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BRIEF REPORT

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Burden of cancer attributable to excess red and processed meat consumption in Japan in 2015

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Abstract: The International Agency for Research on Cancer has evaluated red meat as probably carcinogenic and processed meat as carcinogenic to humans. The World Cancer Research Fund and American Institute for Cancer Research concluded there is convincing evidence that consumption of processed meat increases the risk of colorectal cancer. We estimated the number and fraction of cancer incidence and mortality in 2015 that could be attributed to excess red and processed meat consumption in 2005 among the Japanese population. Data on the consumption of red and ptocessed meat, in g/day, by sex and age group, is available for 2005 from the Japanese National Health and Nutrition Survey. For the present study, the optimal consumption of red meat in Japan was considered as less than 500 g/week, or 71.4 g/day, and 0 g/day for processed meat. Population attributable fractions (PAFs) were calculated for each sex and age group according to a standard formula, and aggregated to obtain the PAF among total cancer incidence and mortality. We found that 0.01% and 0.4% of cancer incidence was attributable to red and processed meat consumption, respectively, while 0.0002% and 0.3% of cancer mortality was attributable to red meat and to processed meat consumption. Based on the current evidence, monitoring red and processed meat consumption may not contribute to reducing cancer incidence and mortality in Japan.

***Keywords*:** cancer, red meat, processed meat, population attributable fraction, Japan

Introduction

Lifestyle factors, including diet, are key determinants of cancer risk (*1*). The International Agency for Research on Cancer (IARC) has rated red meat as probably carcinogenic (Group 2a) and processed meat as carcinogenic to humans (Group 1) (*2*). An expert report by the World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR) titled Food, Nutrition, Physical Activity and Prevention of Cancer concluded there was strong evidence that the consumption of processed meat - defined as meat preserved by smoking, curing, salting, or the addition of chemical preservatives - and of red meat increase the risk of colorectal cancer (*3*). The report recommended limiting weekly consumption to no more than about three portions (350-500 g/week). It also reported that consumption of processed meat was associated with a limited-suggestive increase in risk for nasopharynx, esophagus, lung, stomach, and pancreatic cancer (*3*).

Potential mechanisms by which red and processed meat may effect cancer risk derive from high cooking temperatures: heme iron may catalyze lipid peroxidation, leading to tissue damage (*4,5*) and the formation of carcinogenic *N*-nitroso compounds (*6-8*). Cooking meat at high temperatures also induces the formation of heterocyclic aromatic amines and polycyclic aromatic hydrocarbons, which might also contribute to carcinogenesis of various sites (*9-12*).

Globally, red and processed meat have been linked to an increased risk of colorectal cancer incidence (*3,13*). National-level estimates of the burden for all cancers due to red and processed meat were 2.3% in Australia (*14*), 2.4% in Germany (*15*), and 2.7% in the UK (*16*). In the Japanese setting, red meat was not included in former studies of PAF for cancer (*17*) or non-communicable diseases (*18*) due to relatively low consumption compared to Europe and the US. The 2013 Japanese National Health and Nutrition Survey (JNHNS) (*19*) reported that an individual's average

daily red and processed meat consumption was 63 g and 13 g, respectively - among the lowest in the world (*19-21*). The Japan Public Health Center-based Prospective Study (JPHC Study) (*13*) found no significant association between processed meat consumption and risk of colorectal cancer for Japanese men and women, but did find a significantly increased risk for red meat in the highest level consumption group, suggesting the possibility of a risk difference between Japan and Europe or North America. A Japanese meta-analysis reported a significant risk of colorectal cancer (*22*) with red meat and a non-significant risk with processed meat, providing the rationale for the present study.

In this report, we estimated the number and fraction of cancer incidence and mortality in 2015 that could be attributed to excess red and processed meat consumption in 2005 among the Japanese population.

Materials and Methods

Cancers associated with red and processed meat

IARC rated red meat as probably carcinogenic (Group 2a) and processed meat as carcinogenic to humans (Group 1) (*2*). Additionally, the WCRF and AICR concluded there was strong evidence that the consumption of processed meat, as well as red meat, increases the risk of colorectal cancer (*3*). In the present study, therefore, we evaluated target cancers identified by this evaluation to be associated with red and processed meat. We included colorectal cancer, which showed sufficient evidence for a positive association with red and processed meat and for which relative risk estimates were available in Japan.

Theoretical minimum risk exposure level

For the purpose of this study, we considered the optimal consumption of red meat in Japan - defined as beef, pork, ham, sausage, other animal meat such as mutton, and organ meat such as tripe - was less than 500 g/week. In the present study, 1/7 of 500 g/week, or 71.4 g/day, was adopted as a theoretical minimum risk exposure level. In addition, we considered the optimal consumption of processed meat, defined as ham and sausage, as 0 g/day (*23*).

Prevalence of excess red and processed meat estimates

The latent period, as in the interval between "exposure"to red and processed meat and the increase in the risk of cancer of the colon is unknown. The average follow-up period of the six cohorts included in the systematic review by Pham *et al.* (*22*) was 13 years. For the present study, we assumed that a mean latency of 10 years would be sufficient, and therefore calculated the 2015 fraction of avoidable cancers due to red and processed meat consumption in 2005.

The data on red and processed meat consumption by sex and age group were derived from the JNHNS from 2005 (*24*). For this purpose, we used the 3-year mean of individual datas for 2004-2006, obtained from the Ministry of Health, Labour, and Welfare, Japan, with permission.

Cancer incidence and mortality in Japan in 2015

We estimated cancer incidence data in 2015 using the annual estimate of cancer incidence in 2013 by the Monitoring of Cancer Incidence project in Japan (*25*). We used an age and period spline model, a type used for short-term projection of cancer incidence (*26*). The sex- and age-specific incidence data for target cancers were coded using the International Statistical Classification of Diseases and Related Health Problems, 10th edition (ICD-10), with the morphology code of the International Classification of Disease for Oncology, 3rd edition (ICD-O-3).

The data on total and colon cancer mortality statistics from 2015 were obtained from Japan's vital statistics (*27*). We obtained sex- and age-specific mortality data by cause of death from available data sources from the Health, Labour, and Welfare Statistics Association (*28*). Similar to the cancer incidence data, we used the 4-digit ICD-10 codes to classify the cause of death.

Estimation of relative risk

The relative risk (RR) for colorectal cancer associated with consumption of red and processed meat was sourced from a meta-analysis of Japanese cohort and case-control studies (Table 1) (*22*). First, colon and rectal cancers were considered separately. However, rectum was excluded as the RR was lower than 1.00. Consequently, we estimated PAF for only colon cancer applying the meta-analysis RR value of cohort studies. We used estimated risk (95% confidence interval) of colon cancer for the highest quintile of consumption by 1.20 (1.00-1.44) and 1.18 (0.92-1.53) for red meat and processed meat, respectively (*22*). Increase in the risk by an increment of 1 g/day of red and processed meat consumption, respectively, was calculated, based on an assumption that the relationship between exposure and colon cancer risk is log-linear. The following equation was used for red and processed meat consumption, respectively, and the risk of colon cancer:

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

Estimation of population attributable fractions (PAFs)

PAF was calculated for each sex and age group according to the formula:

Table 1. Summary of risk estimates for the association between red and processed meat consumption and site-specific cancer

Exposure	Theoretical minimum risk exposure level	Cancer type	Estimated risk for the highest quintile of consumption	*Ref.*
Red meat	< 500 g/week or < 71.4 g/day	Colon	1.20 (1.00 - 1.44)	Pham *et al.* (*22*)
Processed meat	0 g/day	Colon	1.18 (0.92 - 1.53)	Pham *et al.* (*22*)

Table 2. Sex- and age-group-specific consumption of red and processed meat, in g/day in Japan in 2005

Age at exposure (2005)	Red meat		Processed meat	
	Mean consumption (g/day)	Excess from 71.4 g/day	Mean consumption (g/day)	Excess from 0 g/day
Men				
0 - 4	34.93	0.00	10.3	10.3
5 - 9	54.66	0.00	13.0	13.0
10 - 14	79.99	8.56	15.8	15.8
15 - 19	106.92	35.49	22.5	22.5
20 - 24	88.76	17.33	16.9	16.9
25 - 29	90.13	18.70	18.1	18.1
30 - 34	88.87	17.44	17.9	17.9
35 - 39	81.45	10.03	14.9	14.9
40 - 44	80.58	9.15	17.0	17.0
45 - 49	76.47	5.04	15.0	15.0
50 - 54	69.84	0.00	12.3	12.3
55 - 59	67.06	0.00	12.5	12.5
60 - 64	59.93	0.00	11.0	11.0
65 - 69	48.35	0.00	8.7	8.7
70 - 74	43.69	0.00	7.8	7.8
≥ 75	34.42	0.00	7.0	7.0
Total	67.54	0.00	13.3	13.3
Women				
0 - 4	33.44	0.00	9.7	9.7
5 - 9	50.61	0.00	11.8	11.8
10 - 14	65.68	0.00	14.3	14.3
15 - 19	78.25	6.82	18.4	18.4
20 - 24	61.06	0.00	13.3	13.3
25 - 29	60.79	0.00	12.9	12.9
30 - 34	58.12	0.00	13.5	13.5
35 - 39	58.51	0.00	12.4	12.4
40 - 44	60.00	0.00	13.3	13.3
45 - 49	56.96	0.00	11.5	11.5
50 - 54	49.84	0.00	10.1	10.1
55 - 59	49.81	0.00	10.3	10.3
60 - 64	41.82	0.00	7.6	7.6
65 - 69	37.98	0.00	7.5	7.5
70 - 74	36.43	0.00	7.5	7.5
≥ 75	27.93	0.00	5.3	5.3
Total	49.53	0.00	10.5	10.5

Red meat: beef, pork, ham, sausage, other meat such as mutton, and organ meat; processed meat: ham and sausage consumption; and excess, reported as mean g/day.

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

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

Results and Discussion

Table 2 shows the age- and sex-stratified red and processed meat mean consumption, in g/day, and the excess over 71.4 g/day for red meat and over 0 g/day for processed meat for the Japanese population, derived from the JNHNS in 2005. Red and processed meat consumption in all categories peaked in the

Table 3. Proportion (%) of cancer in 2015 attributable to excess red and processed meat consumption in Japan

Factors	Incidence			Mortality		
	Men	Women	Both sexes	Men	Women	Both sexes
Red meat						
Colon (C18)	0.1	0.0	0.1	0.1	0.0	0.0
Total cancer (C00-C96)	0.0	0.0	0.0	0.0	0.0	0.0
Processed meat						
Colon (C18)	4.3	3.3	3.8	4.0	3.0	3.0
Total cancer (C00-C96)	0.4	0.4	0.4	0.3	0.3	0.3

15-19-year age group. In men, the trend of excess consumption continued until age 49 for red meat and continued until the oldest age group for processed meat. Japanese women overall consumed less red meat than men. While only 15-19-year-old women consumed red meat in excess, women of all age categories consumed processed meat in excess.

The estimated PAF of cancer incidence and mortality in 2015 attributed to red and processed meat consumption in Japan is summarized in Table 3.

Table S1 (online data, *https://www.ghmopen.com/site/supplementaldata.html?ID=39*) shows the PAF of cancer incidence in Japan in 2015 due to red and processed meat consumption in 2005. Excess red meat consumption was attributable to 0.01% of total cancer incidence in Japan (0.01% in men and 0.0001% in women). Excess processed meat consumption attributed to 0.4% of total cancer incidence in Japan (0.4% for both men and women). Table S2 (online data, *https://www.ghmopen.com/site/supplementaldata.html?ID=39*) shows the PAF of cancer mortality in 2015 attributed to red and processed meat consumption in Japan in 2005, where excess red meat consumption attributed to 0.0002% of total cancer mortality (0.01% in men and 0.0002% in women) and the excess processed meat consumption attributed to 0.3% of total cancer mortality (0.3% for both men and women).

Additionally, using a similar approach as an Australian study (*14*), we performed a sensitivity analysis by changing the cut-off to 0 g/day instead of 71.4 g/day for red meat consumption. The PAFs were 0.6% (0.6% for both men and women) for cancer incidence and 0.5% (0.5% in men and 0.6% women) for cancer mortality.

In summary, our study suggests that 0.01% and 0.4% of cancer incidence may be attributable to red and processed meat consumption, respectively, while 0.0002% and 0.3% of cancer mortality may be attributable to red meat and to processed meat consumption, respectively. The results do not greatly differ from the theoretical minimum risk exposure level of zero. Regarding RR, an IARC monograph reported 17% increased risk for every 100 g/portion of red meat eaten daily (*2*). This is not substantially different from the RR used in this study (13% and 14% for every 100 g of meat consumption among men and women, respectively), based on a meta-analysis of Japanese studies (*22*).

Colorectal cancer incidence and mortality trends in Japan follow a different pattern compared to Europe and the United States (*27*). This difference may be due higher consumption of fish and less meat among Japanesean (*21*).

A recent 2016 review of cancer attributable to modifiable factors by Whiteman *et al.* (*29*) provides an insufficient overview of the global situation for red and processed meat, and includes only two reports, from Australia (*14*) and the UK (*16*). In the UK study, the theoretical minimum risk exposure level for red meat was nil (*16*), and thus was stricter than our study cut off. The study reported that 2.7% of all cancers were attributable to red and processed meat. The Australian study found men aged 19 years and older that consumed 121 g/day of red meat and 64 g/day of processed meat accounted for 2.3% of all cancers (*14*), with a theoretical minimum risk exposure level of zero. In addition to these studies, a 2018 German study reported that 2.4% of all cancers were attributable to red meat, with a theoretical minimum risk exposure level of 500 g red meat/week and 0 g processed meat/week (*15*). Red and processed meat is not as popular or heavily consumed in Japan as in Western countries, resulting in the low attributed PAF in Japan. Therefore, policies to control red and processed meat consumption will likely not be effective to reduce cancer incidents and mortality in Japan.

Conclusion

Our analysis provides evidence for the relatively small burden of cancer attributable to red and processed meat consumption in Japan. From the results, 0.01% and 0.4% of cancer incidence, and 0.0002% and 0.3% of cancer mortality is attributable to red and processed meat consumption, respectively. These findings may provide critical evidence for the priority ranking of programs aimed to reduce the cancer burden in Japan.

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