menopause, body mass index, and the risk of colorectal cancer mortality in the Dutch Diagnostisch Onderzoek Mammacarcinoom (DOM) cohort. *Epidemiology* 2000; **11**: 304–8.
27. Ohno Y, Tamakoshi A; JACC Study Group. Japan collaborative cohort study for evaluation of cancer risk sponsored by Monbusho (JACC study). *J Epidemiol* 2001; **11**: 144–50.
28. Parkin DM, Whelan SL, Ferlay J, Raymond L, Young J. Cancer incidence in five continents. vol. VII. Lyon: International Agency for Research on Cancer; 1997.
29. McMichael AJ, Potter JD. Do intrinsic sex differences in lower alimentary tract physiology influence the sex-specific risks of bowel cancer and other biliary and intestinal diseases? *Am J Epidemiol* 1983; **118**: 620–7.
30. Bjelke E. Epidemiologic studies of cancer of the stomach, colon, and rectum; with special emphasis on the role of diet. *Scand J Gastroenterol Suppl* 1974; **31**: 1–235.
31. Amiel SA, Caprio S, Sherwin RS, Plewe G, Haymond MW, Tamborlane WV. Insulin resistance of puberty: a defect restricted to peripheral glucose metabolism. *J Clin Endocrinol Metab* 1991; **72**: 277–82.
32. de Ridder CM, Bruning PF, Zonderland ML, Thijssen JH, Bonfrer JM, Blankenstein MA, Huisveld IA, Erich WB. Body fat mass, body fat distribution, and plasma hormones in early puberty in females. *J Clin Endocrinol Metab* 1990; **70**: 888–93.
33. Frisancho AR, Flegel PN. Advanced maturation associated with centripetal fat pattern. *Hum Biol* 1982; **54**: 717–27.
34. Giovannucci E. Insulin and colon cancer. *Cancer Causes Control* 1995; **6**: 164–79.
35. Ronnemaa T, Knip M, Lautala P, Viikari J, Uhari M, Leino A, Kaprio EA, Salo MK, Dahl M, Nuutinen EM, Pesonen E, Pietikainen M, Akerblom HK. Serum insulin and other cardiovascular risk indicators in children, adolescents and young adults. *Ann Med* 1991; **23**: 67–72.
36. Rosenberg L, Palmer JR, Kaufman DW, Strom BL, Schottenfeld D, Shapiro S. Breast cancer in relation to the occurrence and time of induced and spontaneous abortion. *Am J Epidemiol* 1988; **127**: 981–9.
37. Cole P, MacMahon B, Brown JB. Oestrogen profiles of parous and nulliparous women. *Lancet* 1976; **ii**: 596–9.
38. Trichopoulos D, Cole P, Brown JB, Goldman MB, MacMahon B. Estrogen profiles of primiparous and nulliparous women in Athens, Greece. *J Natl Cancer Inst* 1980; **65**: 43–6.
39. Martin CJ. Monitoring maternity services by postal questionnaire: congruity between mothers' reports and their obstetric records. *Stat Med* 1987; **6**: 613–27.
40. Paganini-Hill A, Ross RK. Reliability of recall of drug usage and other health-related information. *Am J Epidemiol* 1982; **116**: 114–22.

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Bowel movement frequency and risk of colorectal cancer in a large cohort study of Japanese men and women

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Epidemiology

The relationship between bowel movement (BM) frequency and the risk of colorectal cancer was examined in a large cohort of 25 731 men and 37 198 women living in 24 communities in Japan. At enrolment, each participant completed a self-administrated questionnaire on BM frequency and laxative use. Incidence rate ratios (IRR) with 95% confidence intervals (CI) were estimated using Cox's proportional-hazard model. During the follow-up period (average length 7.6 years), 649 cases of colorectal cancer, including 429 cases of colon cancer, were identified. Among women, subjects who reported a BM every 2–3 days had the lowest risk of developing colorectal (IRR = 0.71, 95% CI = 0.52–0.97) and colon cancer (IRR = 0.70, 95% CI = 0.49–1.00), whereas those reporting a BM every 6 days or less had an increased risk of developing colorectal (IRR = 2.47, 95% CI = 1.01–6.01) and colon cancer (IRR = 2.52, 95% CI = 0.93–6.82) compared with those reporting ⩾1 BM per day. A similar, but nonsignificant, association between the frequency of BM and cancer risk was observed in men. There was no association between colorectal or colon cancer risk and laxative use. Regulating BM frequency might therefore have a role in the prevention of colorectal cancer.
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An association between constipation and the risk of colorectal cancer has long been noted. Prolonged intestinal transit time might not only increase the duration of contact between carcinogens in the stools and the gut wall, but could also concentrate carcinogens by increasing colonic water absorption. A meta-analysis of 14 case–control studies that examined the association between constipation or infrequent bowel movements (BMs) and colorectal cancer and found a statistically significant 48% increase in the pooled odds ratios for colorectal cancer in association with constipation (Sonnenberg and Müller, 1993). Recent case–control studies have also reported a relatively consistent positive relationship between constipation and colorectal cancer (Kotake *et al*, 1995; Le Marchand *et al*, 1997; Ghadirian *et al*, 1998; Jacobs and White, 1998; Roberts *et al*, 2003).

Since bowel habits might be influenced by the presence of colorectal cancer, retrospective studies cannot exclude the effects of the cancer itself, as well as recall bias, on their results. However, few prospective studies have addressed this issue. The only cohort study, which had a 12-year follow-up period involving 84 577 women, of colorectal cancer incidence and BM frequency or laxative use reported negative results (Dukas *et al*, 2000). The influence of BMs on male colorectal cancer has not been previously studied prospectively.

We conducted a large cohort study to investigate the association between bowel habits, laxative use, susceptibility to diarrhoea and the colorectal cancer risk in Japanese men and women.

MATERIALS AND METHODS

All data were taken from the Japan Collaborative Cohort (JACC) Study, the methods of which have been described in detail elsewhere (Ohno and Tamakoshi, 2001). Briefly, the original study population consisted of 110 792 Japanese adults aged 40–79 years. Enrolment began in 1988 and continued until the end of 1990 in 45 areas across Japan. Most subjects were recruited from the general population or when undergoing routine health checks in the municipalities. Written informed consent for participation was obtained individually from subjects, with the exception of a few

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study areas in which informed consent was provided at the group level after explaining the aims of the study and confidentiality of the data to community leaders. The study protocol was approved by the Ethics Committee of Medical Care and Research of the Fujita Health University School of Medicine, Japan.

Analyses were restricted to data from the 65 184 participants who lived in the 24 study areas in which cancer registries were available. A further 58 subjects with a previous history of colorectal cancer, and 2197 subjects for whom information about bowel habits was not available, were excluded. Therefore, a total of 62 929 individuals (25 731 men and 37 198 women) were involved in this analysis.

All participants completed a self-administered questionnaire on enrolment. This covered demographic characteristics and lifestyle factors such as diet, tobacco smoking, alcohol consumption, physical activity, BM frequency, susceptibility to diarrhoea and laxative use over the past year. The alternative answers provided on the questionnaire for the frequency of BM were: 'daily', 'every 2–3 days', 'every 4–5 days' and 'every 6 days or less'. With regard to laxative use, the questionnaire asked only whether the participants used laxatives in the past one year at the time of enrolment; additional data on the type of laxative, the reason for use and the duration of use were not collected. Participants also provided information about susceptibility to diarrhoea by answering 'yes', 'no' or 'neutral' in response to the question: do you often have diarrhoea?

Population registries in the municipalities were used to determine the vital and residential status of subjects. Registration of death is required under the Family Registration Law in Japan, which applies throughout the country. Incidences of cancer were confirmed using records from the population-based cancer registries, which were supplemented by a systematic review of death certificates (Ohno and Tamakoshi, 2001); in some areas, medical records were also reviewed in major local hospitals. The mortality-to-incidence ratio for colorectal cancer was 0.28 in the cohort covered by the cancer registries. This figure is comparable with those calculated in the most accurate population-based cancer registries in Japan (Parkin *et al*, 2003), which indicates that most cases of colorectal cancer were identified in the study population.

The follow-up period ran from the time of the baseline survey through to the end of 1997 in all but three areas (in which it ran until the end of 1994, 1995 and 1996, respectively). The end point of the study was defined as the incidence of colorectal cancer (10th Revision of the International Classification of Diseases, ICD-10: C18–C20) or colon cancer (ICD-10: C18). The risk of rectal cancer was not analysed separately because of the relatively small number of cases observed. Subjects who moved out of the study area or died from causes other than colorectal cancer were treated as censored cases. During the study period, only 3.3% (2071) of the participants were lost from the follow-up as a result of a change of residence.

All analyses were carried out by sex using the SAS statistical package release 8.2 (SAS Inc., Cary, NC, USA). Differences in baseline characteristics between categories of BM frequency were tested using the chi-squared (χ^2) test or one-way analysis of variance (ANOVA). The follow-up period for each participant was calculated as the time between completing the questionnaire and either the diagnosis of colon or rectal cancer, death, moving out of the study area or the end of the study – whichever occurred first.

The incidence rate ratios (IRR) and 95% confidence intervals (CI) for colorectal and colon cancer were estimated, by sex, using Cox's proportional-hazard model according to the levels of BM frequency, laxative use and susceptibility to diarrhoea. The categories of 'every day' for BM, 'nonuse' for laxative use and 'no' or 'neutral' for susceptibility to diarrhoea were used as reference groups.

Analyses were adjusted for the following potential confounding factors: age (continuous variable); body mass index (BMI) calculated as weight (kg) [height (m)]$^{-2}$ and categorised as '$\geqslant 25\,kg\,m^{-2}$' or '$<25\,kg\,m^{-2}$'; intake frequency of green leafy vegetables ('daily' or 'not daily'); intake frequency of alcohol ('$\geqslant 5$ days per week' or '<5 days per week'); current smoking status ('smoker' or 'nonsmoker'); time spent walking per day ('$\leqslant 30$ min or '>30 min'); history of colorectal cancer in parents or siblings ('yes' or 'no'); and age at leaving full-time education ('$\geqslant 20$ years' or '<20 years'). For each covariate, missing values were treated as an additional category and were included in the model. To determine the influence of symptoms of colorectal cancer on bowel habits, analyses were repeated excluding the first 3 years of follow-up. In all cases, two-sided P-values <0.05 were considered to be statistically significant.

RESULTS

Within the study group, 1.1% of men and 4.0% of women reported infrequent BMs (every 4 days or less). The use of laxatives was more common among women (14.7%) than men (6.9%), whereas men were more likely to report frequent diarrhoea (20.3%) than were women (9.7%).

Table 1 shows the baseline characteristics of the study population by BM frequency. Regardless of sex, individuals who reported infrequent BMs – compared with those who reported BMs daily or every 2–3 days – had a lower average BMI, were less likely to spend >30 min walking per day and were more likely to use laxatives.

A significant difference in the intake frequency of green leafy vegetables and in smoking status across the BM groups was observed only among women: those who reported BMs daily or every 2–3 days were more likely to consume green leafy vegetables daily and less likely to be smokers. In addition, women who reported BMs every 2–3 days were, on average, younger than those in the other BM groups. Alcohol consumption did not differ between BM groups in women.

Among men, the number that reported daily alcohol intake increased linearly with BM frequency. Male subjects who reported BMs every 2–3 days had the lowest rate of frequent diarrhoea, whereas the number of women who reported frequent diarrhoea decreased linearly with BM frequency.

During the follow-up period (average length 7.6 years, standard deviation 1.9), a total of 649 cases of colorectal cancer were identified (379 in men and 270 in women), which included 429 cases of colon cancer (225 in men and 204 in women).

Age-adjusted IRRs were calculated for colorectal and colon cancer according to BM frequency (not shown). Regardless of sex, the ratios were <1.00 for subjects who reported BMs every 2–3 days relative to those who reported daily BMs: the IRRs for colorectal cancer were 0.74 in men (95% CI = 0.51–1.09) and 0.71 in women (95% CI = 0.52–0.97), whereas the IRRs for colon cancer were lower in men (0.45; 95% CI = 0.25–0.82) and the same in women (0.71; 95% CI = 0.49–1.00). In contrast, the age-adjusted IRRs for subjects who reported highly infrequent BMs (every 6 days or less) relative to those with daily BMs were >1.00: the IRRs for colorectal cancer were 1.14 in men (95% CI = 0.16–8.10) and 2.53 in women (95% CI = 1.04–6.15), whereas the IRRs for colon cancer were 1.78 in men (95% CI = 0.25–12.7) and 2.59 in women (95% CI = 0.96–6.98).

Adjustment for potential confounding factors (as discussed above) had no significant effects on the IRRs (Table 2). Furthermore, even after excluding the first 3 years of follow-up, there was a lower risk of colorectal or colon cancer in women who reported BMs every 2–3 days relative to those who reported daily BMs: the multivariate-adjusted IRRs were 0.64 for colorectal cancer (95% CI = 0.43–0.96) and 0.68 for colon cancer (95% CI = 0.43–1.05). Increased risks of colorectal and colon cancers were also observed in association with highly infrequent BMs

Table 1 Background characteristics of the participants at baseline by BM frequency by sex

Variable	BM frequency									
	Men					Women				
	⩾1 per day, ($n=22\,930$)	Every 2–3 days, ($n=2526$)	Every 4–5 days, ($n=222$)	Every 6 days or less, ($n=53$)	*P*-value[a]	⩾1 per day, ($n=25\,884$)	Every 2–3 days, ($n=9813$)	Every 4–5 days, ($n=1238$)	Every 6 days or less, ($n=263$)	*P* value[a]
Age (years)										
Mean	57.6	59.7	62.5	65.9	<0.0001	58.4	57.3	57.4	58.8	<0.0001
s.d.	10.2	11.2	11.3	11.6		9.9	10.5	10.8	11.0	
BMI ($kg\,m^{-2}$)										
Mean	22.7	22.2	21.7	21.7	<0.0001	23.1	22.6	22.5	22.0	<0.0001
s.d.	3.0	2.9	3.1	3.6		3.6	3.0	3.1	3.0	
Having green leafy vegetables every day (%)	26.2	26.1	20.7	22.6	0.29	32.5	27.8	27.1	24.7	<0.0001
Daily alcohol drinking (%)	48.4	36.0	33.3	28.3	<0.0001	5.2	4.7	4.3	4.9	0.15
Current smokers (%)	50.3	48.9	51.8	47.2	0.55	4.5	4.7	8.1	11.4	<0.0001
Daily walking time <30 min (%)	25.9	32.3	38.3	50.9	<0.0001	22.4	26.6	31.9	37.3	<0.0001
Having family history of colorectal cancer (%)	2.2	2.1	1.8	0.0	0.71	2.5	2.5	3.1	3.4	0.53
Age of final education completed ⩾20 years (%)	11.8	11.4	8.1	15.1	0.30	5.2	5.6	4.9	4.2	0.29
Use of laxatives (%)	4.6	21.8	46.2	60.5	<0.0001	8.5	24.1	48.5	64.3	<0.0001
Having frequent diarrhoea (%)	20.7	16.5	20.1	18.8	<0.0001	10.7	7.6	6.4	3.8	<0.0001

BM = bowel movement; BMI = body mass index; ANOVA = analysis of variance. [a]Test for homogeneity of characteristics between categories of BM frequency, using ANOVA (age, BMI) and χ^2 (other variables).

Table 2 IRR for colorectal and colon cancer according to BM frequency by sex

BM	Observed person-years	Colorectal cancer			Colon cancer		
		No. of cases	Multivariate-adjusted[a] IRR	95% CI[b]	No. of cases	Multivariate-adjusted[a] IRR	95% CI[b]
Men							
⩾1 per day	175 485	346	1.00		211	1.00	
Every 2–3 days	18 335	30	0.77	0.53–1.12	11	0.46	0.25–0.85
Every 4–5 days	1515	2	0.56	0.14–2.26	2	0.93	0.23–3.75
Every 6 days or less	321	1	1.16	0.16–8.27	1	1.86	0.26–13.4
Women							
⩾1 per day	196 472	204	1.00		155	1.00	
Every 2–3 days	72 891	51	0.71	0.52–0.97	38	0.70	0.49–0.996
Every 4–5 days	8937	10	1.12	0.59–2.11	7	1.01	0.47–2.17
Every 6 days or less	1880	5	2.47	1.01–6.01	4	2.52	0.93–6.82

IRR = incidence rate ratios; BM = bowel movement; BMI = body mass index. [a]Adjusted for age, BMI, intake frequency of green leafy vegetables, daily alcohol drinking, current smoking status, time spent for walking per day, family history of colorectal cancer and education. [b]CI: confidence interval.

(every 6 days or less), although they were not statistically significant.

Table 3 shows the associations between laxative use, susceptibility to diarrhoea and colorectal or colon cancer risk. There were weak nonsignificant positive associations between laxative use and cancer risk in both men and women, but no association between cancer risk and frequent diarrhoea.

DISCUSSION

This is the first prospective study, to our knowledge, that has reported a significant association between BM frequency and colorectal cancer risk. Infrequent BMs were associated with a significantly increased risk of colorectal cancer and a marginally increased risk of colon cancer in women. A similar, but

Table 3 IRR for colorectal and colon cancer according to laxative use and susceptibility to diarrhoea

		Colorectal cancer			Colon cancer		
	Observed person-years	No. of cases	Multivariate-adjusted[a] IRR	95% CI[b]	No. of cases	Multivariate-adjusted[a] IRR	95% CI[b]
Men							
Laxative use							
No	155 068	292	1.00		170	1.00	
Yes	10 015	33	1.28	0.89–1.86	20	1.31	0.81–2.11
Susceptibility to diarrhoea							
Normal	143 808	285	1.00		168	1.00	
Having frequent diarrhoea	35 775	68	1.08	0.82–1.41	40	1.08	0.76–1.53
Women							
Laxative use							
No	206 189	183	1.00		137	1.00	
Yes	33 097	41	1.20	0.85–1.69	33	1.26	0.86–1.85
Susceptibility to diarrhoea							
Normal	230 880	224	1.00		173	1.00	
Having frequent diarrhoea	23 417	26	1.18	0.79–1.78	16	0.95	0.57–1.59

IRR = incidence rate ratios; BMI = body mass index. [a]Adjusted for age, BMI, intake frequency of green leafy vegetables, daily alcohol drinking, current smoking status, time spent for walking per day, family history of colorectal cancer and education. [b]CI: confidence interval.

Epidemiology

nonsignificant, association was found in men. These results were not altered by adjusting for potential confounding factors or excluding the first 3 years of follow-up from the analysis, which indicated that the effects of the cancers themselves on bowel habits were not responsible for the associations.

These results support the findings of recent case–control studies and of the meta-analysis carried out by Sonnenberg and Müller (1993), which reported a significantly increased risk of colorectal cancer in association with constipation or infrequent BMs. However, the findings from the Nurses' Health Study in the United States – only one published prospective data on the association between BM frequency and female colorectal cancer risk (Dukas *et al*, 2000) – did not support an association between infrequent BMs and the risk of colorectal cancer. One possible reason for the discrepancy between these results and those of the present study is that different criteria were used to define 'infrequent BM'. The Nurses' Health Study defined this as an average frequency of 'every third day or less'. However, in the present study, a significantly increased risk of colorectal and colon cancer was found only in subjects who reported BMs every 6 days or less relative to those reporting daily BMs. Therefore, we suggest that only highly infrequent BMs elevate the risk of colorectal cancer.

Daily BMs were found to increase the risk of colorectal and colon cancer compared with BMs every 2–3 days, in both men and women. This observation is in line with the results of a previous case–control study carried out in Japan (Kato *et al*, 1993). However, the Nurses' Health Study (Dukas *et al*, 2000) found no difference in colorectal cancer incidence between subjects who reported $\geqslant 2$ BMs per day and those who reported BMs once per day (multivariate-adjusted IRR = 0.89, 95% CI = 0.65–1.20). Unfortunately, limitations of the questionnaire used in the present study precluded us from determining the risk associated with $\geqslant 2$ BMs per day. On the basis of the combined findings of these studies, we speculate that subgroups that have highly frequent BMs might be at an increased risk of colorectal cancer. Experimental studies have reported elevated levels of prostaglandin E_2 (PGE_2) in the gastrointestinal tract in many diarrhoeal states (Burakoff and Percy, 1992), and increased levels of PGE_2 might be associated with carcinogenesis in the large intestine (Reddy *et al*, 1993). We did not observe a significant association between self-reported susceptibility to diarrhoea and colorectal cancer risk, and the results of previous epidemiological studies (case–control studies only) were inconsistent (Dales *et al*, 1979; Kune *et al*, 1987). Similar to 'constipation', the definition of 'diarrhoea' is equivocal. Some case–control studies have suggested that 'soft' or 'loose' faeces might increase the risk of colorectal cancer (Kato *et al*, 1993; Inoue *et al*, 1995). To have a conclusion, additional data on factors such as faecal consistency should be collected and analysed together with data on susceptibility to diarrhoea and BM frequency.

A weak nonsignificant positive association was found between laxative use and the risk of colorectal cancer in both men and women. Previously, the meta-analysis of Sonnenberg and Müller (1993) revealed a significant 46% increase in the risk of colorectal cancer associated with the use of laxatives. On the other hand, recent case–control studies (Jacobs and White, 1998; Nascimbeni *et al*, 2002; Roberts *et al*, 2003) and a prospective study (Dukas *et al*, 2000) found no relationship between these factors – although Dukas *et al* suggested that some types of laxative might influence intestinal pH and the metabolism of intestinal flora, thereby modifying colorectal cancer risk. The effects of laxative type were not investigated in the present study because of limitations of the questionnaire. Further prospective studies investigating the types of laxative and duration of use will be necessary to resolve this question.

The risk of rectal cancer was not analysed independently because of the small number of cases in the study group. Larger-scale prospective studies will be necessary to reveal the effects of bowel habits on the development of cancers of the large intestine at specific sites.

There were some limitations to the scope of the present study. For example, although the main risk factors for colorectal cancer were adjusted for in the analysis, other factors such as aspirin use and hormone replacement therapy in women might have confounded the results. Also, bowel habits were evaluated only through a self-reported questionnaire that was administered once at the baseline; the reproducibility and validity of the responses of subjects were therefore not confirmed.

In conclusion, this study shows that highly infrequent BMs can increase the risk of colorectal cancer in both men and women. Highly frequent BMs may also enhance this risk. Further

prospective studies are needed to confirm our findings and to clarify the risk associated with BMs for colorectal cancer by subsite.

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REFERENCES

Burakoff R, Percy WH (1992) Studies *in vivo* and *in vitro* on effects of PGE2 on colonic motility in rabbits. *Am J Physiol* **262**: G23–G29

Dales LG, Friedman GD, Ury HK, Grossman S, Williams SR (1979) A case–control study of relationships of diet and other traits to colorectal cancer in American blacks. *Am J Epidemiol* **109**: 132–144

Dukas L, Willett WC, Colditz GA, Fuchs CS, Rosner B, Giovannucci EL (2000) Prospective study of bowel movement, laxative use, and risk of colorectal cancer among women. *Am J Epidemiol* **151**: 958–964

Ghadirian P, Maisonneuve P, Perret C, Lacroix A, Boyle P (1998) Epidemiology of sociodemographic characteristics, lifestyle, medical history, and colon cancer: a case–control study among French Canadians in Montreal. *Cancer Detect Prev* **22**: 396–404

Inoue M, Tajima K, Hirose K, Hamajima N, Takezaki T, Hirai T, Kato T, Ohno Y (1995) Subsite-specific risk factors for colorectal cancer: a hospital-based case–control study in Japan. *Cancer Causes Control* **6**: 14–22

Jacobs EJ, White E (1998) Constipation, laxative use, and colon cancer among middle-aged adults. *Epidemiology* **9**: 385–391

Kato I, Tominaga S, Matsuura A, Yoshi Y, Shirai M, Kobayashi S (1993) Case–control study of bowel habits and colorectal adenoma and cancer. *J Epidemiol* **3**: 1–5

Kotake K, Koyama Y, Nasu J, Fukutomi T, Yamaguchi N (1995) Relation of family history of cancer and environmental factors to the risk of colorectal cancer: a case–control study. *Jpn J Clin Oncol* **25**: 195–202

Kune GA, Kune S, Watson LF (1987) The Melbourne Colorectal Cancer Study. Characterization of patients with a family history of colorectal cancer. *Dis Colon Rectum* **30**: 600–606

Le Marchand L, Wilkens LR, Kolonel LN, Hankin JH, Lyu LC (1997) Associations of sedentary lifestyle, obesity, smoking, alcohol use, and diabetes with the risk of colorectal cancer. *Cancer Res* **57**: 4787–4794

Nascimbeni R, Donato F, Ghirardi M, Mariani P, Villanacci V, Salerni B (2002) Constipation, anthranoid laxatives, melanosis coli, and colon cancer: a risk assessment using aberrant crypt foci. *Cancer Epidemiol Biomarkers Prev* **11**: 753–757

Ohno Y, Tamakoshi A (2001) Japan collaborative cohort study for evaluation of cancer risk sponsored by monbusho (JACC study). *J Epidemiol* **11**: 144–150

Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB (2003) *Cancer Incidence in Five Continents*, Vol . 8 Lyon: IARC Press

Reddy BS, Rao CV, Rivenson A, Kelloff G (1993) Inhibitory effect of aspirin on azoxymethane-induced colon carcinogenesis in F344 rats. *Carcinogenesis* **14**: 1493–1497

Roberts MC, Millikan RC, Galanko JA, Martin C, Sandler RS (2003) Constipation, laxative use, and colon cancer in a North Carolina population. *Am J Gastroenterol* **98**: 857–864 doi;10.1016/S0002-9270(03)00050-9

Sonnenberg A, Müller AD (1993) Constipation and cathartics as risk factors of colorectal cancer: a meta-analysis. *Pharmacology* **47**(Suppl 1): 224–233

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Field Study

A Chronological Decrease in Type A Behavior Patterns among Japanese Male Workers in 1995–1999

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Abstract : A Chronological Decrease in Type A Behavior Patterns among Japanese Male Workers in 1995–1999: Masayo KOJIMA, *et al.* Department of Health Promotion and Preventive Medicine, Nagoya City University Graduate School of Medical Sciences—We examined the chronological change in Type A behavior pattern (TABP) among Japanese male workers for 5 yr. A brief questionnaire to measure TABP was administered to 21,711 male workers who underwent health check-ups at least once during the period from 1995 to 1999 and were born in 1936–1965. The mean TABP scores decreased year by year linearly. Then the repeated measurement analysis of variance was performed with the data of 5,689 subjects who completed the questionnaire successively through the study period. Both year and the age effects were highly significant ($p<0.001$, respectively), whereas the time trends were comparable by baseline age. In conclusion, TABP among Japanese male workers decreased in all generations during the period from 1995 to 1999.
(J Occup Health 2004; 46: 171–174)

Key words: Type A, Psychosocial factor, Economy, Chronological change

"Type A man" was born of the clinical observations of two American Cardiologists in the mid-1950s. Friedman and Rosenman[1, 2] found that their cardiac patients presented an "overt behavior pattern", characterized by intense ambition, competitive drive, constant preoccupation with occupational deadlines, and a sense of time urgency. It was named "Type A behavior pattern (TABP)"[3, 4] and a series of studies were conducted to assess its association with coronary heart disease (CHD). After three large population studies showed a positive relationship between TABP and an increased risk of CHD[5, 6], the Review Panel on Coronary-prone Behavior and Coronary Heart Disease concluded in 1978 that TABP was an independent risk factor for developing CHD[7].

Nevertheless, a number of subsequent prospective epidemiological surveys failed to produce consistent results[8]. Moreover, psychological research, beginning in the mid-1960s, focused on emotions such as anger or hostility in isolation, thus fragmenting the concept of TABP into its component parts. Reviewing the articles concerning TABP from 1965 to 1998, Riska[9] described what happened to the "Type A man" as follows: "having the status of a distinct set of medical risk factors in the late 1960s and most of the 1970s, the Type A man has all but disappeared as a social and diagnostic category in the vocabulary of medicine." Has the "Type A man" disappeared from the world? He might have just become inconspicuous because we have less interest in him than before. Or has he just mellowed with time?

Up until October 2001, just one article could be found on the Medline database reporting the change in the prevalence of TABP over time in the general population. Smith and Sterndorff[10] administered the Jenkins Activity Survey Scale (JAS)[11] to four hundred Danish men and women, once in 1988 and again in 1992. The scores were lower in 1992 than in 1988, and they concluded that TABP had declined in the Danish population, but these were not consecutive reports from the same individuals. We believe this is the first study that demonstrates a chronological decline in TABP in a working male population over a period of 5 yr.

Subjects and Methods

Subjects

The study protocol was approved by the Ethics

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Table 1. Type A Behavior Pattern (TABP) scores in Japanese male workers from 1995 to 1999

Year	n	TABP Score			Age	
		Mean	SD	Chronbach's α	Mean	SD
1995	13,290	12.6	5.9	0.75	46.3	7.1
1996	13,090	12.5	5.9	0.80	47.9	7.1
1997	12,790	12.4	5.9	0.81	47.4	7.0
1998	12,361	12.2	5.8	0.81	47.9	7.1
1999	11,631	12.0	5.8	0.81	48.2	7.2

Committee of Nagoya City University, Graduate School of Medical Sciences. The samples of this study were male Japanese workers born in 1936–1965 who visited Gifu Prefectural Center for Health Check and Health Promotion ("the Center") during the period April 1995 to March 2000. The data on these subjects were taken from the medical records in the Center. Although individual written informed consent was not obtained from each subject, the investigators explained the aim of the study and confidentiality of the data to the Center administrators and got permission to access the data.

The Center is located in Gifu City, a middle-sized city in Central Japan with a population of 407,134 in 1995. According to the requirements of the law of Industrial Safety and Health, it is mandatory for workers to take an annual medical check-up. Therefore, the present sample can be regarded as a working male population of this Japanese semi-urban community.

Between April 1995 and March 2000, a total of 25,574 men underwent health examinations at least once. Those who were born before 1936 or after 1965, or those who reported having no stable job at any point during the study period, were excluded from the analysis. 21,711 subjects met all the criteria. Among the eligible subjects, 5,689 participants visited the center successively for 5 yr (mean age ± SD: 47 ± 6 yr, range from 29 to 60 yr at the baseline in 1995): that was 42.8% of the participants in 1995.

Methods

A self-report 12-item questionnaire developed by Maeda[12, 13] was administered to the participants as one of the routine questionnaires from the Center; inquiring about past and present illness, demographic background, dietary habits, sports, sleep, and so on as part of the health evaluation. Maeda's "Brief Questionnaire" was an original scale, designed to evaluate TABP tendencies in Japanese populations. Each item is rated on a three-point Likert scale ranging from "usually" (scored 2) to "hardly ever" (scored 0), with a double score given to the three items. The total score ranges from 0 to 30, and the author recommends a cut-point score of 17 or more for TABP screening. The correlation coefficient with JAS[11] was reported as 0.72, and the concordance of the Type A judgment by Maeda's scale and by JAS was 75%[12]. A recent cross-sectional study reported the discriminant validity of this scale between non-fatal myocardial infarction patients and healthy controls[14].

The participants were requested to complete the questionnaire in advance, and public health nurses checked all items during individual interviews carried out at the end of the health checkups. If there were missing items, the nurses asked the participants to complete them.

Analyses

Data were analyzed with SAS for Windows version 8.01 (SAS Institute, Cary, NC, USA). All statistical tests were two-sided. p-values ≤ 0.05 were considered statistically significant. In order to evaluate the internal reliability of Maeda's Brief Questionnaire, Cronbach's alpha coefficient was calculated for each year's data.

A repeated-measurement analysis of variance was then performed to examine the year effect and the generation difference on the chronological change in the TABP score. The subjects were divided into three groups by the baseline age (29 to 39 yr old, born in 1956–65; 40 to 49 yr old, born in 1946–55; 50 to 59 yr old, born in 1936–1945). The interaction between baseline age group and year, and the differences in the TABP scores by the baseline age group by year were examined.

Results

Table 1 shows the mean TABP scores ± standard deviation (SD), Chronbach's alpha coefficients, and mean ages ± SD of the each year sample from 1995 to 1999. Alpha coefficients were at an optimal level (above 0.70), indicating good internal consistency of the scale. The mean scores of the total samples by year decreased linearly from 1995 to 1999.

Then, to test the time and generation effect on the score change, a repeated measurement analysis of variance was performed with the data for subjects who took the annual health examination successively through the study period. A total of 5,689 subjects, 42.8% of the study participants in 1995 were included in the analysis. The chronological change in the mean TABP score by generation is shown

in coronary disease. Detection of overt behavior pattern A in patients with coronary disease by a new psychophysiological procedure. JAMA 173 , 1320–1326 (1960)
3) RH Rosenman, M Friedman, R Straus, CD Jenkins, SJ Zyzanski and M Wurm: Coronary heart disease in the Western Collaborative Group Study. A follow-up experience of 4 and one-half years. J Chronic Dis 23, 173–190 (1970)
4) M Friedman and RH Rosenman: Type A Behavior Pattern: its association with coronary heart disease. Ann Clin Res 3, 300–312 (1971)
5) CD Jenkins, RH Rosenman and SJ Zyzansk: Prediction of clinical coronary heart disease by a test of the coronary-prone behaviour pattern. N Engl J Med 290, 1271–1275 (1974)
6) SG Haynes, M Feinleib and WB Kannel: The relationship of psychosocial factors to coronary heart disease in the Framingham study: 3. Eight year incidence of coronary heart disease. Am J Epidemiol 111, 37–58 (1980)
7) The Review Panel on Coronary-Prone Behavior and Coronary Heart Disease, Coronary-Prone Behavior and Coronary Heart Disease: A critical review. Circulation 63; 1199–1215 (1981)
8) H Hemingway and M Marmot: Evidence based cardiology: psychosocial factors in the aetiology and prognosis of coronary heart disease. Systematic review of prospective cohort studies. BMJ 318, 1460–1467 (1999)
9) E Riska: The rise and fall of Type A man. Soc Sci Med 51, 1665–1674 (2000)
10) DF Smith and B Sterndorff: Coronary-prone behavior may be declining in Danish men and women. Scand J Psychol 34, 379–383 (1993)
11) Jenkins CD, Zyzanski SJ, Rosenman RH. Jenkins Activity Survey Manual, The psychological Corporation, Cleveland. 1979.
12) S Maeda: A study on behavior pattern of patients with coronary heart diseases. Seishin-Igaku 25, 297–306 (1985) (in Japanese with English abstract)
13) S Maeda: Application of a brief questionnairefor the behavior pattern survey. Type A 2, 33–40 (1991) (in Japanese with English abstract)
14) K Yoshimasu and The Fukuoka Heart Study Group: Relation of type a behavior pattern and job-related psychosocial factors to nonfatal myocardial infarction: a case-control study of Japanese male workers and women. Psychosom Med 63, 797–804 (2001)
15) KA Matthews and SG Haynes: Type A behavior pattern and coronary disease risk. Update and critical evaluation. Am J Epidemiol 123, 923–960 (1986)
16) Ministry of Labour. Report of Survey on Employment Trends. White paper on labour. Tokyo: Nihon Roudou Kenkyuu Kikou, 2000: 31–38 (in Japanese)
17) Statistics and information department, Ministry of Health, Labour and Welfare. Vital statistics of Japan. Tokyo: Health and welfare statistics association, 2000 (in Japanese)
18) Rosenman, RH, Chesney, M. Stress, type A behavior and coronary disease. Goldberger l., and Brezmitz, S.: Handbook of Stress. New York, Macmillan,1982.
19) Statistics and information department, Ministry of Health, Labour and Welfare. Patient Survey. Tokyo: Health and welfare statistics association, 2000 (in Japanese)
20) S Cohen: Pathways linking affective disturbances and physical disorders. Health Psychol 14, 374–380 (1995)

RESEARCH COMMUNICATION

Association between Type II Diabetes and Colon Cancer among Japanese with Reference to Changes in Food Intake

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Abstract

Many epidemiological studies have provided support for the hypothesis that type II diabetes can increase the risk of colorectal cancer, but time trends, geographical distributions and host factors for the two diseases remain largely to be clarified. To address these issues, we investigated the epidemic pattern of colon cancer and type II diabetes among Japanese in Japan (J-Japanese), with consideration of the westernization of dietary habits. Over the last three decades, the increase in crude mortality rates of colon cancer from the Vital Statistics has closely paralleled the increment in prevalence rates (PRs) from hospital based surveys of diabetes. Age-standardized incidence rates (ASIRs) for colon cancer among Japanese in the United States (US-Japanese) were higher than those among J-Japanese and almost the same as those among US-Whites, while PRs for type II diabetes among US-Japanese were the highest in the three populations. Correlation analysis showed that PRs for type II diabetes had a positive association with ASIRs for colon cancer among both J-Japanese and US-Japanese ($r=0.79$, $p<0.01$). Since 1950, intake of milk, meat, eggs and fat/oil has increased, while that of rice and potatoes has gradually decreased. Our findings indicate that the increment of ASIRs for colon cancer among J-Japanese might be closely associated with the increment of PRs for type II diabetes, reflecting the westernization of food intake.

Key Words: Colon cancer - type II diabetes - food intake - Japanese

Asian Pacific J Cancer Prev, 5, 28-35

Introduction

In Japan, the westernization of lifestyle, especially dietary habits, has progressed remarkably over the last half century, accompanied by trends for change in age-standardized incidence rates (ASIRs) and age-adjusted mortality rates for gastrointestinal cancers, with reduction of gastric cancer and the increment in colorectal cancer (Tominaga and Kuroishi, 1997; Tajima and Tominaga, 1985). The Cancer Incidence in Five Continents books published by the International Agency for Research on Cancer/ International Association of Cancer Registries have documented rapid increase in ASIRs for colon cancer in descendents of Japanese in the United States (US-Japanese), while those for stomach cancer among Japanese in Japan (J-Japanese) have gradually decreased (Muir et al., 1987; Parkin et al., 1992; 1997).

Epidemiological studies have suggested that the westernization of lifestyle is also associated with change in prevalence rates (PRs) for type II diabetes (non-insulin dependent diabetes) (Fujimoto, 1992; King and Rewers, 1993; King et al., 1998). In the early 1980s, PRs for type II diabetes among US-Japanese Nisei (second-generation) were four times higher than those among J-Japanese, based on identical diagnostic criteria (Fujimoto, 1994). Among J-Japanese aged over 40 years, furthermore, the PR of type II diabetes with glycated hemoglobin (HbA1c >= 6.1%) was estimated to be 8.2% from results of the National Nutritional Survey (Ministry of Health, Labor and Welfare, Division of Health and Nutrition, 1999) conducted in 1997.

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Since 1970, many studies have provided support for the hypothesis that type II diabetes increases the risk of colorectal cancer, and several authors have speculated possible biological mechanisms, including impaired glucose tolerance (IGT) and insulin resistance (McKeown-Eyssen, 1994; Will et al., 1998; Bruce et al., 2000; Mori et al., 2000; Giovannucci, 2001; Sandhu et al., 2002). However, time trends, geographic distributions and host factors, such as age, gender and ethnic variation, for the two diseases have not well documented with reference to changes in food intake. The purpose of the present study was to clarify these issues, focusing on the association between colon cancer and type II diabetes, using available information published in Japan and the US.

Materials and Methods

Food consumption data for the period from 1950 to 2000 in Japan were accessed from the National Nutritional Survey (Ministry of Health, Labor and Welfare, Division of Health and Nutrition, 2002). Crude mortality rates for colon cancer [International Classification of Diseases (ICD), 10th] and PRs from hospital based surveys (PRs-HBS) of diabetes (ICD 9th for 1979-1995 and 10th from 1996) were derived from the Vital Statistics of Japan (Ministry of Health and Welfare of Japan, 1995; 2002). PRs-HBS for diabetes (ICD 9th for 1980 and 1990) were not adjusted for age and were defined as rates for all clinic patients (out- and in-patients) with diabetes on the National Patient Surveys in 1972, 1980 and 1990 (Ministry of Health and Welfare of Japan, 1974; 1982; 1992). Age-specific mortality rates (ASMRs) for colon cancer (ICD 9th revision) were obtained from the National Statistics of Japan (1950-1995)(Kuroishi et al., 1997).

ASIRs for colon cancer were obtained from the Cancer Incidence in Five Continents Vols. VI and VII (ICD 9th)(Parkin et al., 1992; 1997). Among J-Japanese, the cancer registries from Osaka prefecture in 1988-92, Tohoku (Yamagata prefectures in 1988-92) and Kyushu areas (Saga prefecture in 1988-92) were corresponded to the below study locations and the periods for type II diabetes, respectively (Figure 1). Likewise, ASIRs among US-Japanese and US-Whites were derived from information as follows; Hawaii and Los Angeles in 1983-87 and 1988-92 for US-Japanese, and Hawaii and Los Angeles, where the majority of US-Japanese live, in 1983-87 and 1988-92 for US-Whites (non-Hispanic Whites), respectively.

PRs for type II diabetes and IGT were derived from Medline-accessed papers, and conducted by large-scale population-based studies (Hara et al., 1994; Harris et al., 1998; Terao et al., 1997). Study location and the periods for type II diabetes and IGT among J-Japanese were as follows; Osaka prefecture in 1992, Tohoku (Yamagata prefectures in 1990) and Kyushu areas (Fukuoka prefecture in 1992), respectively (Figure 1). Those rates were adjusted for the Japanese standard population. With regard to ethnic variation, PRs for type II diabetes among US-Japanese and US-Whites were as follows: Hawaii and Los Angels in 1978-88 for US-Japanese, and the third National Health and Nutrition Examination Survey in 1988-94 for US-Whites, respectively. PRs for IGT among US-Japanese and US-Whites were unobtainable. Age of study subjects, methods of oral glucose tolerance test (OGTT) and the diagnostic criteria for type II diabetes and IGT among J-Japanese, US-Japanese and US-Whites were summarized as follows; >= 40-79y, 75g OGTT, World Health Organization (WHO) for J-Japanese; >=40y, 50g OGTT, the Japan Diabetes Society for US-Japanese in Hawaii; >=40y, 75g OGTT, WHO for US-Japanese in Los Angeles; 40-74y, 75g OGTT, WHO for US-Whites, respectively.

With reference to changes in food intake since 1950, we described the pattern of both colon cancer and type II diabetes since 1970s focusing on issues as follows: 1) time trends; 2) age and gender specificities; 3) geographic distributions; and 4) ethnic variation among J-Japanese, US-Japanese and US-Whites, 5) correlation between colon cancer and type II diabetes. Correlation analyses were performed with the PC-SAS statistical package version 8.1 (SAS Institute IN., Cary, NC, USA).

Results

Food intake in Japan increased most for milk from 1950 to 2000, followed by meat, eggs, fat/oil and fruit, while those of rice and potatoes gradually decreased (Figure 2). Westernized food intake, especially milk, meat, eggs and fat/oil, was increased 5 times or more until 1970, and then maintained up to today or further slightly increased. The intake of rice and potatoes was two-third and half fold decreased in 1975, respectively, but that of fish, beans, green-

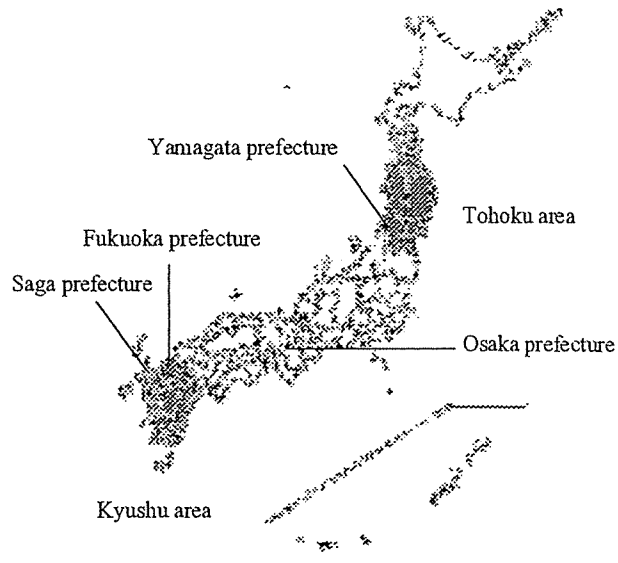

Figure 1. Location of the Representative Areas for Information of Cancer Registries and Data of Type II Diabetes According to Large-scale Population-based Studies in Japan

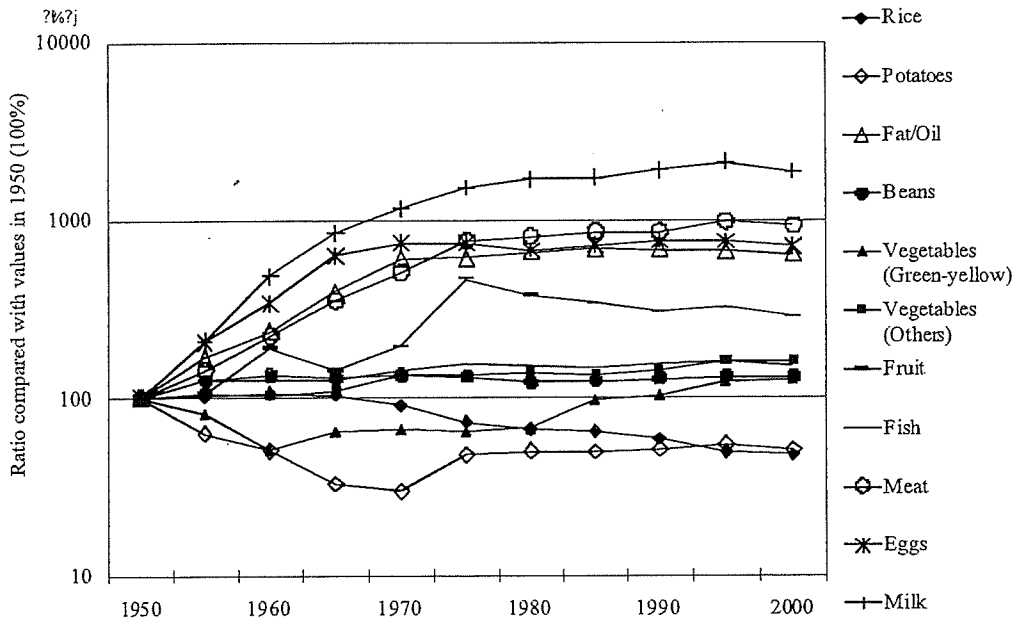

Figure 2. Relative Changes in Selected Food Intake in Japan (1950-2000), Compared with Values for 1950

yellow vegetables and other vegetables remained relatively constant.

Crude mortality rates for colon cancer from 1970 to 2000 among J-Japanese demonstrated 5 and 4.5 fold elevations for men and women, compared with each baseline value, respectively (Figure 3). PRs-HBS for diabetes similarly increased 2-3 times. The rates in 1996 were slightly decreased because of the alteration of ICD from 9th to 10th. Among men and women, ASMRs for colon cancer had gradually increased with age until 1972, followed by rapid elevation until 1980 and further steep increase in 1990 (Figure 4). ASMRs for colon cancer were increased among

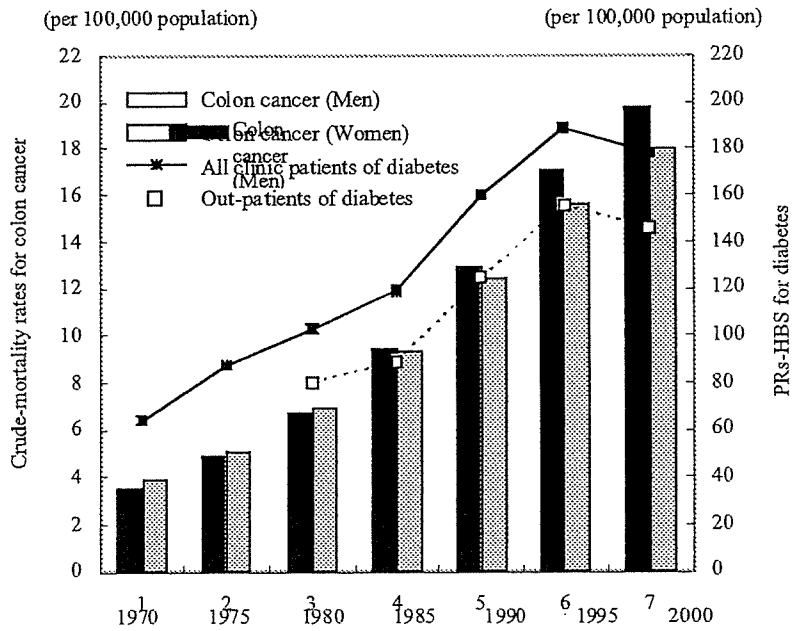

Figure 3. Time Trends in Crude Mortality Rates for Colon Cancer and Prevalence Rates from Hospital Based Surveys (PRs-HBS) for Diabetes among Japanese in Japan, 1970-2000

both genders aged over 45-49y, and those in 1990 were greater among men than among women. As well as ASMRs for colon cancer, PRs-HBS for diabetes among both genders were rapidly increased with age decade by decade. Among men and women, PRs-HBS for diabetes were significantly increased through 45-49y to 70-74y and 75-79y, respectively, but reduced among those who were more elderly. In 1990, PRs-HBS for diabetes among women aged 70-74y, 75-79y and 80-84y were higher than those among the corresponding men, but overall they were higher among men.

Figure 5 shows relations between PRs for type II diabetes and ASIRs for colon cancer among J-Japanese and US-Japanese. In early 1990s, geographical differences in Japan were observed that PRs for type II diabetes were the highest in Kyushu area, but ASIRs for colon cancer, especially for women, were the highest in Tohoku area. Whereas, PRs for IGT among J-Japanese men were higher in Kyushu area and Osaka prefecture, but those among J-Japanese women were higher in Kyushu and Tohoku areas (data not shown). Correlation analysis showed that PRs for type II diabetes among both J-Japanese and US-Japanese had a positive association with ASIRs for colon cancer ($r=0.79$, $p<0.01$).

Regarding ethnic variation, ASIRs for colon cancer among US-Japanese were almost the same as those among US-Whites [26.7 and 28.9, and 20.6 and 20.6 per 100,000 population for US-Japanese and US-Whites men and the corresponding women living in Los Angeles (1988-92), in that order]. Furthermore, PRs for type II diabetes among US-Japanese were the highest in three populations including US-Whites [13.4 per 1,000 subjects for both genders (1988-94)]. With elevating PRs for type II diabetes, ASIRs for colon

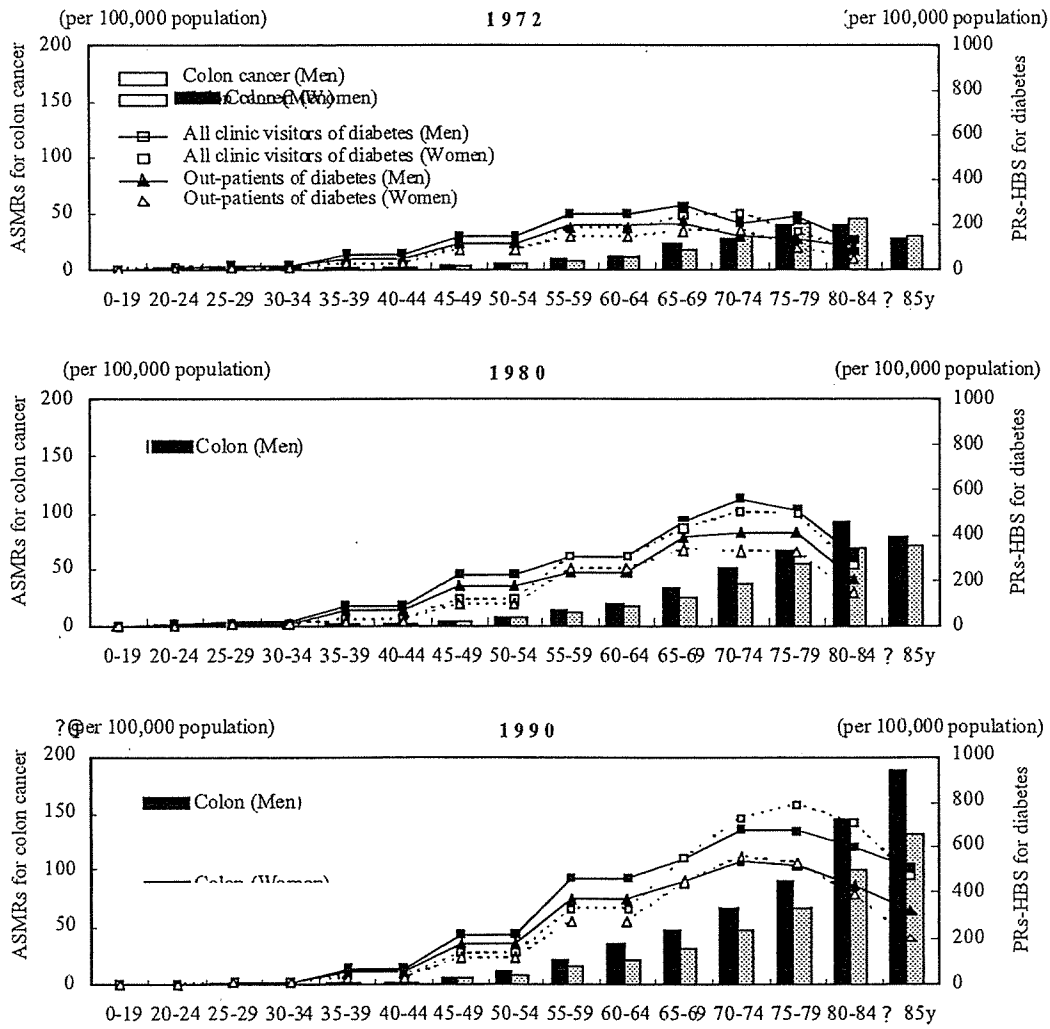

Figure 4. Age-specific Mortality Rates (ASMRs) for Colon Cancer and Prevalence Rates from Hospital Based Surveys (PRs-HBS) for Diabetes among Japanese in Japan by Gender in 1970, 1980 and 1990

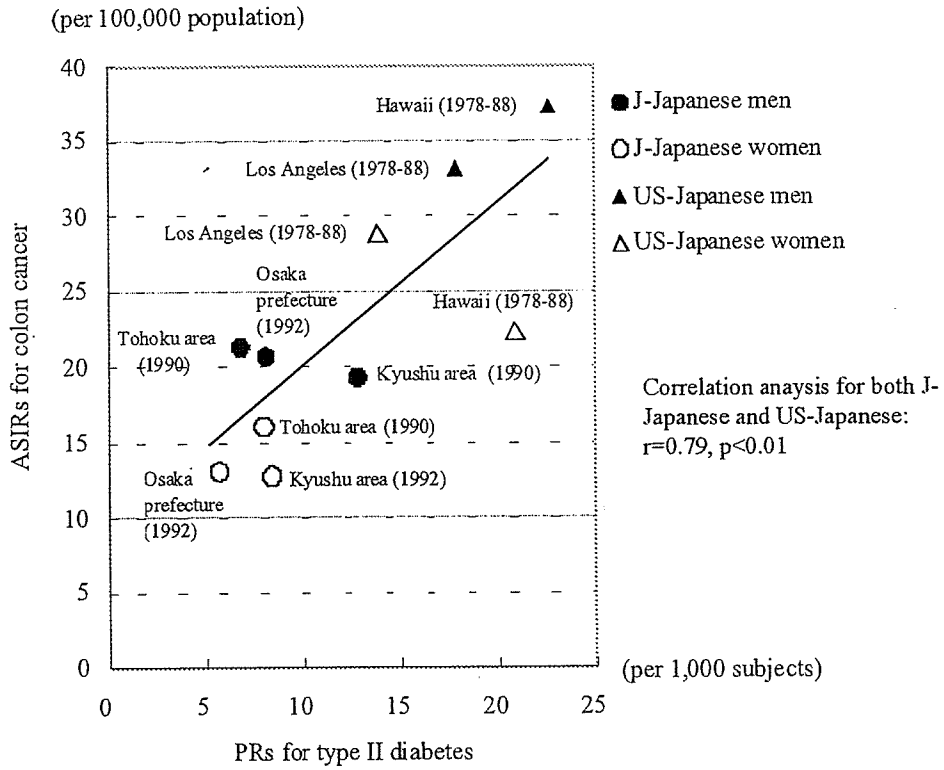

Figure 5. Relation between Prevalence Rates (PRs) for Type II Diabetes and Age-standardized Incidence Rates (ASIRs) for Colon Cancer among Japanese in Japan (J-Japanese) and in the United States (US-Japanese)

cancer among J-Japanese and US-Japanese have been increased, in contrast to changeless or a little reduction of later rates among US-Whites (Data not shown).

Discussion

Although previous studies have suggested that type II diabetes may be a risk factor for colorectal cancer, the epidemic feature of the two diseases have not well documented simultaneously. Here, we described time trends, geographical distributions and host factors, such as age, gender and ethnic variation for both colon cancer and type II diabetes among J-Japanese. A major strength of this study was made allowance for significant changes in food intake among J-Japanese, because dietary habits are clearly very important environmental factors determining risks of colon cancer and type II diabetes.

Time Trends

Among J-Japanese men and women, colorectal cancer is the fourth (11%) and the second (16%) leading cause of cancer deaths, respectively. ASIRs for colorectal cancer are 16-17% and have been elevated among both genders, and especially those for colon cancer are significantly increased for the latest three decades. Regarding food consumption among J-Japanese, dietary intake of milk, meat, eggs and fat/oil had remarkably increased through 1950 to 1970, and then has remained constant. We, therefore, thought that the increment of colon cancer might have a positive causal association with the remarkable changes in food intake. Time-series analysis showed that ratios of fat/total dietary fiber intake through 1947 to 1987 had a highest positive correlation with age-adjusted mortality rates for colon cancer after 16-years delay (Tsuji et al., 1996).

PRs-HBS for diabetes has been increasing abreast with crude mortality rates for colon cancer. Although PRs for type II diabetes may be underestimated because of the lack of an established method to detect this disease readily in large-scale population-based survey, values in 1990 were elevated three times compared with those in 1970. From results of polynominal regression analyses, PRs for type II diabetes in 1970, 1980 and 1990 were estimated to be 16, 27 and 60 per 1,000 population and 9, 16 and 40 per 1000 population among J-Japanese men and women, respectively (Islam et al., 1999). We have to pay enough caution that PRs for type II diabetes and IGT were not adjusted for the world standard population, and diagnostic criteria for type II diabetes were not unified.

Age and Gender

The incidence rates for colon cancer increase with advancing age. ASMRs for colon cancer have increased,

and especially among both men and women aged over 45-49y. Age for colon cancer incidence has shown a tendency to shift the younger age decade by decade. Colon cancer occurs more frequently among men than among women, and sex ratios for colon cancer incidence were 1.2 in 1970s, 1.5 in 1980s and 2.0 in 1990s, respectively. Although there is not sufficient information on age-specific PRs for type II diabetes, considerable increase has been reported in individuals older than 45y, with a peak at 65-69y to 70-74y (Kuzuya et al., 1994). PRs for type II diabetes were higher among men than among women, but in 1990, those were higher among women aged 70-74y, 75-79y and 80-84y than among the corresponding men.

Geographical Differences

From 1969 to 1981, age-adjusted mortality rates of colon cancer, especially for men, were higher in urban areas than in rural areas in line with more rapid change in lifestyle in city communities (Tajima et al., 1985). Recently, ASIRs for colon cancer in Tohoku and Kyushu areas have become the same or rather higher than those in Osaka prefecture, because the food consumption among J-Japanese has become westernized throughout the country and previous geographical differences have disappeared. Data conducted from the National Nutritional Survey has shown that regional differences for food consumption in Japan were diminished year by year. ASIRs for colon cancer, however, were slightly higher in metropolitan cities than in other areas (data not shown). Regarding available indicators of registration completeness and the validity of the diagnostic information for colon cancer in 1988-92, the percentage of cases with diagnosis based on death certificate information only, the ratio of death versus incidence registered, and the percentage of cases with morphological verification of diagnosis among both genders were as follows; 8-10%, 47-54 and 73-76% for Osaka prefecture, 15-19%, 49-59 and 63-70% for Saga prefecture, 9-11%, 43-47 and 78-83% for Yamagata prefecture, 0%, unobtainable and 95-98% for US-Japanese in Los Angeles, and 1%, 48 and 96-98% for US-Whites in Los Angeles, respectively (Parkin et al., 1997). Like ASIRs for colon cancer, PRs for type II diabetes and IGT have been increased in all areas of Japan (data not shown), the validity of the diagnostic information for type II diabetes were adequately not evaluated.

Varieties among Ethnic Groups

Studies of migrants are very important for determination of host and environmental factors. Over much of the latest three decades, ASIRs for colon cancer among US-Japanese were almost the same as those among US-Whites. PRs of type II diabetes and IGT among US-Japanese were also higher than those among J-Japanese, and were the highest in three populations. Several reports have shown ASIRs for colon cancer and PRs for type II diabetes to be higher among US-Japanese Issei (first-generation) than among J-Japanese, and higher among US-Japanese Nisei than among US-Whites (Tokudome, 1996; King et al., 1993). Dietary analysis have reported that US-Japanese Nisei men with diabetes consumed significantly greater amount of animal fat and animal protein than normal men, but energy intake was similar (Fujimoto et al., 1989). The same was the case for Brazilian-Japanese (Tsugane et al., 1989). Recently, ASIRs for colon cancer among US-Japanese were higher than those among US-Whites (27.7 and 26.1, and 21.8 and 19.7 per 100,000 population among US-Japanese and US-Whites men and the corresponding women in Los Angeles (1993-97), in that order (Parkin et al., 2002).

In 1975-93, PRs for type II diabetes and IGT adjusted for the world standard population were reported to be 10.1% and 17.3% among J-Japanese men aged 40-74y, and 6.0% and 15.8% among their female counterparts (Broder, 1993). Those rates among US-Whites aged 40-74y were reported to be 11.4% and 15.6% in 1976-80, and 14.3% and 15.6% in 1988-94, respectively (Harris et al., 1998). PRs for type II diabetes among J-Japanese men and women are moderate compared to levels in other population of the world, whereas PRs for IGT have been ranked moderate for men and high-moderate for women (Broder, 1993). Sasaki et al (1998) have reported that PRs for diabetes and IGT among US-Whites were almost same levels, but PRs for IGT among J-Japanese and US-Japanese were about 1.5 times higher than PRs for diabetes. We speculate that this reason may be not only changes in lifestyle factors such as dietary habits, but also interactions with Japanese inherent genetic predispositions with regard to the system for regulation of circulating glucose or abilities of metabolizing enzymes acting on meat and fat/oil may be operating.

Association between Colon Cancer and Diabetes

On this correlation analysis, we demonstrated that PRs for type II diabetes had a positive association with ASIRs for colon cancer among both J-Japanese and US-Japanese. In three case-control studies among J-Japanese men, type II diabetes demonstrated positive associations with colon adenomas (Kono et al., 1998; Nishi et al., 2001; Marugame et al., 2002). The prevalence and history of diabetes as the risk factor of colorectal cancer have been documented in a number of case-control and large-scale cohort studies (La Vecchia et al., 1991; 1997; Hardell et al., 1995; Le Marchand et al., 1997; Will et al., 1998; Hu et al., 1999; Nilsen and Vatten, 2001; Levi et al., 2002). Type II diabetes and plasma insulin level demonstrated positive associations with colorectal cancer in two reports as follows: 1) a long-term and large-scale cohort study for diabetes patients at baseline (Weiderpass et al., 1997), and 2) a study for persons aged 60y and older at baseline with other than heart diseases at an early age (Schoen et al., 1999). From a Nurses' Health Study, the group of Hu firmly concluded that women had diabetes first, and later developed colon cancer (Volkers, 2000).

In four out of five reports, IGT, insulin resistance and plasma levels of glucose or insulin demonstrated positive associations with the incidence and the death for colorectal cancer (Smith et al., 1992; Colangelo et al., 2002; Trevisan

et al., 2001; Nilsen and Vatten, 2001; Schoen et al., 1999). Insulin is one of important growth factors for colonic epithelial cells, and McKeown-Eyssen (1994) and Giovannucci (1995) have suggested that lifestyle factors first lead to insulin resistance and this promotes the development of colon cancer. Many studies has suggested insulin-like growth factor (IGF)-I, IGF binding-protein-3, the ratio of IGF-I/IGF binding protein-3 and C-peptide as biomarkers for colorectal cancer through insulin resistance (Ma et al., 1999; Kaaks et al., 2000; Shandhu et al., 2002). Those were involved in somatic growth, cell proliferation, transformation and p53-dependent apoptosis, IGF-I bioavailability and pancreatic insulin secretion, respectively.

Conclusions

Increment in ASIRs for colon cancer among J-Japanese might be closely associated with the increment in PRs for type II diabetes linked to changes in food intake toward the westernization of the diet. Our study demonstrated a positive association between PRs for type II diabetes and ASIRs for colon cancer among both J-Japanese and US-Japanese. Compared with US-Whites, we speculate that J-Japanese and US-Japanese may have low resistance against both colon cancer and type II diabetes due to their responses to common risk factors such as meat and oil/fat. In future research, we should encourage evaluation of colon cancer in association with PRs for type II diabetes and make good use of the findings for primary prevention by lifestyle modification.

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References

Broder S (1993). Perspectives on cancer in Japan and the United States. *Jpn J Cancer Res*, **84**, 821-30.

Bruce WR, Wolever TMS, Giacca A (2000). Mechanisms linking diet and colorectal caner: The possible role of insulin resistance. *Nutr Cancer*, **37**, 19-26.

Colangelo LA, Gapstur SM, Gann PH, Dyer AR, Liu K (2002). Colorectal cancer mortality and factors related to the insulin resistance syndrome. *Cancer Epidemiol Biomark Prev*, **11**, 385-91.

Fujimoto WY (1992). The growing prevalence of non-insulin-dependent diabetes in migrant Asian populations and its implications for Asia. *Diabetes Res Clin Pract*, **15**, 167-83.

Fujimoto WY, Bergstrom RW, Boyko EJ, et al (1994). Diabetes and diabetes risk factors in second- and third-generation Japanese Americans in Seattle, Washington. *Diabetes Res Clin Pract*, **24 (Suppl)**, 43-52.

Fujimoto WY, Bergstrom RW, Newell-Morris L, Leonetti DL (1989). Nature and nurture in the etiology of type 2 diabetes mellitus in Japanese Americans. *Diabetes Metab Rev*, **5**, 607-25.

Giovannucci E (1995). Insulin and colon cancer. *Cancer Causes Control*, **6**, 164-79.

Giovannucci E (2001). Insulin, insulin-like growth factors and colon cancer: a review of the evidence. *J Nutr*, **131 (Suppl)**, 3109-29.

Hara H, Egusa G, Yamakido M Kawate R (1994). The high prevalence of diabetes mellitus and hyperinsulinemia among the Japanese-Americans living in Hawaii and Los Angeles. *Diabetes Res Clin Pract*, **24 (Suppl)**, S37-42.

Hardell L, Fredrikson M, Axelson O (1995). Case-control study on colon cancer regarding previous diseases and drug intake. *Int J Oncol*, **8**, 439-44.

Harris MI, Flegal KM, Cowie CC, et al (1998). Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. *Diabetes Care*, **21**, 518-24.

Hu FB, Manson JE, Liu S, et al (1999). Prospective study of adult onset diabetes mellitus (type 2) and risk of colorectal cancer in women. *J Natl Cancer Inst*, **91**, 542-7.

Islam MM, Horibe H, Kobayashi F (1999). Current trend in prevalence of diabetes mellitus in Japan, 1964-1992. *J Epidemiol*, **9**, 155-62.

Kaaks R, Toniolo P, Akhmedkhanov A, et al (2000). Serum C-peptide, insulin-like growth factor (IGF)-I, IGF-binding proteins, and colorectal cancer risk in women. *J Natl Cancer Inst*, **92**, 1592-600.

King H, Aubert RE, Herman WH (1998). Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. *Diabetes Care*, **21**, 1414-31.

rieve&db=PubMed&list_uids=8123057&dopt=Abstracté King H, Rewers M (1993). Global estimates for prevalence of diabetes mellitus and impaired glucose tolerance in adults. WHO Ad Hoc Diabetes Reporting Group. *Diabetes Care*, **16**, 157-77.

Kono S, Honjo S, Todoroki I, et al (1998). Glucose intorelance and adenomas of the sigmoid colon in Japanese men (Japan). *Cancer Causes Control*, **9**, 441-6.

Kuroishi T, Hirose K, Tajima K, Tominaga S (1997). Cancer mortality in Japan (1950-1995). *Gann Monogr Cancer Res*, **47**, 1-82.

Kuzuya T (1994). Prevalence of diabetes mellitus in Japan compiled from literature. *Diabetes Res Clin Pract*, **24 (Suppl)**, 15-21.

La Vecchia C, D'Avanzo B, Negri E, Franceschi S (1991). History of selected diseases and the risk of colorectal cancer. *Eur J Cancer*, **27**, 582-6.

La Vecchia C, Negri E, Decarli A, Franceschi S (1997). Diabetes mellitus and the risk of primary liver cancer. *Int J Cancer*, **73**, 204-7.

Le Marchand L, Wilkens LR, Kolonel LN, Hankin JH, Lyu LC (1997). Associations of sedentary lifestyle, obesity, smoking, alcohol use, and diabetes with the risk of colorectal cancer. *Cancer Res*, **57**, 4787-94.

Levi F, Pasche C, Lucchini F, La Vecchia C (2002). Diabetes mellitus, family history, and colorectal cancer. *J Epidemiol Community Health*, **56**, 479-80.

Ma J, Pollak MN, Giovannucci E, et al (1999). Prospective study of colorectal cancer risk in men and plasma levels of insulin-

like growth factor (IGF)-I and IGF-binding protein-3. *J Natl Cancer Inst*, **91**, 620-5.
Marugame T, Lee K, Eguchi H, et al (2002). Relation of impaired glucose tolerance and diabetes mellitus to colorectal adenomas in Japan. *Cancer Causes Control*, **13**, 917-21.
McKeown-Eyssen G (1994). Epidemiology of colorectal cancer revisited: are serum triglycerides and/or plasma glucose associated with risk? *Cancer Epidemiol Biomark Prev*, **3**, 687-95.
Ministry of Health and Welfare of Japan, Health and Welfare Statistics and Information Department (1995; 2002), Journal of Health and Welfare Statistics, 42; 49. Tokyo: Health and Welfare Statistics Association. (in Japanese)
Ministry of Health and Welfare of Japan, Statistics and Information Department Minister's Secretariat (1974; 1982; 1992), Patients survey 1972; 1980; 1990. Tokyo: Health and Welfare Statistics Association. (in Japanese)
Ministry of Health, Labor and Welfare, Division of Health and Nutrition (1999; 2002), Kokumin-Eiyo-no-Genjo (Current Status of National Nutrition) 1997; 2000, Tokyo: Dai-ichi Shuppann. (in Japanese)
Mori M, Saitoh S, Takagi S, et al (2000). A review of cohort studies on the association between history of diabetes mellitus and occurrence of cancer. *Asian Pac J Cancer Prev*, **1**, 269-76.
Muir C, Waterhouse J, Mack T, Powell J, Whelan S (1987). Cancer Incidence in Five Continents V. No.88. Lyon: IARC.
Nilsen TIL, Vatten LJ (2001). Prospective study of colorectal cancer risk and physical activity, diabetes, blood glucose and BMI: exploring the hyperinsulinaemia hypothesis. *Brit J Cancer*, **84**, 417-22.
Nishii T, Kono S, Abe H, et al (2001). Glucose intolerance, plasma insulin levels, and colorectal adenomas in Japanese men. *Jpn J Cancer Res*, **92**, 836-40.
Parkin DM, Muir CS, Whelan SL, et al (1992). Cancer Incidence in Five Continents VI. No.120. Lyon: IARC.
Parkin DM, Whelan SL, Ferlay J, Raymond L, Young J (1997). Cancer Incidence in Five Continents VII. No.143. Lyon: IARC.
Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB (2002). Cancer Incidence in Five Continents VIII. No.155. Lyon: IARC.
The Research Group for Population-based Cancer Registration in Japan (1990; 1992). Hanai A.
Sasaki A, Tominaga M, Eguchi H, et al (1998). Comparison of the prevalence of diabetes mellitus and impaired glucose tolerance in Japan and other countries. *J Jpn Diab Soc*, **41**, 355-62. (in Japanese)
Schoen RE, Tangen CM, Kuller LH, et al (1999). Increased blood glucose and insulin, body size, and incident colorectal cancer. *J Natl Cancer Inst*, **91**, 1147-54.
Shandhu MS, Dunger DB, Giovannucci EL (2002). Insulin, insulin-like growth factor-I (IGF-I), IGF binding proteins, their biologic interactions, and colorectal cancer. *J Natl Cancer Inst*, **94**, 972-80.
Smith GD, Egger M, Shipley MJ, Marmot MG (1992). Post-challenge glucose concentration, impaired glucose tolerance, diabetes, and cancer mortality in men. *Am J Epidemiol*, **136**, 1110-4.
Tajima K, Hirose K, Nakagawa N, Kuroishi T, Tominaga S (1985). Urban-rural difference in the trend of colorectal cancer mortality with special reference to the subsites of colon cancer in Japan. *Jpn J Cancer Res* (Gann), **76**, 717-28.
Tajima K, Tominaga S (1985). Dietary habits and gastro-intestinal cancers: a comparative case-control study of stomach and large intestinal cancers in Nagoya. *Jpn J Cancer Res* (Gann), **76**, 705-16.
Terao A, Konishi M, Baba S, Mannami T (1997). Prevalence of glucose intolerance, diabetes mellitus, and high serum insulin levels in a Japanese urban population. *Nippon Koshu Eisei Zasshi*, **44**, 283-91. (in Japanese)
Tokudome S (1996). Frequency and distribution of cancer and interaction between host and environmental factors. *Gann Monogr Cancer Res*, **44**, 21-8.
Tominaga S, Kuroishi T (1997). An ecological study on diet/nutrition and cancer in Japan. *Int J Cancer*, 10 (Suppl), 2-6.
Trevisan M, Liu J, Muti P, et al (2001). Markers of insulin resistance and colorectal cancer mortality. *Cancer Epidemiol Biomark Prev*, **10**, 937-41.
Tsugane S, Gotlieb SL, Laurenti R, Souza JM, Watanabe S (1989). Mortality and cause of death among first-generation Japanese in Sao Paulo, Brazil. *Int J Epidemiol*, **18**, 647-51.
Tsuji K, Harashima E, Nakagawa Y, Urata G, Shirataka M (1996). Time-lag effect of dietary fiber and fat intake ratio on Japanese colon cancer mortality. *Biomed Environ Sci*, **9**, 223-8.
Volkers N (2000). Diabetes and Cancer: Scientists search for a possible link. *J Natl Cancer Inst*, **92**, 192-4.
Weiderpass E, Gridley G, Nyren O, et al (1997). Diabetes mellitus and risk of large bowel cancer. *J Natl Cancer Inst*, **89**, 660-1.
Will JC, Galuska DA, Vinicor F, Calle EE (1998). Colorectal cancer: Another complication of diabetes mellitus? *Am J Epidemiol*, **147**, 816-25.

RESEARCH COMMUNICATION

Development of a Data-based Short Food Frequency Questionnaire for Assessing Nutrient Intake by Middle-aged Japanese

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Abstract

Objective: Development of a data-based short food frequency questionnaire (FFQ) for evaluating intake of nutrients by middle-aged Japanese. Methods: Of 102 foods listed in the formerly developed semi-quantitative FFQ, foods having similar nutrient contents were combined into 72 foods/food groups by research dietitians. Nutrient contents were computed by multiplying the weight of foods consumed and its nutrient contents. Next, a cumulative multiple regression coefficient up to 0.85 was applied, and 47 foods/food groups were chosen for a brief FFQ for assessing intake of 21 nutrients including energy, protein, fat, carbohydrate, vitamins, minerals, and dietary fibers. Results: The 47 foods/food groups comprised rice, bread and noodles (3), margarine/butter (2), eggs (1), milk and dairy products (2), soybean and soybean products (3), miso-soup (1), meat including beef, pork and chicken (4), fish (3), other fish, shellfish and fish products (4), green-yellow vegetables (5), other vegetables and mushrooms (3), edible roots (4), seaweeds (1), mayonnaise (1), fried dishes (2), seeds (1), fruit (2), beverages, including alcohol (3), and confectioneries (2). Conclusions: The evidence-based short FFQ efficiently covered the intake of 21 nutrients, and may be competent to rank the middle-aged general public Japanese according to intake of nutrients.

Key Words: food frequency questionnaire - food intake - nutrient intake - multiple regression - weighed diet record

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Introduction

In order to assess population/individual intake of foods and nutrients, several methods are available, including the diet record (DR) /weighed diet record (WDR), 24 hour recall, and duplicate method, as well as biomarker approaches, taking advantage of blood and urine parameters (Margetts and Nelson, 1990; Thompson and Byers, 1994; Willett, 1998). There are strengths and weaknesses for each procedure. Selection criteria may depend on the nature of the protocol, including the aim, time frame, dietary elements and subjects studied. For example, 24 hour recall or DR/WDR may be chosen for evaluating *population* values. For collecting information on *individual* habitual intake of foods/food groups for cohort and case-control studies, the food frequency questionnaire (FFQ)/semi-quantitative food frequency questionnaire (SQFFQ) is more often employed.

Recently, using multiple regression analysis (MRA) (Byers et al., 1985; Hankin et al., 1968; Overvad et al., 1991) as well as contribution analysis (CA) (Block et al., 1985; Freudenheim et al., 1993), we designed an evidence-based SQFFQ on the basis of WDRs from 351 participants (Tokudome et al., 1998). Calibration/validation and reproducibility studies in terms of the food list, intake frequency, and portion size were executed, as detailed elsewhere (Imaeda et al., 2002; Tokudome et al., 2001); however, the SQFFQ was primarily designed for the JADE (Japanese Dietitians' Epidemiologic) Study. For epidemiologic studies of the general middle-aged populace, we here evolved a self-administered brief FFQ by MRA.

Subjects and Methods

Subjects and Selection of Foods/Food Groups

The subjects and methods for developing the SQFFQ were described elsewhere (Tokudome et al., 1998). In brief, nutrient intake by food was computed by multiplying the food intake (in grams) and the nutrient content (per gram)

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of food as listed in the Standard Tables of Food Composition, Version 4 and the Follow-up of the Standard Tables of Food Composition, Version 4 (Resources Council, 1982; ibid, 1992). In all, 102 foods/food groups were listed in the SQFFQ. Those foods/food groups having similar nutrient contents were combined into 72 foods/food groups by research nutritionists (Figure 1). Next, forward MRA was performed with total intake of specific nutrients as the dependent variables and overall amounts of nutrients from 72 foods/food groups as the independent variables from 351 individuals (Byers et al., 1985; Hankin et al., 1968; Overvad et al., 1991). Foods/food groups with a cumulative multiple regression coefficient/cumulative R^2 up to 0.85 were chosen (SAS, 1999).

Nutrients Selected

The following 21 nutrients were selected: energy, protein, fat, carbohydrate, vitamins (including carotene, and vitamins A, C, D and E), minerals (calcium and iron) and total dietary fiber (TDF) (including soluble DF and insoluble DF). The fat was divided into cholesterol, saturated fatty acid, mono-unsaturated fatty acid (including oleic acid), poly-unsaturated fatty acid (PUFA), n-6 PUFA, n-3 PUFA, and n-3 HUFA (including eicosapentaenoic acid [EPA, 20: 5n-3] and docosahexaenoic acid [DHA, 22: 6n-3]).

Food Intake Frequency and Weight Assigned

Food intake frequencies were classified into eight categories: that is, never or seldom, 1-3 times per month, 1-2 times per week, 3-4 times per week, 5-6 times per week, once a day, twice a day, and 3 or more times a day, and weights assigned were shown in Table 1.

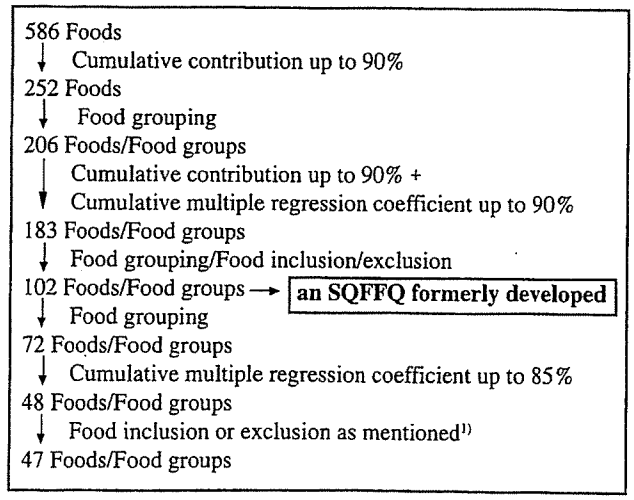

Figure 1. Flow Chart for Development of the Short FFQ

[1)] Stirr-fried dishes were grouped into fried dishes. Fried dish was categorized into deep fried and light fried because the oil portion size differs. For *Tofu*, *Hiyayakko* (chilled *tofu*) and *Yu-dofu* (hot *tofu*) were inquired separately but *Abura-age* (fried *tofu*) was included in *Miso* soup. Cookie and cake were deleted because they were miscategorized into Western style confectioneries. Sesame was deleted because it is difficult to estimate portion size. Green tea was included because it typically contains flavonoids and folate.

Portion Size

The mean portion size was calculated for respective foods from the one-day WDRs, and typical/standard values and/or natural units from the literature were also cited for evaluating intake of nutrients of interest.

Staple Foods

Rice, bread and noodles are the Japanese staple foods which provide most nutrients. They were here investigated in a special manner: namely, taking into account the intake frequency and portion size for breakfast, lunch, and supper, separately. The intake frequencies were categorized as follows: never or seldom, 1-3 times per month, 1-2 times per week, 3-4 times per week, 5-6 times per week and daily. The portion size was also determined in an open-ended manner..

Lifestyle Items

In addition, lifestyle items were included in the questionnaire, with parameters such as smoking, drinking, physical exercise, sleeping hours, and intake of vitamin and mineral supplements, as well as functional (or designer) foods.

Results

Number of Foods/Food Groups Contributing to Nutrients Selected

The foods/food groups contributing to the nutrients selected are listed in Table 2. For example, the n-3 HUFAs and vitamin D were each provided by specific foods/food groups, while iron was contributed by a total of 17 foods/food groups.

List of Foods/Food Groups

The 47 foods/food groups were included in the questionnaire: rice, bread and noodles (3), margarine/butter (2), eggs (1), milk and dairy products (2), soybean and soybean products (3), *miso*-soup (1), meat including beef, pork and chicken (4), fish (3), other fish, shellfish and fish products (4), green-yellow vegetables (5), other vegetables and mushrooms (3), edible roots (4), seaweeds (1), mayonnaise (1), fried dishes (2), seeds (1), fruit (2), beverages, including alcohol (3), and confectioneries (2) (Appendix).

Table 1. Food Intake Frequency and Weight Assigned

Frequency	Weight
Never or seldom	0
1-3 times per month	0.1
1-2 times per week	0.2
3-4 times per week	0.5
5-6 times per week	0.8
Once a day	1
Twice a day	2
Three or more times a day	3

Discussion

Following a systematic data-based procedure, we chose 47 foods/food groups for categorizing people according to 21 nutrients estimated. The questionnaire is concise and brief, and it could be self-administered to the general public. The food list was arranged considering Japanese dietary habits and lifestyle. Staple foods, for example, were listed first and related foods/food groups were itemized adjacent to one another. Although we included inquiries about intake of vitamin and mineral supplements and functional (or designer) foods, data on type (liquid, granule, tablet), quantity (portion size) and frequency were not sufficient to validly estimate consumption. Vitamin and mineral supplements are actually not so popular in Japan; however, we should take into account this drawback, particularly when executing relevant studies.

For choosing foods/food groups, there are two contrasting methods (Margetts and Nelson, 1990; Mark et al., 1996; Stryker et al., 1991; Thompson and Byers, 1994; Willett, 1998): one is based on CA (Block et al., 1985; Freudenheim et al., 1993), and the other on MRA (Byers et al., 1985; Hankin et al., 1968; Overvad et al., 1991). Each method has its respective advantages and disadvantages. The former approach is based on absolute intake of nutrients. Thus, the procedure is especially suitable for studies to clarify the association with energy intake and energy-adjusted intake of nutrients. The latter is based on the variance of nutrient intakes. The cumulative R^2 can generally be explained by a smaller number of foods than the cumulative % contribution. Substantial foods/food groups selected by MRA were covered by those chosen by CA; in addition, specific foods were chosen by MRA. Thus, the latter may be efficient for categorizing individuals, although it is unsuitable to compute absolute nutrient levels.

Table 2. Number of Foods/food Groups Contributing to 21 Nutrients with a Cumulative R^2 up to 0.85

Nutrient	Cumulative R^2	Number of food groups
Energy	0.861	14
Protein	0.858	15
Fat	0.856	11
Cholesterol	0.868	3
SFAs	0.867	8
MUFAs	0.873	7
PUFAs	0.864	8
n-6 PUFAs	0.872	7
n-3 PUFAs	0.904	4
n-3 HUFAs	0.872	1
Carbohydrate	0.869	7
Calcium (Ca)	0.852	10
Iron (Fe)	0.851	17
Carotene	0.928	2
Vitamin A	0.933	4
Vitamin C	0.894	7
Vitamin D	0.942	1
Vitamin E	0.856	9
TDF	0.855	13
SDF	0.854	10
IDF	0.866	13

Admittedly, the sample size for the one-day WDRs was not large, and the survey was performed in a selected area and in a specific season in Japan. It is known that within-individual variation is greater than inter-individual variation (Beaton et al.,1983; Margetts and Nelson, 1990; Mark et al., 1996; Nelson et al., 1989; Stryker et al., 1991; Thompson and Byers, 1994; Tokudome et al., 2002; Willett, 1998); however, we were here naturally unable to estimate inter- and within-individual variation on the basis of one-day WDRs. Although Japan is relatively small country in terms of area, the length from the North (latitude ca 45 degree) to the South (latitude ca 25 degree) is rather great. Accordingly there are wide varieties of foods consumed even though mass-transportation systems have been developed throughout the country. Furthermore, there are four seasons in Japan and seasonal variations in intake of foods, vegetables and fruit, in particular (Shahar et al., 1999; Tokudome et al., 2003; Ziegler et al., 1987). We should therefore take into account these variations in evaluating intake of foods and nutrients.

In epidemiological studies, validity and reproducibility are two important components. Validity is defined as being free from bias, and reproducibility as being low in random variation. Those should be evaluated prior to actually applying an FFQ for investigations, including case-control and cohort studies. We thus propose relative validation of the present FFQ versus 7 day WDRs and blood parameters. With the latter, we would validate the FFQ against concentrations of plasma fatty acids because we are particularly interested in lifestyle-related diseases, including cancers, cerebrovascular disease and chronic heart disease, related to excess/imbalanced intake of fats/oils. Reproducibility studies are now underway with the public in community and company employee settings.

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References

Beaton GH, Milner J, McGuire V, Feather TE, Little JA (1983). Source of variance in 24-hour dietary recall data: implications for nutrition study design and interpretation. Carbohydrate sources, vitamins and minerals. *Am J Clin Nutr*, **37**, 986-95.

Block G, Dresser CM, Hartman AM, Carrol MD (1985). Nutrient sources in the American diet: quantitative data from the NHANES II survey. I. Vitamins and minerals. *Am J Epidemiol*, **122**, 13-26.

Byers T, Marshall J, Fiedler R, Zielenzny M, Graham S (1985). Assessing nutrients intake with an abbreviated dietary interview.