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Burden of cancer attributable to excess bodyweight and physical inactivity in Japan in 2015

Mayo Hirabayashi[1], Sarah Krull Abe[1], Norie Sawada[2], Eiko Saito[3], Megumi Hori[3], Kota Katanoda[3], Tomohiro Matsuda[4], Manami Inoue[1,2,*]; the Cancer PAF Japan Collaborators

[1] Division of Prevention, Center for Public Health Sciences, National Cancer Center, Tokyo, Japan;
[2] Division of Cohort Research, Center for Public Health Sciences, National Cancer Center, Tokyo, Japan;
[3] Division of Cancer Statistics Integration, Center for Cancer Control and Information Services, National Cancer Center, Tokyo, Japan;
[4] National Cancer Registry Section, Center for Cancer Registries, Center for Cancer Control and Information Services/Office of International Affairs, Strategic Planning Bureau National Cancer Center, National Cancer Center, Tokyo, Japan.

Abstract: Overweight and obesity are known contributors to many non-communicable diseases, including cancer, and affect over one-tenth of the global population. One way to maintain a healthy weight and reduce the risk for cancer is through increased physical activity. We estimated the fraction of cancer incidence and mortality in 2015 attributable to excess bodyweight as well as lack of physical activity among the Japanese population. The optimal body-mass index (BMI) for the purposes of this study was determined to be less than 23 kg/m^2. Mean BMI for each sex and age group was calculated using measured weight and height data extracted from the 2005 Japanese National Health and Nutrition Survey (JNHNS). For the data on physical activity, we extracted the answers from the same survey from a question regarding whether the respondent did regular exercise. Population attributable fractions (PAFs) for each cancer positively associated with excess bodyweight - esophageal adenocarcinoma, stomach (cardia), colorectum, liver, gallbladder, pancreas, female breast (pre- and post- menopausal), ovary, endometrium, advanced prostate and kidney - and for those positively associated with physical inactivity - colorectum, female breast and endometrium - were calculated for each sex and age group and aggregated to obtain the PAF among total cancer incidence and mortality. Excess bodyweight was attributable to 0.7% of cancer incidence and mortality, while lack of regular exercise was attributable to 1.3% of cancer incidence and 0.8% of cancer mortality. Around 1% of cancer incidence and mortality in Japan in 2015 are attributable to excess bodyweight and physical inactivity.

***Keywords*:** cancer, excess bodyweight, physical inactivity, population attributable fraction, Japan

Introduction

The World Health Organization (WHO) defines overweight (body-mass index (BMI) greater than or equal to 25) and obesity (BMI 30 or over) as abnormal or excessive fat accumulation that may impair health (*1*). Since 1975, worldwide obesity has nearly tripled. In 2016, more than 1.9 billion adults aged 18 years or over were overweight- of these, over 650 million (13% of the global population) were obese (*1*). Overweight and obesity are known to be major risk factors for non-communicable diseases (*1*). In 2016, the International Agency for Research on Cancer (IARC) reaffirmed that overweight and obesity increase risk for cancers of the colon, rectum, gastric cardia, liver, gallbladder, pancreas, kidney, and esophageal adenocarcinoma, with positive dose-response relationships (*2*). The same report also noted positive associations between adult obesity and postmenopausal breast cancer and endometrial cancer (*2*).

The fundamental cause of excess bodyweight is an energy imbalance between calories consumed and calories expended. One of the ways to maintain a healthy bodyweight is through exercise. Regular physical activity is essential for optimal health. Exercising regularly has significant benefits, even at a modest level, including lower cancer incidence (*3*). The World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR) have reported that there is a probable association between physical inactivity and risk of cancers of colon, breast and endometrium (*3*).

Here, we estimated the fraction of cancer incidence and mortality in 2015 attributable to excess bodyweight and physical inactivity in the Japanese population.

Materials and Methods

Cancers associated with excess bodyweight and physical inactivity

For the purposes of this study, we selected cancer sites associated with overweight and obesity, and physical activity, for which IARC or WCRF/AICR found sufficient evidence to indicate a positive association, and with data available on relative risk. The cancer sites included in this study are the esophagus (adenocarcinoma), stomach (cardia), colorectum, liver, gallbladder, pancreas, breast, endometrium, ovary, prostate (advanced), and kidney for excess bodyweight; and colorectum, breast, and endometrium for physical inactivity.

Prevalence of excess bodyweight and physical inactivity estimates

Data on the prevalence of excess bodyweight were obtained from the Japanese National Health and Nutrition Survey (JNHNS) from 2005 (*4*). This survey reports mean BMI by age group and sex. BMI was calculated using measured weight and height in kg/m^2. Table 1 shows the sex- and age-group-specific prevalence of excess bodyweight in Japanese derived from the 2005 JNHNS. In 2005, mean BMI slightly exceeded 23 in men aged between 30 and 70 and women aged between 55 and 74.

Similarly, we used data from the 2005 JNHNS to determine physical activity level in the Japanese population. The survey provides data on the proportion of people (by sex and age group) who answered "yes" to a question regarding whether they do regular exercise. Table 2 shows the sex- and age-group-specific prevalence derived from 2005 JNHNS of those who do regular exercise in Japanese. Among men, the proportion who answered yes to whether they got regular exercise was highest in the 70-74 years age group, but in the 65-69 years age group among women.

The duration of the latent period between 'exposure' to excess bodyweight, physical inactivity and an appropriate increase in the risk of cancers has not been well established. We assumed that 10 years would be sufficient time for latency between exposure and outcome, and therefore examined the effects of cancers occurring in 2015 due to sub-optimal bodyweight and physical activity in the year 2005.

Theoretical minimum risk exposure level

The optimal BMI in Japan for the purposes of this study was determined to be less than 23 kg/m^2. Because mean BMI across all sex- and age-specific categories was below 25 kg/m^2, the PAF of excess body weight would be 0 if the definition of excess overweight were BMI ≥ 25 kg/m^2. Moreover, there has been controversy when applying international criteria for obesity to Asian populations; in response, the WHO expert consultation recommended a new overweight category of BMI ≥ 23 kg/m^2 and obesity of BMI ≥ 25 kg/m^2 (*5*). Accordingly, as a practical solution to estimating the PAF of excess bodyweight in a Japanese population, we defined the optimal BMI as less than 23 kg/m^2. The optimal amount of physical exercise in Japan for the purposes of this study was defined as regular exercise.

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 (*6*) by an age and period spline model. This type of model is used for short-term projections of cancer incidence in Japan (*7*).

Table 1. Sex- and age-group-specific prevalence of excess bodyweight in Japanese in 2005

Men			Women		
Age at exposure (2005)	Average body-mass index (BMI) (kg/m^2)	Excess from BMI 23 kg/m^2	Age at exposure (2005)	Average body-mass index (BMI) (kg/m^2)	Excess from BMI 23 kg/m^2
0 - 4	16.0	0	0 - 4	15.8	0
5 - 9	16.2	0	5 - 9	15.9	0
10 - 14	18.6	0	10 - 14	18.6	0
15 - 19	21.3	0	15 - 19	20.9	0
20 - 24	22.0	0	20 - 24	20.4	0
25 - 29	22.9	0	25 - 29	20.6	0
30 - 34	23.4	1.43	30 - 34	21.1	0
35 - 39	23.7	0.73	35 - 39	21.5	0
40 - 44	24.0	1.01	40 - 44	22.2	0
45 - 49	24.1	1.05	45 - 49	22.6	0
50 - 54	23.9	0.90	50 - 54	22.9	0
55 - 59	23.6	0.61	55 - 59	23.1	0.10
60 - 64	23.8	0.77	60 - 64	23.3	0.29
65 - 69	23.8	0.83	65 - 69	23.6	0.57
70 - 74	23.5	0.49	70 - 74	23.2	0.21
≥ 75	22.7	0	≥ 75	22.9	0

Data source: The National Health and Nutrition Survey, Japan, 2005.

Table 2. Sex- and age-group-specific prevalence of Japanese who do regular exercise, 2005

Men		Women	
Age at exposure (2005)	Proportion of those who answered "yes" to regular exercise in the population (%)	Age at exposure (2005)	Proportion of those who answered "yes" to regular exercise in the population (%)
0 - 4	0.0	0 - 4	0.0
5 - 9	0.0	5 - 9	0.0
10 - 14	0.0	10 - 14	0.0
15 - 19	0.0	15 - 19	0.0
20 - 24	24.5	20 - 24	17.6
25 - 29	19.9	25 - 29	17.3
30 - 34	15.4	30 - 34	14.2
35 - 39	18.0	35 - 39	17.3
40 - 44	19.2	40 - 44	17.0
45 - 49	20.7	45 - 49	25.4
50 - 54	20.4	50 - 54	26.9
55 - 59	24.9	55 - 59	30.6
60 - 64	38.8	60 - 64	37.2
65 - 69	46.4	65 - 69	40.2
70 - 74	46.7	70 - 74	38.7
≥ 75	38.0	≥ 75	28.4

Data source: The National Health and Nutrition Survey, Japan, 2005.

The sex- and age-specific incidence data for the target cancers were coded in accordance with the International Statistical Classification of Diseases and Related Health Problems, 10th edition (ICD-10), using the morphology codes of the International Classification of Disease for Oncology, 3rd edition (ICD-O-3).

The statistical data on cancer mortality from 2015 were based on the vital statistics of Japan (*8*). We obtained sex- and age-specific mortality data by cause of death from an available data source provided by the Health, Labour, and Welfare Statistics Association (*9*). Similarly to the cancer incidence data, 4-digit ICD-10 codes were used to classify the cause of death.

Due to a lack of information in these statistics, we regarded the number of case of esophagus adenocarcinoma as 5% of total esophageal cancer. For prostate cancer, 30% of prostate cancer incidence and all for prostate cancer mortality were regarded as advanced cancer.

Estimation of relative risks

The relative risk (RR) estimates associated with excess weight (BMI ≥ 23 kg/m^2) and physical activity are shown in Tables 3 and 4, respectively. We prioritized meta-analyses or pooled analyses published for Japanese populations, followed by Asian populations, then studies from other nations. RRs from our own meta-analyses or a single study were used if there was not enough evidence or if no preceding meta-analysis was available. If no Japanese data were available, WCRF/AICR's summary RR was used.

For BMI, RRs for esophageal, gastric cardia, kidney, gallbladder, liver, prostate, colorectal, and post-menopausal breast cancers were derived from epidemiological studies included in the WCRF/AICR reports (*3*). For the risk of ovarian cancer, a Japanese study (*10*) published in 2012 was used as a reference. For endometrial cancer, the summary RR of a Japanese study included in the WCRF/AICR (*11*) and a study published in 2019 (*12*) was used. For pancreatic cancer, the results of a pooled analysis of nine Japanese studies was used (*13*).

Increase in risk for a 1-unit increase in BMI was calculated based on the assumption that the relationship between exposure and risk factor is log-linear. Accordingly, the following equation was used:

$$Risk = exp^{[\ln(\text{risk per 1 BMI unit})\times(\text{Excess BMI}-23)]}$$

For physical activity, many previous studies that looked at the effect of physical activity on cancer risk presented their results in categories of activity (such as high/medium/low, or in quantiles). In this study, consistent with the available data, we categorized the population into two - those who do regular exercise (three or more days/week for breast cancer; three or more hours/day for colorectal cancer; and three or more times/week for endometrial cancer) and those who do not. The RR for all of cancer sites (post-menopausal breast cancer, colorectal, and endometrial (*14*)) were derived from the WCRF/AICR (*3*).

Estimation of population fractions (PAFs)

For excess bodyweight, PAFs were calculated for each sex and age group according to the formula (*15*):

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

Table 3. Relative risk associated with overweight and obesity

Cancer type	Study	BMI unit for calculated risk (kg/m^2)	RR (95% CI)
Esophageal adenocarcinoma[a]	Summary RR from WCRF-CUP (*3*)	5	1.48 (1.35 - 1.62)
Cardia gastric cancer[**]	Kuriyama *et al.* (2005) (*11*)[*]	5	1.41 (0.85 - 2.34)
Kidney cancer	Summary RR of three Japanese studies[*] (*11,23,24*)	5	1.35 (1.02 - 1.79)
Gallbladder cancer	Summary RR of three Japanese studies[*] (*11,24,25*)	5	1.30 (0.86 - 1.96)
Liver cancer	Summary RR of four Japanese studies[*] (*11,24,26,27*)	5	1.36 (0.95 - 1.93)
Pancreas	Koyanagi *et al.* (2018) (*13*)	1	1.00 (0.95-1.05)
Advanced prostate cancer[c]	Summary RR of two Japanese studies[*] (*24,28*)	5	1.44 (1.07 - 1.92)
Ovarian cancer[d]	Weiderpass *et al.* (2012) (*10*)	1	1.00 (0.94 - 1.08)
Endometrial cancer[d]	Summary RR of Kuriyama *et al.* (2005) (*11*)[*] and Kawachi *et al.* (2019) (*12*)	5	1.39 (1.13 - 1.70)
Post-menopausal breast cancer	Wada *et al.* (2014) (*29*)[*]	5	1.28 (1.16 - 1.40)
Colorectal cancer	Summary RR of Yamamoto *et al.* (2010) (*30*)[*] and Matsuo *et al.* (2012) (*31*)	5	1.24 (1.20 - 1.29)

[*]Included in WCRF/AICR. [a]Considered as 5% of all esophageal cancer. [b]Calculated by excluding unknown cases. [c]Calculated for men only; all death cases are considered as advanced. [d]Calculated for women only. Abbreviations: BMI = body mass index; RR = relative risk; CI = confidence interval; WCRF/AICR = World Cancer Research Fund, American Institute for Cancer Research.

Table 4. Relative risk associated with physical activity

Cancer type	Study	Reference group	Decrease in risk due to physical activity
Breast	Suzuki *et al.* (2011) (32)[*]	≥ 3 days/week	0.83 (0.64 - 1.45)
Colorectal	Lee *et al.* (2007) (33)[*]		
Men		≥ 3 hours/day	0.82 (0.65 - 1.05)
Women		≥ 3 hours/day	1.06 (0.78 - 1.45)
Endometrial[a]	Hirose *et al.* (1996) (34)[*]	≥ 3 times/week	0.60 (0.38 - 0.93)

[*]Included in WCRF/AICR. [a]Calculated for women only. Abbreviations: RR = relative risk; CI = confidence interval; WCRF/AICR= World Cancer Research Fund, American Institute for Cancer Research.

For physical inactivity, PAFs were calculated using the formula (*16*):

$$\mathrm{PAF} = \frac{P \times (RR - 1)}{P \times (RR - 1) + 1}$$

where P refers to the proportion of those who are physically inactive in the total population.

By summing these site-specific attributed numbers of cancer incidence and mortality, we obtained the attributed number of total cancer incidence and mortality. Total cancer PAF was then obtained by dividing the number of attributed total cancer incidence and mortality by the number of observed total cancer incidence and mortality.

Results

The estimated PAF of cancer incidence and mortality in 2015 attributed to excess bodyweight and lack of physical activity is summarized in Table 5.

Excess bodyweight: For cancer incidence, the site with the highest PAF value was esophageal adenocarcinoma for men (5.5%) and liver for women (1.2%). For cancer mortality, the site with the highest PAF attributed to overweight was esophageal adenocarcinoma for both men and women (5.0% for men, 1.2% for women). In total, overweight was attributed to 0.7% of all cancer incidence and mortality (1.0% in men and 0.3% in women).

Physical inactivity: Physical inactivity attributed the most to the cancer incidence of colorectal for men (6.8%) and endometrium for women (14.7%). The trend remained the same for cancer mortality, although the PAF was slightly increased for both sexes (7.2% of colorectal cancer for men, and 16.9% of endometrium cancer for women). In total, physical inactivity was attributed to 1.3% of all cancer incidence (1.0% for men, 1.6% for women) and 0.8% of cancer mortality (0.9% for men, 0.8% for women).

Detailed results for each cancer, sex, and age-group are shown for excess bodyweight in Tables S1-S2 (online data, *https://www.ghmopen.com/site/supplementaldata.html?ID=34*) and for lack of physical activity in Tables S3-S4 (online data, *https://www.ghmopen.com/site/supplementaldata.html?ID=34*)

Discussion

Several previous estimates of the fraction of cancer in Japan attributable to excess bodyweight and physical inactivity have been published. In 2005, Kuriyama *et al.* (*11*) reported PAFs attributable to overweight and

Table 5. Proportion (%) of cancer in 2015 attributable to excess bodyweight (Body-mass index (BMI) ≥ 23 kg/m²) and physical inactivity in Japan

Variables	Incidence			Mortality		
	Men	Women	Both sexes	Men	Women	Both sexes
Excess bodyweight (Body-mass index (BMI) ≥ 23 kg/m²)						
Esophagus (C15)	0.4	0.1	0.3	0.2	0.1	0.2
Esophagus adenocarcinoma (C15)	5.5	1.2		5.0	1.2	
Stomach (C16)	0.4	0.1	0.3	1.1	0.2	0.8
Cardia gastric cancer (C16.0)	4.6	1.2		3.8	0.9	
Colorectum (C18-C20)	2.8	0.7	1.9	2.5	0.6	1.6
Liver (C22)	4.0	1.2	3.0	3.6	1.1	2.8
Gallbladder (C23)	3.1	0.9	1.8	2.7	0.8	1.6
Pancreas (C25)	0.0	0.0	0.0	0.0	0.0	0.0
Breast (C50)		0.4	0.4		0.6	0.6
Endometrium (C54)		0.6	0.6		1.0	1.0
Ovary (C56)		0.0	0.0		0.0	0.0
Advanced prostate (C61)	1.4		1.4	3.0		3.0
Kidney (C64)	3.1	1.0	2.5	2.5	0.9	1.9
Total	1.0	0.3	0.7	1.0	0.3	0.7
Physical inactivity						
Colorectum (C18-C20)	6.8	0.0	3.9	7.2	0.0	3.9
Breast (C50)		5.0	5.0		5.6	5.6
Endometrium (C54)		14.7	14.7		16.9	16.9
Total	1.0	1.6	1.3	0.9	0.8	0.8

obesity of -0.2% for men and 4.5% for women. In 2012, Inoue *et al.* (*17*) attributed overweight (BMI ≥ 25 kg/m²) to 0.8% of cancer incidence and 0.5% of cancer mortality among men, and 1.6% and 1.1% among women. The same study found that physical inactivity, defined as the lack of three metabolic equivalents (METs) per day, attributed 0.6% of cancer incidence and 0.4% of cancer mortality in men, and 0.4% and 0.3% in women. These numbers slightly differ to our findings, namely that PAFs were lower in men than women, due to the different definition of physical inactivity and data source between these estimates.

In an international setting, a recent report from Canada (*18*) calculated that country's current burden of cancer attributable to excess bodyweight (BMI ≥ 25 kg/m²) to be 3.1%. Brown *et al.* estimated that overweight and obesity were attributable to 6.3% of all cancers in the United Kingdom (UK) (*19*). The greater number of attributable cases in Europe and Northern America may be explained by the larger proportion of overweight and obesity in these populations. In the UK, 36% and 28% of the population are considered to be overweight and obese, respectively, in 2019 (*20*); while in Canada, over 61% were overweight or obese in 2015 (*21*). On the other hand, the prevalence of obesity among Japanese adults in 2018 is 3.8% (4.1% in men and 3.6% in women) (*22*), suggesting a possible gap in the obesity burden between Japan and Western countries. According to 2018 National Health and Nutrition Survey (*22*), the prevalence of overweight and obesity among the Japanese population has not changed statistically in the past decade. As long as Japan can maintain the current trend, the cancer burden attributable to excess bodyweight will continue to be marginal. Although physical inactivity was associated with an increase of certain types of cancer, the overall contribution was small, perhaps due to insufficient exposure level. Furthermore, lifestyle factors such as physical inactivity are associated with other factors such as poor diet and high bodyweight. Given that most cancers are have a multifactorial etiology, a multivariate estimation of the PAF would provide a better estimation of the burden.

There are several limitations to this study. Our cut-off for excess bodyweight was defined as a BMI of 23 and over, due to practicality of estimation for Japanese. This cut-off differs to the WHO overweight standard (BMI of 25 and over), which is often used in studies from other nations. The PAF of physical inactivity was calculated using a binominal category only, and the definition of regular exercise differed for each cancer site. This prevented us from being able to directly compare our results to previous studies. As evidence was insufficient, some of the RRs used for this study were not derived from a Japanese population. Additionally, many RRs used to calculate PAF were derived from a single cohort study. This may have led to over- or underestimation of the risk. When more data is available, it will be necessary to update the evidence by re-calculating these PAFs using RRs from meta-analyses or pooled analyses.

Despite the limitations listed above, these estimates have major implications for Japan's national health policy for cancer prevention and control strategies. Although the current Japanese obesity rate is low, policymakers and public health agencies must be prepared to intervene if necessary.

Conclusion

Our analysis provides evidence for the current burden of cancer attributable to excess bodyweight and physical inactivity. Excess bodyweight and physical inactivity contributed to 0.7% and 1.3% of cancer incidence, and 0.7% and 0.8% of cancer mortality, respectively. The results of this study may provide useful evidence for appropriately reducing the cancer burden in Japan.

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**Address correspondence to*:
Manami Inoue, Division of Prevention, Center for Public Health Sciences, National Cancer Center, 5-1-1 Tsukiji Chuo-ku, Tokyo 104-0045, Japan
E-mail: mnminoue@ncc.go.jp