Table 3. Number and PAF (%) of cancer incidence and mortality attributable to selected risk factors in Japan in 2005

Risk factor	Definition of exposure category	Incidence		Mortality	
		PAF (%) (95% CI)	Number	PAF (%) (95% CI)	Number
Men					
Total number			379 436		196 603
Tobacco smoking	Ever smoking	29.7 (29.6–29.8)	112 622	34.4 (34.3–34.5)	67 697
Passive smoking	Passive smoking	0.2 (0.2–0.2)	913	0.4 (0.4–0.4)	708
Infection	Positive (*Helicobacter pylori*, HCV, HBV, HPV, EBV, HTLV-I)	22.8 (22.8–22.8)	86 529	23.2 (23.2–23.2)	45 619
Alcohol drinking	Alcohol intake	9.0 (9.0–9.0)	34 151	8.6 (8.6–8.6)	16 905
Salt intake	>6 g/day	1.9 (1.8–1.9)	7137	1.5 (1.4–1.5)	2908
Body mass index	≥25 (overweight and obesity)	0.8 (0.7–0.8)	2848	0.5 (0.5–0.5)	1046
Fruit intake	Lowest intake group	0.7 (0.7–0.7)	2621	0.7 (0.7–0.8)	1441
Vegetable intake	Lowest intake group	0.7 (0.7–0.7)	2549	0.7 (0.7–0.7)	1395
Physical inactivity	Without three METs/day exercise	0.3 (0.3–0.3)	1169	0.2 (0.2–0.2)	423
All above risk factors (adjusted for overlaps)		53.3 (53.2–53.4)	202 257	56.9 (56.8–57.0)	111 901
Women					
Total number			267 366		129 338
Tobacco smoking	Ever smoking	5.0 (4.9–5.0)	13 276	6.2 (6.1–6.2)	8002
Passive smoking	Passive smoking	1.2 (1.2–1.2)	3238	1.6 (1.6–1.7)	2133
Infection	Positive (*H. pylori*, HCV, HBV, HPV, EBV, HTLV-I)	17.5 (17.5–17.6)	46 869	19.4 (19.3–19.4)	25 040
Alcohol drinking	Alcohol intake	2.5 (2.5–2.6)	6769	2.5 (2.4–2.5)	3176
Salt intake	>6 g/day	1.2 (1.2–1.3)	3300	1.2 (1.2–1.2)	1574
Body mass index	≥25 (overweight and obesity)	1.6 (1.5–1.6)	4167	1.1 (1.1–1.1)	1431
Fruit intake	Lowest intake group	0.8 (0.8–0.8)	2162	0.8 (0.8–0.9)	1079
Vegetable intake	Lowest intake group	0.4 (0.4–0.4)	1082	0.4 (0.4–0.5)	562
Physical inactivity	Without three METs/day exercise	0.6 (0.5–0.6)	1462	0.4 (0.4–0.4)	521
Exogenous hormone use	Current use	0.4 (0.4–0.4)	999	0.2 (0.2–0.2)	241
All above risk factors (adjusted for overlaps)		27.8 (27.6–27.9)	74 234	29.9 (29.8–30.1)	38 736
Both sexes					
Total number			646 802		325 941
Tobacco smoking	Ever smoking	19.5 (19.4–19.5)	125 898	23.2 (23.2–23.3)	75 699
Passive smoking	Passive smoking	0.6 (0.6–0.7)	4152	0.9 (0.9–0.9)	2842
Infection	Positive (*H. pylori*, HCV, HBV, HPV, EBV, HTLV-I)	20.6 (19.7–21.5)	133 398	21.7 (20.4–22.9)	70 660
Alcohol drinking	Alcohol intake	6.3 (6.3–6.4)	40 920	6.2 (6.1–6.2)	20 081
Salt intake	>6 g/day	1.6 (1.6–1.6)	10 437	1.4 (1.3–1.4)	4483
Body mass index	≥25 (overweight and obesity)	1.1 (1.1–1.1)	7014	0.8 (0.7–0.8)	2476
Fruit intake	Lowest intake group	0.7 (0.7–0.8)	4783	0.8 (0.8–0.8)	2520
Vegetable intake	Lowest intake group	0.6 (0.5–0.6)	3631	0.6 (0.6–0.6)	1957
Physical inactivity	Without three METs/day exercise	0.4 (0.4–0.4)	2631	0.3 (0.3–0.3)	945
Exogenous hormone use	Current use	0.2 (0.2–0.2)	999	0.1 (0.1–0.1)	241
All above risk factors (adjusted for overlaps)		42.7 (42.6–42.9)	276 491	46.2 (46.1–46.3)	150 637

PAF, population attributable fraction; CI, confidence interval; HCV, hepatitis C virus; HBV, hepatitis B virus; EBV, Epstein–Barr virus; HPV, human papillomavirus; HTLV-I, human T-cell leukemia type I; MET, metabolic equivalents.

H. pylori infection in Japan. Hepatocellular carcinoma, which accounts for 90% of all liver cancer cases, is primarily caused by chronic HCV infection in Japan. The peak incidence between the 1970s and the 1990s in Japanese men was affected by the birth cohort effect among those born during 1931–1935, which was attributed to HCV outbreaks in Japan [35]. This spread was ended by the early 1990s by the control of parenteral HCV transmission and interferon therapy for patients with chronic HCV infection, followed by a community-based anti-HCV screening system started in 2002. Japanese liver cancer incidence is therefore likely to decline further in the next decade [35].

Other important infections in Japan include human T-cell leukemia type I (HTLV-I), which is the main cause of adult T-cell leukemia (ATL). However, the attribution of this agent to total cancer burden is small due to the low prevalence of

Table 4. PAF (%) of incidence and mortality attributable to known risk factors by site of cancer in Japan in 2005

Site	ICD-10	Men Incidence/mortality, PAF (%) (95% CI)	Women Incidence/mortality, PAF (%) (95% CI)	Both sexes Incidence, PAF (%) (95% CI)	Both sexes Mortality, PAF (%) (95% CI)
Oral cavity	C00–C09	72.8 (72.5–73.1)	30.3 (30.0–30.7)	54.9 (54.6–55.3)	56.1 (55.8–56.4)
Oropharynx	C10	75.3 (75.0–75.6)	36.8 (36.5–37.1)	71.2 (70.9–71.5)	70.5 (70.2–70.9)
Nasopharynx	C11	97.2 (97.2–97.2)	92.8 (92.8–92.9)	95.9 (95.7–95.9)	96.3 (96.3–96.3)
Hypopharynx, etc.	C12–C14	71.9 (71.6–72.3)	28.2 (27.8–28.5)	64.9 (64.5–65.2)	66.9 (66.5–67.2)
Esophagus	C15	84.8 (84.7–85.0)	51.6 (51.2–52.0)	79.7 (79.5–80.0)	79.7 (79.5–79.9)
Stomach	C16	82.5 (82.3–82.6)	72.0 (71.7–72.2)	79.1 (79.0–79.3)	78.8 (78.6–79.0)
Colon	C18	51.0 (50.8–51.1)	12.8 (12.6–13.0)	33.6 (33.4–33.8)	31.7 (31.5–31.9)
Rectum	C19–C20	46.6 (46.5–46.7)	6.5 (6.4–6.6)	31.5 (31.3–31.6)	31.9 (31.8–32.1)
Anus	C21	90.0 (90.0–90.0)	90.0 (90.0–90.0)	90.0 (90.0–90.0)	89.9 (89.9–89.9)
Liver	C22	92.2 (92.1–92.3)	91.8 (91.6–92.0)	92.1 (91.9–92.2)	92.1 (91.9–92.2)
Pancreas	C25	23.9 (23.7–24.1)	11.6 (11.5–11.8)	18.1 (18.0–18.3)	18.2 (18.0–18.4)
Larynx	C32	71.9 (71.5–72.2)	30.1 (29.7–30.5)	69.7 (69.3–70.1)	68.6 (68.3–69.1)
Lung	C33–C34	69.1 (69.0–69.2)	36.5 (36.3–36.8)	59.2 (59.0–59.3)	60.2 (60.1–60.4)
Breast	C50		10.5 (10.4–10.7)/11.0 (10.8–11.1)	10.5 (10.4–10.7)	11.0 (10.8–11.1)
Vulva	C51		40.0 (40.0–40.0)	40.1 (40.1–40.1)	39.8 (39.8–39.8)
Vagina	C52		40.0 (40.0–40.0)	39.8 (39.8–39.8)	40.2 (40.2–40.2)
Cervix uteri	C53		100 (100.0–100.0)	100 (100.0–100.0)	100 (100.0–100.0)
Corpus uteri	C54		15.5 (15.2–15.8)	15.5 (15.2–15.8)	15.5 (15.2–15.8)
Ovary	C56		0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)
Penis	C60	40.0 (40.0–40.0)		39.9 (39.9–39.9)	39.8 (39.8–39.8)
Prostate	C61	0.0 (0.0–0.0)		0.0 (0.0–0.0)	0.0 (0.0–0.0)
Kidney	C64	37.4 (37.0–37.8)	12.0 (11.7–12.2)	29.4 (29.0–29.7)	29.2 (28.9–29.6)
Renal pelvis	C65–C66, C68	70.7 (70.5–70.9)	3.6 (3.4–3.7)	45.5 (45.3–45.7)	45.0 (44.8–45.2)
Bladder	C67	70.7 (70.5–70.9)	3.6 (3.4–3.7)	54.9 (54.8–55.1)	49.6 (49.5–49.8)
Hodgkin disease	C81	48.0 (48.0–48.0)	48.0 (48.0–48.0)	48.0 (48.0–48.0)	48.5 (48.5–48.5)
NHL	C82–C85, C96	4.0 (4.0–4.0)	3.8 (3.9–3.9)	3.9 (3.9–4.0)	3.8 (3.8–3.8)
Leukemia	C91–C95	29.2 (29.0–29.4)/32.0 (31.8–32.2)	14.7 (14.7–14.7)	23.0 (22.9–23.1)	25.0 (20.8–25.1)

PAF, population attributable fraction; CI, confidence interval; ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th Revision; NHL, non-Hodgkin lymphoma.

HTLV-I and small proportion of carriers (6% and 2% among men and women, respectively) who develop ATL [36].

Alcohol consumption in Japan and the proportion of heavy drinkers increased for decades until 1990 and have now peaked [2]. Our estimates of the PAF of alcohol drinking should be interpreted with caution because Japanese have a high prevalence of an aldehyde dehydrogenase 2-deficient phenotype, a deficiency that results in greater exposure to acetaldehyde, which is a known carcinogen in alcohol. This genetic difference may be one reason for the stronger RR in Japanese than Western populations [37]. In addition, the nonexposure referent group in many Japanese studies includes lifetime abstainers who are genetically unable to metabolize acetaldehyde, as well as past drinkers who quit drinking due to symptoms caused by alcohol drinking, which may have resulted in the underestimation of RR.

Other risk factors tended to contribute only a relatively small portion of the overall burden. For example, the prevalence of overweight and obesity (BMI ≥25) in Japan has gradually increased in men (22% in 1990 and 29% in 2005) but has been stable in women at ~21%–22% for decades according to the National Nutrition Survey [38]. In addition, the prevalence of obesity (BMI ≥30) has been ~3% in both sexes. As long as the Japanese maintain current BMI levels, the overall cancer burden derived from excess BMI may be small. Rather, the prevalence of underweight (BMI <18.5) in Japan has been greater (5% in men and 10% in women) than that of obesity. Given that many previous studies in Japanese and Asian populations have associated low BMI with an increased risk of cancer [28, 39], PAF for low BMI may warrant further investigation.

Physical inactivity, high salt intake, low vegetable and fruit intake, and female exogenous hormone use are associated with an increased risk of some cancers, but the contribution from these exposures based on our definition of exposed category was modest, due to the low prevalence of exposed category and/or an insufficient or inadequate definition of exposure level. It is notable that the intake of highly salt-concentrated preserved foods rather than salt intake as a whole salt equivalent is suggested to increase the risk of cancer [40], and estimation by the latter instead of the former may underestimate the real PAF. In addition, the prevalence of exogenous hormone use in Japan was and remains significantly low compared with Western populations, which may have led to its small contribution. More accurate estimates of the impact of these factors in Japanese will require a better scientific understanding of the association and more reliable data for Japanese.

Several limitations of these estimates warrant mention. Due to a lack of reliable prevalence data in Japan, we did not include

risk factors such as occupational, air pollution, or ultraviolet or radiation exposures. From previous estimates from Western populations [41], the PAF of occupational exposure may be expected to be ~5% in men, which is not negligible, while the PAF of other factors may not be substantial. Regarding infectious agents, we substituted our estimates with the PAF obtained in a previous estimate [25] due to a lack of prevalence and RR data in Japan, such as for human papillomavirus and Epstein–Barr virus, or excluded them from the present estimate due to the very small number of cases in this population. In addition, the RR estimates and prevalence data were extracted independently. Combining biases by using data from multiple sources would increase the bias of PAF estimation. More generally, most cancers have a multifactorial etiology, and a logically multivariate approach is more realistic. Due to an absence of information on most interactions and the joint prevalence of multiple exposures, we took account of the overlap of risk factors. Nevertheless, the results should be interpreted with caution due to uncertainties over the interactions among risk factors of cancer [8, 11, 42]. Since we used the best estimate of RR and prevalence currently available for Japanese, measured with the most suitable methodology, we believe that our estimates of PAFs are the best that can be currently calculated for Japanese. Nevertheless, many PAFs in the present analysis were based on RRs derived from a single study, not from pooled or meta-analyses, and estimates based on them will require updating when more appropriate evidence become available. At the same time, the cause of more than half of Japanese cancers remains unexplained. Solving this issue will require more research targeted at cancer etiology.

Allowing for these methodological issues, this first comprehensive assessment of cancer burden attributable to multiple risk factors in Japan showed that ~55% of cancer in men, 30% of cancer in women, and 45% of cancer in both sexes was attributable to known risk factors. Our estimate also confirmed that tobacco smoking and infectious agents are currently the main causes of cancer in Japan. These estimates have major implications for national health policy for cancer prevention and control strategies in Japan, namely that public health targeting aimed at substantial reductions in current Japanese cancer incidence and mortality should more strongly focus on the control of tobacco smoking and reduction of chronic infections such as *H. pylori* and HCV.

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Contributors—MIn and ST developed the study concept. MIn, NS, MIw, SS, and TS undertook reviews of published studies. TM and KS prepared statistical data for analysis. MIn and NS analyzed the data and prepared the results. MIn wrote the draft of the report. NS, TM, MIw, SS, TS, KS, and ST critically revised the manuscript. All authors have seen and approved the final version.

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disclosure

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Appendix tables

Appendix Table 1-1. Relative risks (RR) of site-specific cancers associated with tobacco smoking [1]

Cancer site	ICD-10	Relative risk (Ever smokers) Men RR	(95%CI)	Women RR	(95%CI)	Source for RR	Type of study
Oral pharynx	C00-C14	2.37	(1.34- 4.20)	1.76	(0.68- 4.59)	[2]	Pooled analysis
Esophagus	C15	2.96	(1.98- 4.42)	2.40	(1.15- 5.02)	[2]	Pooled analysis
Stomach	C16	1.42	(1.22- 1.66)	1.29	(1.00- 1.66)	[2]	Pooled analysis
Colorectum	C18-20	1.35	(1.13- 1.63)	1.38	(0.86- 2.22)	[3]	Large-scale cohort study
Liver	C22	1.74	(1.44- 2.11)	1.59	(1.15- 2.20)	[2]	Pooled analysis
Pancreas	C25	1.43	(1.08- 1.90)	1.85	(1.37- 2.50)	[2]	Pooled analysis
Larynx	C32	4.50	(1.08- 18.72)	4.50[a]	(1.08- 18.72)	[2]	Pooled analysis
Lung (Active smoking)	C33-C34	3.85	(3.12- 4.74)	3.55	(2.86- 4.40)	[2]	Pooled analysis
Uterine cervix	C53	-		1.99	(1.16- 3.41)	[2]	Pooled analysis
Ovary	C56	-		0.90	(0.40- 2.10)	[4]	Large-scale cohort study
Kidney, except renal pelvis	C64	1.53	(0.81- 2.90)	0.86	(0.20- 3.69)	[2]	Pooled analysis
Renal pelvis, Ureter, Bladder	C65-68	4.30	(2.01- 9.23)	1.30	(0.59- 2.88)	[2]	Pooled analysis
Myeloid leukemia	C92	1.69	(0.89- 3.18)	0.96	(0.34- 2.68)	[2]	Pooled analysis

[a] RR in men served as a substitute for that in women due to a lack of data.

Appendix Table 1-2. Prevalence of ever smokers in Japan in 1990 -National Nutrition Survey [5]

Smoking status	Men	Women
Never	27.0	87.7
Former	19.8	2.6
Current	53.1	9.7

Appendix Table 1-3. Number and population attributable fraction (PAF) of cancer cases and deaths attributable to active tobacco smoking in Japan in 2005

Cancer site	ICD-10	PAF (%)	(95%CI)	Cases	(95%CI)	Deaths	(95%CI)
Men							
Lip, oral cavity, and pharynx	C00-C14	50.0	(49.8- 50.2)	3,709	(3,690- 3,727)	2,076	(2,065- 2,086)
Esophagus	C15	58.9	(58.7- 59.0)	8,722	(8,700- 8,744)	5,571	(5,557- 5,585)
Stomach	C16	23.5	(23.4- 23.6)	18,796	(18,721- 18,871)	7,660	(7,629- 7,690)
Colorectum	C18-C20	20.4	(20.2- 20.5)	12,102	(12,034- 12,171)	4,507	(4,481- 4,532)
Liver	C22	35.1	(35.0- 35.2)	10,076	(10,047- 10,106)	8,138	(8,114- 8,162)
Pancreas	C25	23.9	(23.7- 24.1)	3,132	(3,109- 3,154)	2,935	(2,914- 2,956)
Larynx	C32	71.9	(71.5- 72.2)	2,805	(2,791- 2,820)	723	(719- 727)
Lung (Active smoking)	C33-C34	67.5	(67.5- 67.6)	39,350	(39,314- 39,386)	30,520	(30,492- 30,548)
Kidney	C64	27.9	(27.5- 28.3)	1,917	(1,891- 1,942)	725	(716- 735)
Renal pelvis, Ureter, Bladder	C65-68	70.7	(70.5- 70.9)	10,957	(10,926- 10,989)	3,929	(3,918- 3,940)
Myeloid leukemia	C92	33.5	(33.1- 33.8)	1,056	(1,045- 1,066)	914	(904- 923)
Total				112,622	(112,269- 112,976)	67,697	(67,510- 67,884)
% of all cancers (95%CI)				*29.7*	*(29.6- 29.8)*	*34.4*	*(34.3- 34.5)*
Women							
Lip, oral cavity, and pharynx	C00-C14	8.5	(8.4- 8.7)	299	(293- 305)	131	(128- 133)
Esophagus	C15	14.7	(14.5- 14.8)	393	(389- 398)	252	(250- 255)
Stomach	C16	3.4	(3.4- 3.5)	1,276	(1,262- 1,289)	609	(602- 615)
Colorectum	C18-C20	4.5	(4.4- 4.5)	1,991	(1,958- 2,024)	834	(821- 848)
Liver	C22	6.8	(6.7- 6.8)	911	(904- 918)	749	(743- 755)
Pancreas	C25	9.5	(9.4- 9.5)	1,107	(1,100- 1,113)	1,007	(1,001- 1,013)
Larynx	C32	30.1	(29.7- 30.5)	64	(64- 65)	25	(25- 26)
Lung (Active smoking)	C33-C34	23.9	(23.8- 23.9)	6,116	(6,102- 6,130)	4,029	(4,020- 4,038)
Uterine cervix	C53	10.9	(10.8- 11.0)	920	(911- 929)	268	(265- 270)
Ovary	C56	-		-		-	
Kidney	C64	-		-		-	
Renal pelvis, Ureter, Bladder	C65-68	3.6	(3.4- 3.7)	199	(192- 205)	99	(95- 102)
Myeloid leukemia	C92	-		-		-	
Total				13,276	(13,175- 13,377)	8,002	(7,949- 8,055)
% of all cancers (95%CI)				*5.0*	*(4.9- 5.0)*	*6.2*	*(6.1- 6.2)*
Both sex				125,898	(125,444- 126,353)	75,699	(75,459- 75,939)
% of all cancers (95%CI)				*19.5*	*(19.4- 19.5)*	*23.2*	*(23.2- 23.3)*

Appendix Table1-4 Prevalence, relative risks (RR), number, and population attributable fraction (PAF) of cancer cases and deaths attributable to passive smoking in Japan in 2005

	Prevalence of passive smoking (%) [6] [a]	RR of lung cancer (95%CI) [7] [b]	PAF (%) (95%CI)	Passive smoking-related lung cancer cases (95%CI)	Passive smoking-related lung cancer deaths (95%CI)
Men					
Exposure to smoking spouse	8	1.34 (0.81- 2.21)	2.6 [c] (2.6- 2.7)	135 (133- 138)	105 (103- 107)
Exposure to smoking at workplace	58	1.32 (0.85- 2.04)	15.7 [d] (15.4- 15.9)	799 (787- 812)	620 (611- 629)
Exposure to smoking spouse or at workplace			17.9 [e] (17.6- 18.2)	913 (899- 928)	708 (698- 719)
% of lung cancer				*1.6 (1.5- 1.6)*	*1.6 (1.5- 1.6)*
% of all cancer				*0.2 (0.2- 0.2)*	*0.4 (0.4- 0.4)*
Women					
Exposure to smoking spouse	35	1.34 (0.81- 2.21)	10.6 [c] (10.4- 10.8)	1,819 (1,787- 1,851)	1,198 (1,177- 1,219)
Exposure to smoking at workplace	32	1.32 (0.85- 2.04)	9.3 [d] (9.1- 9.4)	1,589 (1,563- 1,615)	1,046 (1,029- 1,064)
Exposure to smoking spouse or at workplace			18.9 [e] (18.6- 19.2)	3,238 (3,186- 3,291)	2,133 (2,099- 2,168)
% of lung cancer				*12.6 (12.4- 12.9)*	*12.6 (12.4- 12.9)*
% of all cancer				*1.2 (1.2- 1.2)*	*1.6 (1.6- 1.7)*
Both Sexes				4,152 (4,073- 4,231)	2,842 (2,787- 2,896)
% of lung cancer				*4.9 (4.9- 5.0)*	*4.6 (4.5- 4.7)*
% of all cancer				*0.6 (0.6- 0.7)*	*0.9 (0.9- 0.9)*

[a] Prevalence among men was re-calculated from the same study as reference 6.
[b] RR in women served as a substitute for that in men due to a lack of data.
[c] PAF1
[d] PAF2
[e] Combined PAF was calculated by the following formula: $\mathrm{PAF} = \mathrm{PAF1} \times \mathrm{PAF2} + \mathrm{PAF1} \times (1 - PAF2) + PAF2 \times (1 - PAF1)$

Appendix Table2-1. Relative risks (RR) of site-specific cancers associated with alcohol drinking [1]

Cancer site	ICD-10	Relative risk (Drinkers) Men RR	(95%CI)		Women RR	(95%CI)		Source for RR	Type of study
Oral and pharynx	C00-C14	2.02	(0.98-	4.21)	2.02[a]	(0.98-	4.21)	[8]	Large-scale cohort study
Esophagus	C15	2.52	(1.90-	3.33)	2.52[a]	(1.90-	3.33)	[9]	Large-scale cohort study
Colorectum	C18-C20	1.64	(1.50-	1.79)	1.08	(0.91-	1.30)	[10]	Pooled analysis
Liver	C22	1.19	(0.97-	1.46)	1.90	(0.85-	4.26)	[11]	Pooled analysis
Breast	C50				1.22	(1.02-	1.48)	[12]	Large-scale cohort study

[a] RR in men served as a substitute for that in women due to a lack of data.

Appendix Table2-2. Prevalence of alcohol drinkers in Japan around 1990 -Prevalence data from pooled analysis of 6 prospective cohort studies [13]

Alcohol drinking	Men	Women
Nondrinker	23.3	73.2
Drinker	76.7	26.8

Appendix Table 2-3. Number and population attributable fraction (PAF) of cancer cases and deaths attributable to alcohol drinking by sex in Japan in 2005

Cancer site	ICD-10	PAF (%)	(95%CI)	Cases	(95%CI)	Deaths	(95%CI)
Men							
Lip, oral cavity, and pharynx	C00-C14	43.9	(43.5- 44.2)	3,256	(3,229- 3,282)	1,822	(1,807- 1,837)
Esophagus	C15	53.8	(53.7- 53.9)	7,976	(7,959- 7,993)	5,095	(5,084- 5,106)
Colorectum	C18-C20	32.9	(32.9- 33.0)	19,581	(19,551- 19,611)	7,292	(7,272- 7,303)
Liver	C22	11.6	(11.5- 11.8)	3,338	(3,301- 3,376)	2,696	(2,666- 2,727)
Total				34,151	(34,040- 34,262)	16,905	(16,828- 16,972)
% of all cancers (95%CI)				*9.0*	*(9.0- 9.0)*	*8.6*	*(8.6- 8.6)*
Women							
Lip, oral cavity, and pharynx	C00-C14	21.5	(21.2- 21.7)	751	(742- 759)	328	(324- 332)
Esophagus	C15	28.9	(28.8- 29.0)	775	(773- 778)	497	(495- 499)
Colorectum	C18-C20	2.1	(2.0- 2.1)	936	(914- 958)	392	(383- 401)
Liver	C22	12.3	(12.1- 12.5)	1,658	(1,633- 1,682)	1,362	(1,342- 1,383)
Breast	C50	5.6	(5.5- 5.6)	2,649	(2,623- 2,675)	597	(591- 603)
Total				6,769	(6,685- 6,853)	3,176	(3,136- 3,217)
% of all cancers (95%CI)				*2.5*	*(2.5- 2.6)*	*2.5*	*(2.4- 2.5)*
Both sex				40,920	(40,725- 41,115)	20,081	(19,964- 20,189)
% of all cancers (95%CI)				*6.3*	*(6.3- 6.4)*	*6.2*	*(6.1- 6.2)*

Appendix Table 3-1. Relative risks (RR) of site-specific cancers associated with body mass index [14]

Cancer site	ICD-10	Relative risk (BMI≥25) Men RR	(95%CI)	Women RR	(95%CI)	Source for RR	Type of study
Colon	C18	1.24	(1.11- 1.39)	1.17	(1.03- 1.33)	[15]	Pooled analysis
Pancreas	C25	0.70	(0.40- 1.10)	1.10	(0.70- 1.60)	[16]	Large-scale cohort study
Postmenopausal breast	C50			1.12	(0.86- 1.45)	[17]	Large-scale cohort study
Corpus uteri	C54			1.73	(0.80- 3.77)	[18]	Large-scale cohort study
Kidney	C64	1.66	(1.05- 2.61)	1.55	(0.76- 3.18)	[19]	Large-scale cohort study

Appendix Table 3-2. Distribution of body mass index in Japan in 1990 -Prevalence data from pooled analysis of 6 prospective cohort studies [20]

	Prevalence (%)	
BMI	Men	Women
<25	77.0	75.3
≥25	23.0	24.7

Appendix Table 3-3. Number and population attributable fraction (PAF) of cancer cases and deaths attributable to overweight and obesity (BMI≥25) in Japan in 2005

Cancer site	ICD-10	PAF (%)	(95%CI)	Cases	(95%CI)	Deaths	(95%CI)
Men							
Colon	C18	5.2	(5.2- 5.3)	1,942	(1,931- 1,953)	703	(699- 707)
Pancreas	C25	-		-		-	
Kidney	C64	13.2	(13.0- 13.3)	906	(897- 915)	343	(339- 346)
Total				2,848	(2,828- 2,867)	1,046	(1,038- 1,053)
% of all cancers (95%CI)				*0.8*	*(0.7- 0.8)*	*0.5*	*(0.5- 0.5)*
Women							
Colon	C18	4.0	(4.0- 4.1)	1,252	(1,241- 1,263)	551	(547- 556)
Pancreas	C25	2.4	(2.3- 2.5)	282	(269- 294)	257	(245- 268)
Postmenopausal breast	C50 (≥50y)	2.9	(2.8- 2.9)	1,005	(981- 1,029)	262	(255- 268)
% of total breast cancer				*2.1*	*(2.1- 2.2)*	*2.4*	*(2.4- 2.5)*
Corpus uteri	C54	15.3	(15.0- 15.5)	1,251	(1,232- 1,270)	214	(210- 217)
Kidney	C64	12.0	(11.7- 12.2)	377	(370- 384)	147	(145- 150)
Total				4,167	(4,094- 4,240)	1,431	(1,403- 1,459)
% of all cancers (95%CI)				*1.6*	*(1.5- 1.6)*	*1.1*	*(1.1- 1.1)*
Both sex				7,014	(6,922- 7,107)	2,476	(2,441- 2,512)
% of all cancers (95%CI)				*1.1*	*(1.1- 1.1)*	*0.8*	*(0.7- 0.8)*

Appendix Table 4. Relative risks (RR) (per unit), number, and population attributable fraction (PAF) of cancer cases and deaths attributable to physical inactivity [14] in Japan in 2005

Cancer	ICD-10	Ln (Risk per 1 MET) [21] [a]	RR for average physical activity level [b]	RR for average physical activity level+3 METs [b]	PAF (%)	(95%CI)	Cases	(95%CI)	Deaths	(95%CI)
Men										
Colon	C18	0.03	2.8	3.08	3.2	(3.0- 3.3)	1,169	(1,126- 1,213)	423	(408- 439)
Total							1,169	(1,126- 1,213)	423	(408- 439)
% of all cancers							*0.3*	*(0.3- 0.3)*	*0.2*	*(0.2- 0.2)*
Women										
Colon	C18	0.02	1.84	1.94	2.9	(2.8- 3.0)	898	(872- 924)	395	(384- 407)
Breast	C50	0.004	1.16	1.18	1.1	(1.1- 1.2)	542	(532- 553)	122	(120- 125)
Corpus uteri	C54	0.0008	1.03	1.03	0.3	(0.2- 0.3)	21	(16- 27)	4	(3- 5)
Total							1,462	(1,420- 1,503)	521	(507- 536)
% of all cancers							*0.6*	*(0.5- 0.6)*	*0.4*	*(0.4- 0.4)*
Both sex							2,631	(2,547- 2,715)	945	(914- 975)
% of all cancers							*0.4*	*(0.4- 0.4)*	*0.3*	*(0.3- 0.3)*

[a] Large-scale cohort study

[b] Average daily total physical activity level (33.5 METs/day [21]) plus 3 METs/day was defined as exposures with the lowest burden of cancer.

Appendix Table 5-1. Relative risks (RR) of site-specific cancers associated with intake of vegetables and fruit [14]

Cancer site	ICD-10	Relative risk (higher than the lowest intake group) Men RR	(95%CI)	Women RR	(95%CI)	Source for RR	Type of study
Vegetables							
Esophagus	C15	0.74	(0.54- 1.03)	0.74	(0.54- 1.03)	[22]	Large-scale cohort study
Stomach	C16	0.94	(0.87- 1.00)	0.90	(0.81- 1.00)	[23]	Pooled analysis
Fruit							
Esophagus	C15	0.73	(0.53- 1.02)	0.73	(0.53- 1.02)	[22]	Large-scale cohort study
Stomach	C16	0.88	(0.80- 0.96)	0.79	(0.71- 0.89)	[23]	Pooled analysis
Lung	C33-C34	1.14	(0.87- 1.48)	1.14	(0.87- 1.48)	[24]	Large-scale cohort study

Appendix Table 5-2. Number and population attributable fraction (PAF) of cancer cases and deaths attributable to insufficient intake of vegetables and fruit in 2005

Cancer site	ICD-10	PAF (%)	(95%CI)	Cases	(95%CI)	Deaths	(95%CI)
Vegetables							
Men							
Esophagus	C15	10.4	(10.2- 10.6)	1,540	(1,505- 1,574)	983	(961- 1,005)
Stomach	C16	1.3	(1.2- 1.3)	1,009	(963- 1,056)	411	(392- 430)
Total				2,549	(2,468- 2,630)	1,395	(1,354- 1,436)
% of all cancers (95%CI)				*0.7*	*(0.7- 0.7)*	*0.7*	*(0.7- 0.7)*
Women							
Esophagus	C15	10.4	(10.2- 10.6)	278	(272- 284)	178	(174- 182)
Stomach	C16	2.2	(2.1- 2.3)	804	(770- 837)	383	(368- 399)
Total				1,082	(1,042- 1,121)	562	(542- 582)
% of all cancers (95%CI)				*0.4*	*(0.4- 0.4)*	*0.4*	*(0.4- 0.5)*
Both sex				3,631	(3,511- 3,751)	1,957	(1,896- 2,017)
% of all cancers (95%CI)				*0.6*	*(0.5- 0.6)*	*0.6*	*(0.6- 0.6)*
Fruit							
Men							
Esophagus	C15	10.9	(10.6- 11.1)	1,612	(1,577- 1,647)	1,030	(1,007- 1,052)
Stomach	C16	1.3	(1.2- 1.3)	1,009	(946- 1,072)	411	(386- 437)
Lung	C33-C34	-		-		-	
Total				2,621	(2,524- 2,719)	1,441	(1,393- 1,489)
% of all cancers (95%CI)				*0.7*	*(0.7- 0.7)*	*0.7*	*(0.7- 0.8)*
Women							
Esophagus	C15	10.9	(10.6- 11.1)	291	(285- 298)	187	(183- 191)
Stomach	C16	5.1	(5.0- 5.2)	1,870	(1,832- 1,908)	892	(874- 910)
Lung	C33-C34	-		-		-	
				2,162	(2,117- 2,206)	1,079	(1,057- 1,101)
				0.8	*(0.8- 0.8)*	*0.8*	*(0.8- 0.9)*
Both sex				4,783	(4,641- 4,926)	2,520	(2,450- 2,590)
% of all cancers (95%CI)				*0.7*	*(0.7- 0.8)*	*0.8*	*(0.8- 0.8)*

Appendix Table 6. Relative risks (RR) (per unit), number, and population attributable fraction (PAF) of cancer cases and deaths attributable to excess salt intake (>6g) [14] in Japan in 2005

Cancer	ICD-10	Ln (Risk per 1 g) [25] [a]	RR for average salt intake (12.5g) [b]	RR for ideal salt intake (6g) [c]	Prevalence (≤6g) (%)	PAF (%)	(95%CI)	Cases	(95%CI)	Deaths	(95%CI)
Men											
Stomach	C16	0.0159	1.22	1.1	2.9	8.91	(8.7- 9.1)	7,137	(6,993- 7,281)	2,908	(2,850- 2,967)
Total								7,137	(6,993- 7,281)	2,908	(2,850- 2,967)
% of all cancers								*1.9*	*(1.8- 1.9)*	*1.5*	*(1.4- 1.5)*
Women											
Stomach	C16	0.0159	1.22	1.1	3.9	8.91	(8.7- 9.2)	3,300	(3,211- 3,389)	1,574	(1,532- 1,617)
Total								3,300	(3,211- 3,389)	1,574	(1,532- 1,617)
% of all cancers								*1.2*	*(1.2- 1.3)*	*1.2*	*(1.2- 1.2)*
Both sex								10,437	(10,204- 10,670)	4,483	(4,382- 4,584)
% of all cancers								*1.6*	*(1.6- 1.6)*	*1.4*	*(1.3- 1.4)*

[a] Large-scale cohort study
[b] From National Nutrition Survey Japan, 1990 [5]
[c] Daily salt intake of ≤6g/day was defined as exposures with the lowest burden of cancer.

Appendix Table 7-1. Prevalence and relative risks (RR) of cancer cases and deaths attributable to infectious agents[26] in Japan in 2005

Agent	Cancer site	ICD-10	Prevalence among cases (%)		Men			Women			Source for RR	
			Men	Women	RR	(95%CI)		RR	(95%CI)			Type of study
H. pylori	Noncardia Stomach	C16 but C160	95.6 [27]	89.3[27]	6.8	(3.6-	12.6)	4.6	(2.1-	9.9)	[27]	Large-scale cohort study
	Gastric MALT Lymphoma	5% of NHL	90 [28]	90 [28]	6.3	(2.0-	19.9)	6.3	(2.0-	19.9)	[29]	Global estimate
HBV	Liver	C22	12.6 [30]	8.9 [30]	102	(79-	202)	102	(79-	202)	[30]	Large-scale cohort study
HCV	Liver	C22	72.7 [30]	80.5 [30]	126	(63-	165)	126	(63-	165)	[30]	Large-scale cohort study
HCV&HBV	Liver	C22	1.8 [30]	1.3 [30]	572	(173-	1887)	572	(173-	1887)	[30]	Large-scale cohort study
HPV	Cervix uteri	C53	-					∞				
	Penis	C60	-		-			-				
	Vulva	C51	-		-			-				
	Vagina	C52	-		-			-				
	Anus	C21	-		-			-				
	Oral cavity	C00-C09	-		-			-				
	Oropharynx	C10	-		-			-				
EBV	Nasopharynx	C11	-		-			-				
	Birkitt Lymphoma	C837	-		-			-				
	Hodgkin Lymphoma	C81	-		-			-				
HTLV-1	ATL	C915	-		∞			∞				

Appendix Table 7-2. Population attributable fraction (PAF) of cancer cases and deaths attributable to infectious agents in Japan in 2005

Agent	Cancer site	ICD-10	PAF (%)	(95%CI)	Cases	(95%CI)	Deaths	(95%CI)
Men								
H. pylori	Noncardia Stomach [a]	C16 but C160	81.5	(81.4- 81.6)	59,438	(59,368- 59,507)	24,222	(24,194- 24,250)
	Gastric MALT Lymphoma	5% of NHL	75.7	(75.5- 75.9)	325	(324- 326)	181	(180- 181)
HBV	Liver	C22	12.5	(12.4- 12.5)	3,584	(3,575- 3,594)	2,895	(2,887- 2,902)
HCV	Liver	C22	72.1	(72.1- 72.1)	20,720	(20,719- 20,722)	16,735	(16,733- 16,736)
HCV&HBV	Liver	C22	1.8	(1.7- 1.9)	516	(488- 544)	417	(394- 439)
HPV	Cervix uteri	C53						
	Penis	C60	40.0 [29]		123		51	
	Vulva	C51						
	Vagina	C52						
	Anus	C21	90.0 [29]		387		123	
	Oral cavity	C00-C09	3.0 [29]		115		54	
	Oropharynx	C10	12.0 [29]		120		79	
EBV	Nasopharynx	C11	90.0 [29]		399		224	
	Birkitt Lymphoma	C837	20.0 [29]		19		3	
	Hodgkin Lymphoma	C81	48.0 [29]		203		43	
HTLV-1	ATL	C915	100.0 [b]		580		593	
	Total				86,529	(86,421- 86,638)	45,619	(45,560- 45,679)
	% of all cancers				*22.8*	*(22.8- 22.8)*	*23.2*	*(23.2- 23.2)*
Women								
H. pylori	Noncardia Stomach [a]	C16 but C160	69.9	(69.7- 70.1)	24,330	(24,267- 24,392)	11,607	(11,577- 11,637)
	Gastric MALT Lymphoma	5% of NHL	75.7	(75.5- 75.9)	279	(279- 280)	139	(139- 140)
HBV	Liver	C22	8.8	(8.8- 8.9)	1,187	(1,181- 1,192)	975	(970- 980)
HCV	Liver	C22	79.9	(79.9- 79.9)	10,753	(10,753- 10,754)	8,837	(8,836- 8,837)
HCV&HBV	Liver	C22	1.3	(1.2- 1.4)	175	(158- 192)	144	(130- 157)
HPV	Cervix uteri	C53	100.0 [b]		8,474		2,465	
	Penis	C60						
	Vulva	C51	40.0 [29]		282		90	
	Vagina	C52	40.0 [29]		88		41	
	Anus	C21	90.0 [29]		223		117	
	Oral cavity	C00-C09	3.0 [29]		83		35	
	Oropharynx	C10	12.0 [29]		14		11	
EBV	Nasopharynx	C11	90.0 [29]		172		65	
	Birkitt Lymphoma	C837	20.0 [29]		6		1	
	Hodgkin Lymphoma	C81	48.0 [29]		240		21	
HTLV-1	ATL	C915	100.0 [b]		563		493	
	Total				46,869	(46,782- 46,955)	25,040	(24,991- 25,090)
	% of all cancers				*17.5*	*(17.5- 17.6)*	*19.4*	*(19.3- 19.4)*
	Both sex				133,398	(133,203- 133,593)	70,660	(70,551- 70,769)
	% of all cancers				*20.6*	*(20.6- 20.7)*	*21.7*	*(21.6- 21.7)*

[a] 91% in men and 94% in women among all gastric cancer in 2000. [31]
[b] PAF was regarded as 100%.

Appendix Table 8. Prevalence and relative risks (RR), number, and population attributable fraction (PAF) of cancer cases and deaths attributable to exogenous hormone use in Japan in 2005

	Current Users				Women					
Exogenous Hormones	RR	(95%CI)	Prevalence (%)	PAF (%)	(95%CI)	Cases	(95%CI)	Deaths	(95%CI)	
Oral Contraceptives (age <45)										
25-29	1.07 [32] [a]	(1.05- 1.09)	5.6 [b]	0.4	(0.4- 0.4)	1	(1- 1)	0	(0- 0)	
30-34	1.07 [32] [a]	(1.05- 1.09)	3.6 [b]	0.3	(0.3- 0.3)	2	(2- 2)	0	(0- 0)	
35-39	1.07 [32] [a]	(1.05- 1.09)	3.2 [b]	0.2	(0.2- 0.2)	4	(4- 4)	1	(1- 1)	
40-44	1.07 [32] [a]	(1.05- 1.09)	1.1 [b]	0.1	(0.1- 0.1)	3	(3- 3)	0	(0- 0)	
Hormone replacement therapy (age≥45)	1.43 [33] [c]	(1.36- 1.50)	5.8 [b]	2.4	(2.4- 2.4)	989	(987- 990)	239	(239- 240)	
Total						999	(997- 1,000)	241	(240- 241)	
% of breast cancers (C50)						*2.1*	*(2.1- 2.1)*	*2.2*	*(2.2- 2.2)*	
% of all cancers						*0.4*	*(0.4- 0.4)*	*0.2*	*(0.2- 0.2)*	
% of all cancers (both sexes)						*0.2*	*(0.2- 0.2)*	*0.1*	*(0.1- 0.1)*	

[a] Meta-analysis
[b] Unpublished data by the Japan Nurses' Health Study (JNHS). [34]
[c] Other population (Large-scale cohort study)

Appendix-references

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