption of vegetables, fruit and dietary fiber in the Japanese population. Consumption of vegetables, fruit and dietary fiber in grams per day, by sex and age group, is available for 2005 from the Japanese National Health and Nutrition Survey. Optimal consumption of vegetables and fruits for this study was assumed to be over 350g and 100g/day, respectively. Optimal consumption of dietary fiber was defined by age group according to the Dietary Reference consumption for Japanese. Population attributable fractions (PAFs) were estimated for each sex and age group according to a standard formula, and aggregated to obtain the PAF among total cancer incidence and mortality. Insufficient consumption of vegetables, fruit, and dietary fiber contributed 0.2%, 0.1% and 1.0% of all cancer incidence, and 0.2%, 0.1% and 0.9% of cancer mortality, respectively. The results of this study may provide useful evidence in reducing the cancer burden attributable to insufficient consumption of vegetables, fruit and dietary fiber in Japan.

Keywords: cancer, vegetable and fruit, dietary fiber, population attributable fraction, Japan

Introduction

In 2018, the World Cancer Research Fund and American Institute for Cancer Research confirmed that consumption of non-starchy vegetables and fruit together was a probable protective factor for colorectal cancer (1). Individually, consumption of non-starchy vegetables was classified as a "limited-suggestive" protective factor for cancer of the oral cavity, pharynx, larynx, nasopharynx, esophagus, lung, and breast. Consumption of fruits was classified as a limitedsuggestive protective factor for cancer of the esophagus and lung. Consumption of citrus fruits was classified as a limited-suggestive protective factor for cancer of the stomach (1). Foods containing dietary fiber were classified as a convincing protective factor of colorectal cancer. Consumption of these plant-source foods together might substantially influence cancer incidence and mortality in the population; specifically, when consumption level is insufficient.

The population attributable fraction (PAF) for all-

cause cancer associated with insufficient vegetable and fruit consumption has previously been estimated for several countries, including Australia (2), Brazil (3), Germany (4), and the United Kingdom (5). The results indicated that while the risk attributed to insufficient consumption varied among countries, it was not low in any. Additionally, PAF for all cancer associated with inadequate dietary fiber consumption was estimated for Australia (2) and Germany (4). Because dietary consumption is a modifiable factor, identifying the proportion of cancers attributed to this factor could have important implications for cancer prevention strategies.

We previously reported that the fractions of cancer attributable to insufficient consumption of vegetables and fruit in 2005 in Japan were 0.4% and 0.8%, respectively (6). PAFs were the same for incidence and mortality. In the present report, we updated this to the fraction of cancer incidence and mortality in Japan for 2015, and also estimated the fraction attributed to dietary fiber consumption.

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Materials and Methods

Cancers associated with insufficient vegetables, fruit and dietary fiber

The WCRF/AICR classified consumption of non-starchy vegetables and fruits together as a probable protective factor for colorectal cancer (1). Individually, consumption of non-starchy vegetables was classified as a limited-suggestive protective factor for cancer of the oral cavity, pharynx, larynx, nasopharynx, esophagus, lung, and breast. Consumption of fruits was classified as a limited-suggestive protective factor for cancer of esophagus and lung. Consumption of citrus fruits was classified as a limited-suggestive protective factor for cancer of the stomach. In addition, non-starchy vegetables and fruit in the aggregate were classified as a probable protective factor for cancers.

Foods containing dietary fiber were classified as probable protective factors of colorectal cancer (1). Therefore, we applied the target cancers associated with vegetables, fruit and dietary fiber identified by this evaluation, namely those which showed sufficient evidence for a positive association with vegetables, fruit and dietary fiber, and for which relative risk estimates in Japan were available, namely stomach, lung and colorectal cancer.

Theoretical minimum risk exposure level

The optimal consumption of vegetables and fruits in Japan for this purpose was defined as over 350 and 100 g/day, respectively. These values were based on goals established for the National Health Promotion Movement in the 21^{st} Century (7). The optimal consumption of dietary fiber was defined by age group according to the Dietary Reference Consumption for Japanese (8).

Prevalence of vegetables, fruit and dietary fiber consumption

The latent period - the interval between "exposure" to insufficient consumption and the increase in risk of cancer - is unknown. For the purpose of this study, the latent period between being "exposed" to insufficient consumption and the consequent increase in cancer was assumed to be 10 years. The 2015 fraction of avoidable cancers calculated for this study is therefore based on an estimate of insufficient consumption in 2005.

The data on vegetable, fruit and dietary fiber consumption by sex and age group were derived from the Japanese National Health and Nutrition Survey (JNHNS) from 2005 (9), taking the 3-year mean of individual year data for 2004-2006 obtained from the Ministry of Health, Labour, and Welfare, Japan with permission.

Sex and age group-specific consumption of vegetables, fruit and dietary fiber in g/day by the

Japanese population in 2005, as derived from the JNHNS, are shown in Table 1. The optimal consumption levels and the deficit from each for the estimation of PAF are given by sex and 5-year age group.

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 (10). We used an age and period spline model. This type of model is used for short-term projections of cancer incidence in Japan (11). 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, 10^{th} edition (ICD-10), using the morphology code of the International Classification of Disease for Oncology, 3^{rd} edition (ICD-O-3).

The data on cancer mortality statistics from 2015 were based on the vital statistics of Japan (12). We obtained sex- and age-specific mortality data by cause of death from available data sources from the Health, Labour, and Welfare Statistics Association (13), and used 4-digit ICD-10 codes to classify the cause of death.

Estimation of relative risks

Risk estimates for the association between site-specific cancer and consumption of vegetable, fruit and dietary fiber are summarized in Table 2. We used relative risk of the highest consumption (quartile or quintile) for the point estimate of risk, with the lowest respective category (first quartile or quintile) as reference. Relative risk for the association between stomach cancer and vegetable consumption was sourced from a pooled analysis of four Japanese cohorts (14). Because a decrease in risk with higher consumption of vegetables was observed only for the distal subsite of stomach cancer, we limited this research to distal stomach cancer only, which nevertheless accounted for 95% of total stomach cancer cases. Relative risk for the association between fruit consumption and lung cancer was sourced from a pooled analysis of four Japanese cohorts (15). Relative risk for the association between highest consumption of dietary fiber and colon cancer was sourced from a published analysis by Wakai et al. (16) using the method by Levin et al. (17). The risk for a deficit of one gram in decreased consumption was calculated using the following formula:

 $Risk = exp^{[\ln(risk \text{ per gram of deficit}) \times average exposure level]}$

where gram of deficit is 3-year mean of individual data by age group derived from the JNHNS.

Estimation of population attributable fractions (PAFs)

Age at exposure (2005) co	Mean onsumption (g/day)	Optimal consumption	Deficit from	Mean					
		(g/day)	optimal consumption (g/day)	consumption (g/day)	Optimal consumption (g/day)	Deficit from optimal consumption (g/day)	Mean consumption (g/day)	Optimal consumption (g/day)	Deficit from optimal consumption (g/day)
Men									
0 - 4	137	350	213	109	100	0	8.4	-	0.0
5 - 9	196	350	154	108	100	0	11.9	11.5	0.0
10 - 14	258	350	92	108	100	0	14.9	15.0	0.1
15 - 19	253	350	97	110	100	0	14.0	19.5	5.5
20 - 24	240	350	110	72	100	28	12.5	20.0	7.5
25 - 29	268	350	82	68	100	32	13.5	20.0	6.5
30 - 34	276	350	74	53	100	47	13.6	20.0	6.4
35 - 39	255	350	95	52	100	48	13.1	20.0	6.9
40 - 44	260	350	90	67	100	33	13.5	20.0	6.5
45 - 49	284	350	66	79	100	21	14.4	20.0	5.6
50 - 54	296	350	54	80	100	20	14.8	20.0	5.2
55 - 59	316	350	34	117	100	0	16.4	20.0	3.6
60 - 64	337	350	13	144	100	0	17.6	20.0	2.4
65 - 69	336	350	13	156	100	0	17.7	20.0	2.3
70 - 74	329	350	21	163	100	0	17.6	19.0	1.4
≥ 75	307	350	43	150	100	0	16.3	19.0	2.7
Women	507	550	15	150	100	0	10.5	19.0	2.,
0 - 4	137	350	213	114	100	0	8.2	-	0.0
5 - 9	195	350	155	111	100	0	11.5	11.0	0.0
10 - 14	261	350	89	115	100	0	14.3	14.5	0.0
15 - 19	245	350	105	109	100	0	12.9	17.5	4.6
20 - 24	231	350	119	82	100	18	12.3	18.0	5.7
25 - 29	243	350	107	79	100	21	12.5	18.0	5.3
30 - 34	237	350	113	79	100	21	12.7	18.0	5.4
35 - 39	240	350	110	73	100	27	12.0	18.0	5.3
40 - 44	240	350	110	86	100	14	12.7	18.0	5.0
45 - 49	240	350	76	110	100	0	13.0	18.0	3.3
43 - 49 50 - 54	292	350	58	137	100	0	14.7	18.0	2.4
50 - 54 55 - 59	312	350	38	162	100	0	15.0	18.0	1.3
60 - 64	312	350	38	172	100	0	17.3	18.0	0.7
65 - 69	322	350	28	172	100	0	17.5	18.0	0.7
03 - 09 70 - 74	313	350	28 37	167	100	0	17.5	18.0	0.3 2.4
>70 - 74 ≥75	285	350	57 65	153	100	0	15.2	19.0	2.4

Table 1. Sex and age group-specific consumption of vegetables, fruit and dietary fiber in g/day in Japan in 2005

Table 2. Summary of risk estimates for the association between consumption of vegetables, fruit, and dietary fiber and site-specific cancer

Cancer site	Studies	Reference group	Estimated risk for the highest (quartile of quintile) consumption		
Stomach	Shimazu et al. (2014) (14)				
Men		First quintile	0.78 (0.63 - 0.97)		
Women		First quintile	0.89 (0.62 - 1.29)		
Lung	Wakai et al. (2015) (15)	*			
Men		First quintile	0.88 (0.66 - 1.16)		
Women		First quintile			
Colon	Wakai et al. (2007) (16)	*			
Men		First quartile	0.52 (0.28 - 0.96)		
Women		First quartile	0.64 (0.36 - 1.13)		
	Stomach Men Uung Men Women Colon Men	Stomach Shimazu et al. (2014) (14) Men	Stomach Shimazu et al. (2014) (14) Men First quintile Women First quintile Lung Wakai et al. (2015) (15) Men First quintile Women First quintile Colon Wakai et al. (2007) (16) Men First quartile		

PAFs were calculated for each sex and age group according to the formula:

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

The number of attributable cancers was then totaled

across all sex and age categories to show a percentage of the total number of all incident cases and deaths of cancer in Japan in 2015.

Results

Sex and age group-specific consumption of vegetables,

fruit and dietary fiber among Japanese people in 2005 is shown in Table 1. The deficit from optimal consumption to mean vegetable intake was high in younger generations (up to 40-44 years-old) and decreased for both sexes thereafter. A similar tendency was seen for fruit, but the decrease was observed slightly later for men (55-59 years-old). The deficit from optimal consumption to mean dietary fiber intake was highest among 20-24-year-olds.

Risk estimates for the association between consumption of vegetables, fruit, and dietary fiber and site-specific cancer in Japan are summarized in Table 2. For vegetables, the estimated risk of stomach cancer was 0.78 for men and 0.89 for women. We used these values to calculate PAF. For fruit, the estimated risk of lung cancer was 0.88 for men and women; while for dietary fiber, the estimated risk of colon cancer was 0.52 for men and 0.64 for women.

The estimated PAF of cancer incidence and mortality in 2015 attributed to insufficient vegetable, fruit and dietary fiber consumption in Japan is summarized in Table 3. Insufficient consumption of vegetables was attributed to 1.7% (1.8% in men and 1.3% in women) of gastric cancer incidence, and to 0.2% (0.3% in men and 0.1% in women) of total cancer incidence. Insufficient consumption of fruits was attributed to 0.5% (0.7% in men and 0.2% in women) of lung cancer incidence, and to 0.1% (0.1% in men and 0.02% in women) of total cancer incidence. Insufficient consumption of vegetables was attributed to 1.3% (1.3% in men and 1.2% in women) of mortality from gastric cancer, and to 0.2% (0.2% in men and 0.1% in women) of total cancer mortality. Insufficient consumption of fruits was attributed to 0.4% (0.5% in men and 0.1% in women) of mortality from lung cancer, and to 0.1% (0.1% in men and 0.01% in women) of total cancer mortality.

Insufficient consumption of dietary fiber was attributed to 10.5% (13.6% in men and 7.1% in women) of colon cancer incidence, and to 1.0% (1.2% in men and 0.8% in women) of total cancer incidence. It was

Total cancer (C00 - C96)

attributed to 10.2% (12.4% in men and 7.9% in women) of mortality from colon cancer, and to 0.9% (1.0% in men and 0.9% in women) of total cancer mortality.

Detailed results for each cancer, sex, and agegroup are shown for insufficient vegetable and fruit consumption in Tables S1-S2 (online data, *https://www. ghmopen.com/site/supplementaldata.html?ID=36*) and for insufficient fiber consumption in Tables S3-S4 (online data, *https://www.ghmopen.com/site/ supplementaldata.html?ID=36*).

Discussion

In this report, we estimated the proportion and absolute number of cancer incidence and mortality in Japan in 2015 that was attributable to insufficient vegetable, fruit and dietary fiber consumption. According to the results from a large prospective cohort study or pooled/ meta-analysis of cohort studies in Japan, insufficient consumption of vegetables, fruit and dietary fiber was attributed to stomach cancer, lung cancer, and colon cancer, respectively. The results indicate that insufficient consumption of vegetables and fruit contributed 0.1-0.2% of both total cancer incidence and mortality. In addition, insufficient dietary fiber consumption contributed approximately 1% of total cancer incidence and mortality.

In a previous study which estimated the effects of 16 risk factors on cause-specific mortality (18), the number of cancer deaths attributable to low fruit and vegetable consumption was 3.8 in thousands, similar to that of our study. In that study, the risk of low consumption of vegetables and fruit was relatively minor, at only one-third that of high dietary sodium consumption, the highest dietary risk factor for cancer in Japan. Further, low dietary fiber consumption was not included.

In contrast, several previous estimates of the fraction of cancer attributable to insufficient consumption of vegetables, fruits and dietary fiber have been published

1.0

0.9

0.9

τ.	Incidence			Mortality		
Items –	Men	Women	Both sexes	Men	Women	Both sexes
Insufficient vegetable consumption						
Stomach (C16)	1.8	1.3	1.7	1.3	1.2	1.3
Total cancer (C00 - C96)	0.3	0.1	0.2	0.2	0.1	0.2
Insufficient fruit consumption						
Lung (C33 - C34)	0.7	0.2	0.5	0.5	0.1	0.4
Total cancer (C00 - C96)	0.1	0.0	0.1	0.1	0.0	0.1
Insufficient vegetable and fruit consumption						
Total cancer (C00 - C96)	0.4	0.2	0.3	0.3	0.1	0.2
Insufficient dietary fiber consumption						
Colon (C18)	13.6	7.1	10.5	12.4	7.9	10.2

Table 3. Proportion (%) of cancer in 2015 attributable to insufficient consumption of vegetable, fruit, and dietary fiber in Japan

1.0

0.8

1.2

from Western countries. PAFs of all cancer attributed to vegetables and fruits combined for all cancer cases were 4.7% in the UK in 2010 (5) and 2.1% in Germany in 2018 (4). In Australia in 2010, PAFs of all cancer attributed to insufficient fruits and vegetables were 1.4% and 0.3%, respectively (2). In France, PAFs of all cancer in 2015 attributed to insufficient fruits and vegetables were 1.4% and 0.5%, respectively (19). Compared to these percentages, the PAF of all cancer in Japan in the present study is rather low.

According to the National Health and Nutrition Survey, average consumption of vegetables by Japanese increased until the mid-1990s, and has since then maintained a steady level between 260-300g/day for about two decades (20). On the other hand, stomach cancer decreased rapidly during this period, both in incidence and mortality. If these trends continue, the burden of all cancer attributed to insufficient consumption of vegetables in the future will be even lower than now. In contrast, average consumption of fruit in Japan decreased drastically up to the 2000s, to around 120g/day, and has since continued to decrease slowly (20). Considering the increasing trend of lung cancer in Japanese women, all cancers attributed to the low consumption of fruit might increase in the future. Consumption of dietary fiber, on the other hand, has remained at approximately 15g/day for the past two decades (20). Foods which make the greatest contribution to the total consumption of dietary fiber include not only fruits and vegetables, but also grains. Since the incidence of colon cancer is increasing in Japanese women, all cancers attributable to insufficient dietary fiber consumption might increase in the future.

There are a few limitations to this study. First, the methodology used to estimate dietary consumption differed. We adopted the mean consumption levels from the results of 1-day dietary records collected in the National Nutrition Survey to take advantage of representative data. Among the various methods available, dietary records also have the advantage of accurately estimating the quantity of consumption. On the other hand, relative risks were estimated using FFQs, which are designed for ranking by consumption level. Moreover, levels of consumption in categories such as quintiles may vary in the meta- and pooled analyses. Our present analysis was based on the hypothesis of a dose-response association between exposure and outcome; however, the differences in cutoff point caused by the different methods might have resulted in error if this hypothesis was not applicable to dietary consumption. Secondly, the RR used to calculate the PAF for insufficient dietary fiber consumption was derived from a single study. This may have led to the over- or underestimation of risk. When additional data are available, re-calculation of the PAF using RR from a meta-analysis or pooled analysis will be essential for

updating the evidence.

Despite the limitations, these estimates have major implications for Japan's national health policy for cancer prevention and control strategies.

Conclusion

Our analysis provides evidence for the current burden of cancer attributable to insufficient consumption of vegetables, fruit and dietary fiber. Insufficient consumption of vegetables, fruit, and dietary fiber contributed 0.2%, 0.1% and 1.0% of all cancer incidence, and 0.2%, 0.1% and 0.9% of cancer mortality, respectively. These results may provide useful evidence in efforts to reduce the cancer burden in Japan.

Funding: This study was supported by JSPS KAKENHI Grant Number 16H05244.

Conflict of Interest: The authors have no conflicts of interest to disclose.

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Received June 12, 2021; Revised November 17, 2021; Accepted December 7, 2021.

Released online in J-STAGE as advance publication December 11, 2021.

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