Table 2 Trends for sex-specific age-adjusted mean dietary intakes of β-carotene, retinol, vitamin C and vitamin E by food group in men and women aged 40–69 years in Ikawa and Kyowa, Japan

Nutrient/sex/ community	Survey years	Green/yellow vegetables		Other vegetables		Fruits		Cereals		Potatoes		Algae		Fish/shellfish		Meats		Eggs		Milk/dairy products		Fats/oils		Green tea	
		Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
β-Carotene (μg/d)																									
Men																									
Ikawa	1974–1977	4057	195·5	59	7·5	186	27·8	0·0	0·86	0·1	0·09	149	12·1	3·2	1·28	–		4·4	0·35	2·8	0·62	0·4	0·24		
	1978–1981	4078	256·2	55	9·9	145	36·5	0·0	1·13	0·3	0·12	111	15·9	1·9	1·68	–		5·0	0·46	5·3	0·82	0·4	0·32		
	1982–1985	5119***	176·7	77	6·8	103	25·1	0·0	0·78	0·3	0·08	152	11·0	3·4	1·16	–		6·2***	0·32	5·6**	0·56	0·6	0·22		
	1986–1989	4292	194·3	88*	7·5	135	27·6	1·0	0·86	0·1	0·09	84***	12·0	3·1	1·28	–		6·5***	0·35	5·6**	0·62	0·7	0·24		
	1990–1993	4476	210·7	83	8·1	128	30·0	4·4**	0·93	0·1	0·10	50***	13·1	6·4	1·38	–		6·0**	0·38	7·6***	0·67	0·8	0·26		
	1994–1997	4766	204·9	99**	7·9	125	29·2	2·6	0·90	0·2	0·10	51***	12·7	3·3	1·35	–		5·5	0·37	8·7***	0·65	0·4	0·25	0	0
	1998–2000	4187	227·2	93*	8·8	44**	32·3	2·0	1·00	0·2	0·11	96*	14·1	2·6	1·49	–		5·3	0·41	8·1***	0·72	1·5**	0·28	0	0
Kyowa	1982–1986	2500	107·1	81	5·1	1004	51·9	2·2	1·13	2·3	0·22	104	11·0	1·9	0·80	–		4·4	0·24	4·4	0·48	1·4	0·30		
	1990–1993	2147	142·0	93	6·7	735**	68·8	3·8	1·49	1·8	0·30	131	14·6	3·8	1·06	–		5·3*	0·32	5·6	0·63	2·4	0·40		
	1994–1997	2550	137·3	92	6·5	837	66·6	4·3	1·44	2·1	0·29	91	14·1	4·8	1·02	–		4·9	0·31	6·2	0·61	1·7	0·39	0	3
	1998–2001	2668	130·2	110***	6·1	739**	63·1	5·3	1·37	2·2	0·27	112	13·4	4·8	0·97	–		4·4	0·29	6·1	0·58	1·5	0·37	5	3
Women																									
Ikawa	1974–1977	3572	199·9	79	7·9	312	33·0	0·6	0·76	0·2	0·20	135	10·5	0·6	1·89	–		4·1	0·36	1·7	0·62	0·3	0·37		
	1978–1981	3843	275·6	67	10·9	228	45·5	0·2	1·04	1·1*	0·28	154	14·5	6·7	2·61	–		5·7*	0·49	3·8	0·86	1·0	0·51		
	1982–1985	4582**	191·5	105	7·6	200	31·6	0·8	0·72	0·8	0·19	140	10·1	4·2	1·81	–		5·1	0·34	5·0***	0·60	0·5	0·35		
	1986–1989	4200	194·1	86	7·7	170*	32·0	0·2	0·73	0·5	0·19	66***	10·2	5·2	1·84	–		5·5*	0·35	5·8***	0·60	1·6	0·36		
	1990–1993	4520**	175·9	100	7·0	179*	29·0	1·4	0·66	0·3	0·18	55***	9·2	5·2	1·66	–		5·3*	0·31	8·3***	0·55	1·4	0·32		
	1994–1997	4867***	177·5	103	7·0	144***	29·3	1·1	0·67	0·4	0·18	50***	9·3	2·7	1·68	–		5·2	0·32	9·4***	0·55	1·4	0·33	2	3
	1998–2000	4996***	203·5	91	8·0	103***	33·6	2·1	0·77	0·5	0·20	66***	10·7	4·0	1·93	–		3·9	0·36	8·4***	0·63	2·3***	0·38	5	4
Kyowa	1982–1986	3049	112·4	87	5·1	1208	54·5	1·1	0·90	3·8	0·31	114	13·7	1·2	0·40	–		4·6	0·23	4·9	0·51	2·0	0·34		
	1990–1993	2749	129·2	94	5·9	1165	62·7	3·1	1·03	3·5	0·36	152	15·7	2·9*	0·46	–		5·1	0·26	8·4***	0·59	2·0	0·39		
	1994–1997	3234	127·0	107*	5·8	1089	61·6	3·6	1·01	2·6*	0·35	124	15·4	2·9*	0·46	–		3·9	0·25	7·3**	0·58	1·6	0·39	1	0
	1998–2001	3099	124·8	108*	5·7	1134	60·6	2·6	1·00	3·4	0·35	144	15·2	1·8	0·45	–		4·3	0·25	7·9***	0·57	2·8	0·38	0	0
Retinol (μg/d)																									
Men																									
Ikawa	1974–1977	–		–		–		–		–		–		45	7·2	27	11·7	36	2·9	17	2·8	1·6	1·36		
	1978–1981	–		–		–		–		–		–		41	9·5	23	15·4	41	3·8	28	3·7	2·1	1·78		
	1982–1985	–		–		–		–		–		–		37	6·5	20	10·6	52***	2·6	32***	2·6	3·1	1·23		
	1986–1989	–		–		–		–		–		–		51	7·2	21	11·7	53***	2·9	34***	2·8	4·2	1·35		
	1990–1993	–		–		–		–		–		–		53	7·8	46	12·6	50**	3·1	43***	3·1	4·3	1·47		
	1994–1997	–		–		–		–		–		–		55	7·6	11	12·3	45	3·0	48***	3·0	2·1	1·42	–	
	1998–2000	–		–		–		–		–		–		83**	8·4	21	13·6	44	3·3	39***	3·3	7·9*	1·58	–	
Kyowa	1982–1986	–		–		–		–		–		–		39	6·0	9	2·5	36	2·0	24	1·8	7·7	1·82		
	1990–1993	–		–		–		–		–		–		62	7·9	13	3·4	44	2·6	31*	2·4	13·2	2·41		
	1994–1997	–		–		–		–		–		–		52	7·7	6	3·3	41	2·6	32**	2·3	9·4	2·33	–	
	1998–2001	–		–		–		–		–		–		47	7·3	6	3·1	37	2·4	27	2·2	8·2	2·21	–	
Women																									
Ikawa	1974–1977	–		–		–		–		–		–		23	7·3	10	13·9	33	2·9	11	2·8	1·2	2·16		
	1978–1981	–		–		–		–		–		–		34	10·1	5	19·1	47	4·0	23*	3·8	6·0	2·98		
	1982–1985	–		–		–		–		–		–		26	7·0	35	13·3	42	2·8	29***	2·7	2·2	2·07		
	1986–1989	–		–		–		–		–		–		40	7·1	25	13·5	45*	2·8	31***	2·7	8·8	2·10		
	1990–1993	–		–		–		–		–		–		30	6·5	26	12·2	43*	2·6	45***	2·4	7·8	1·90		
	1994–1997	–		–		–		–		–		–		49*	6·5	24	12·3	42	2·6	52***	2·5	8·4	1·92	–	
	1998–2000	–		–		–		–		–		–		51*	7·5	16	14·1	32	3·0	47***	2·8	11·9**	2·20	–	
Kyowa	1982–1986	–		–		–		–		–		–		23	5·3	11	3·5	38	1·9	27	2·0	11·3	1·99		
	1990–1993	–		–		–		–		–		–		48**	6·1	7	4·0	42	2·2	38**	2·3	11·0	2·29		
	1994–1997	–		–		–		–		–		–		35	6·0	5	4·0	32	2·1	40***	2·3	7·9	2·25	–	
	1998–2001	–		–		–		–		–		–		32	5·9	12	3·9	36	2·1	37**	2·2	15·3	2·21	–	

Table 2 *Continued*

Nutrient/sex/ community	Survey years	Green/yellow vegetables		Other vegetables		Fruits		Cereals		Potatoes		Algae		Fish/shellfish		Meats		Eggs		Milk/dairy products		Fats/oils		Green tea	
		Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Vitamin C (mg/d)																									
Men																									
Ikawa	1974–1977	33	2·1	15	1·1	19	1·9	–		9·0	0·82	–		–		1·7	0·22	–		–		–			
	1978–1981	36	2·7	19	1·4	24	2·4	–		11·0	1·08	–		–		1·9	0·28	–		–		–			
	1982–1985	58***	1·9	15	1·0	19	1·7	–		4·9*	0·74	–		–		1·7	0·20	–		–		–			
	1986–1989	35	2·0	18	1·1	15	1·8	–		7·7	0·82	–		–		2·0	0·22	–		–		–			
	1990–1993	35	2·2	20**	1·2	13	2·0	–		7·4	0·88	–		–		2·3	0·23	–		–		–			
	1994–1997	39	2·2	20*	1·1	15	1·9	–		9·3	0·86	–		–		2·2	0·23	–		–		–		14	1·1
	1998–2000	40	2·4	20**	1·3	11*	2·2	–		12·4*	0·95	–		–		1·9	0·25	–		–		–		12	1·2
Kyowa	1982–1986	19	1·4	30	1·1	65	3·0	–		10·2	0·72	–		–		2·4	0·23	–		–		–			
	1990–1993	20	1·9	32	1·5	46***	4·0	–		9·2	0·95	–		–		2·9	0·31	–		–		–			
	1994–1997	25*	1·8	34	1·5	54	3·9	–		10·2	0·92	–		–		2·5	0·30	–		–		–		36	1·0
	1998–2001	22	1·7	32	1·4	43***	3·7	–		10·5	0·87	–		–		2·8	0·28	–		–		–		33	0·9
Women												–		–				–		–					
Ikawa	1974–1977	26	2·1	16	1·1	35	2·6	–		9·6	0·89	–		–		0·7	0·19	–		–		–			
	1978–1981	37**	2·9	16	1·5	44	3·6	–		10·5	1·23	–		–		1·2	0·26	–		–		–			
	1982–1985	47***	2·0	15	1·0	37	2·5	–		6·6	0·85	–		–		1·4	0·18	–		–		–			
	1986–1989	35**	2·1	16	1·0	27	2·5	–		7·1	0·86	–		–		1·8***	0·18	–		–		–			
	1990–1993	39***	1·9	21**	0·9	28	2·3	–		8·3	0·78	–		–		2·0***	0·17	–		–		–			
	1994–1997	44***	1·9	22***	0·9	24**	2·3	–		10·4	0·79	–		–		1·8***	0·17	–		–		–		11	0·7
	1998–2000	47***	2·2	23***	1·1	27	2·6	–		13·1*	0·91	–		–		1·8***	0·19	–		–		–		13	0·8
Kyowa	1982–1986	26	1·6	27	1·0	77	3·4	–		13·0	0·80	–		–		2·6	0·21	–		–		–			
	1990–1993	24	1·8	32***	1·1	77	3·9	–		11·4	0·92	–		–		2·3	0·24	–		–		–			
	1994–1997	32	1·8	29	1·1	76	3·8	–		12·0	0·90	–		–		2·7	0·24	–		–		–		32	0·9
	1998–2001	30	1·7	29	1·1	72	3·8	–		12·0	0·89	–		–		2·5	0·23	–		–		–		34	0·8
Vitamin E (mg/d)																									
Men																									
Ikawa	1974–1977	1·78	0·102	0·14	0·030	0·27	0·020	0·43	0·024	–		–		2·06	0·099	0·21	0·015	0·26	0·021	0·04	0·008	0·31	0·042		
	1978–1981	1·59	0·134	0·15	0·039	0·24	0·026	0·38	0·032	–		–		2·03	0·130	0·17	0·020	0·29	0·027	0·08	0·011	0·46	0·055		
	1982–1985	2·99***	0·092	0·32***	0·027	0·23	0·018	0·42	0·022	–		–		1·99	0·090	0·19	0·014	0·37***	0·019	0·09***	0·007	0·55***	0·038		
	1986–1989	2·13	0·101	0·38***	0·030	0·21	0·020	0·39	0·024	–		–		2·03	0·099	0·19	0·015	0·38***	0·021	0·10***	0·008	0·71***	0·042		
	1990–1993	2·12	0·110	0·28**	0·032	0·18*	0·021	0·50	0·026	–		–		2·05	0·107	0·23	0·016	0·36**	0·022	0·13***	0·009	0·64***	0·045		
	1994–1997	2·20*	0·107	0·30**	0·031	0·23	0·021	0·42	0·025	–		–		2·11	0·104	0·19	0·016	0·32	0·022	0·14***	0·009	0·57***	0·044	–	
	1998–2000	1·91	0·119	0·24	0·035	0·19	0·023	0·43	0·028	–		–		1·89	0·116	0·21	0·018	0·31	0·024	0·11***	0·010	0·82***	0·049	–	
Kyowa	1982–1986	0·99	0·055	0·29	0·020	0·41	0·022	0·49	0·024	0·26	0·022	–		1·23	0·058	0·15	0·009	0·26	0·014	0·07	0·005	1·27	0·054		
	1990–1993	0·89	0·074	0·31	0·027	0·34	0·029	0·52	0·031	0·17*	0·029	–		1·47*	0·077	0·18	0·011	0·32*	0·019	0·09*	0·007	1·13	0·071		
	1994–1997	1·09	0·071	0·32	0·026	0·36	0·028	0·50	0·030	0·19	0·028	–		1·41	0·075	0·17	0·011	0·29	0·018	0·09**	0·007	1·32	0·069	–	
	1998–2001	1·05	0·067	0·35	0·024	0·35	0·026	0·45	0·029	0·21	0·026	–		1·22	0·071	0·17	0·010	0·26	0·017	0·08	0·006	1·40	0·065	–	
Women																									
Ikawa	1974–1977	1·35	0·102	0·17	0·024	0·46	0·028	0·42	0·022	0·03	0·015	–		1·63	0·082	0·08	0·010	0·24	0·021	0·03	0·008	0·54	0·050		
	1978–1981	1·63	0·140	0·17	0·033	0·48	0·038	0·28**	0·030	0·10*	0·021	–		1·36	0·113	0·10	0·013	0·33*	0·029	0·07*	0·012	0·70	0·069		
	1982–1985	2·55***	0·097	0·29**	0·023	0·42	0·027	0·30***	0·021	0·06	0·014	–		1·48	0·079	0·13**	0·009	0·30	0·020	0·08***	0·008	0·66	0·048		
	1986–1989	2·08***	0·099	0·33***	0·023	0·37	0·027	0·32***	0·021	0·05	0·015	–		1·46	0·080	0·14***	0·009	0·32*	0·020	0·10***	0·008	0·85***	0·049		
	1990–1993	2·20***	0·089	0·28**	0·021	0·34**	0·024	0·35	0·019	0·02	0·013	–		1·49	0·072	0·13**	0·008	0·31*	0·018	0·13***	0·007	0·86***	0·044		
	1994–1997	2·12***	0·090	0·30***	0·021	0·31***	0·025	0·29***	0·019	0·04	0·013	–		1·60	0·073	0·11	0·008	0·30	0·019	0·15***	0·008	0·76**	0·045	–	
	1998–2000	2·12***	0·103	0·24	0·025	0·33**	0·023	0·34	0·022	0·05	0·015	–		1·42	0·084	0·11	0·010	0·23	0·021	0·13***	0·009	0·83***	0·051	–	
Kyowa	1982–1986	1·28	0·061	0·38	0·024	0·51	0·026	0·38	0·019	0·34	0·024	–		0·82	0·047	0·12	0·007	0·27	0·013	0·08	0·006	1·29	0·053		
	1990–1993	1·10	0·070	0·32	0·027	0·56	0·025	0·35	0·022	0·30	0·028	–		1·16	0·053	0·13	0·008	0·30	0·015	0·11***	0·007	1·23	0·061		
	1994–1997	1·38	0·069	0·33	0·027	0·49	0·025	0·40	0·021	0·23*	0·028	–		1·02***	0·053	0·13	0·007	0·23	0·015	0·12***	0·007	1·31	0·060	–	
	1998–2001	1·32	0·068	0·36	0·026	0·54	0·023	0·35	0·021	0·28	0·027	–		0·92**	0·052	0·13	0·007	0·26	0·015	0·11***	0·006	1·38	0·059	–	

Intake of green tea was not taken into account; intakes of nutrients were evaluated in conditions before cooking.
Mean values were significantly different from those of the first survey: $^{*}P<0·05$, $^{**}P<0·01$, $^{***}P<0·001$.

Ikawa, and did not change substantially among men and women from 1982–1986 to 1990–1993 in Kyowa. Mean intake of retinol from, eggs, milk/dairy products and fats/oils increased among men and women from 1974–1977 to 1998–2000 in Ikawa. In Kyowa, mean intake of retinol from milk/dairy products increased from 1982–1986 to 1990–1993, and then plateaued thereafter.

Mean intake of vitamin C from green/yellow and other vegetables, primary food sources, increased among men and women from 1974–1977 to 1982–1985 and plateaued thereafter in Ikawa, while that from fruits tended to decrease after the 1980s. In Kyowa, mean intake of vitamin C from green/yellow and other vegetables and fruits did not change substantially among men and women from 1982–1986 to 1998–2001.

Mean intake of vitamin E from green/yellow and other vegetables and fats/oils increased among men and women from 1974–1977 to 1982–1985, and plateaued thereafter in Ikawa, while intake from these foods did not change substantially among men and women in Kyowa.

The proportions of β-carotene intake according to food group in the latest survey period (1998–2001 for Ikawa, 1998–2000 for Kyowa) are shown in Fig. 1. The major food sources for β-carotene intake were green/yellow (92–93 %) and other vegetables (1–2 %) and fruits (1–2 %) among men and women in Ikawa, with 68–72 %, 3 % and 20–25 %, respectively, among men and women in Kyowa. The retinol intake comprised 30–41 % from fish/shellfish, 19–22 % from eggs and 19–28 % from milk/dairy products among men and women in Ikawa. The respective proportions in Kyowa were 21–34 %, 24–27 % and 20–24 %.

Vitamin C intake consisted of 35–37 % from green/yellow vegetables, 17–18 % from other vegetables, 10–20 % from fruits and 10–11 % from green tea among men and women in Ikawa. The respective proportions in Kyowa were 15–16 %, 16–22 %, 29–39 % and 19–22 %.

The vitamin E intake comprised 27–31 % from green/yellow vegetables, 3 % from other vegetables, 21–27 % from fish/shellfish and 11–12 % from fats/oils among men and women in Ikawa. The respective proportions in Kyowa were 15–18 %, 6 %, 13–18 % and 20–21 %.

Discussion

The present study of long-term nutritional trends in Japan revealed that both men and women in Ikawa had increased dietary intakes of β-carotene and vitamin C, primarily from green/yellow and other vegetables; increased intake of retinol from fish/shellfish, eggs, milk/dairy products and fats/oils; and increased intake of vitamin E from green/yellow and other vegetables, milk/dairy products and fats/oils between the 1970s and the 1990s. In Kyowa, mean intake of retinol from fish/shellfish and milk/dairy products increased among men and women; while mean intake of vitamin C from fruits decreased among men between the 1980s and the 1990s.

Ikawa comprises areas of plains and mountains where people have traditionally worked mainly on rice farms. New factories for heavy industry were founded in the late 1970s and many farmers changed to work in these factories. According to local government statistics, 67 % of the population worked on farms and 12 % in factories in 1975, but this had changed to 41 % and 42 %, respectively, by 1980. Consequently, the mean income of people in this community increased from the 1970s to the 1980s, which improved eating habits in terms of nutrition. In contrast, Kyowa is located on the plains where a large percentage of people worked on fruit and vegetable farms or for light-industry companies; there have been no substantial changes in industry since the 1980s.

Mean intakes of vitamins A, C and E in Ikawa and Kyowa were similar to those of the national samples in Japan. According to the national nutritional survey[23,24], the daily per capita intake of total vitamin A increased from 1974 (552 μg RE) to 2001 (981 μg RE). The daily per capita intake of vitamin C remained over 100 mg: 120 mg in 1974 and 106 mg in 2001. The daily per capita intake of vitamin E was 8.5 mg in 2001[24].

For ages 30–69 years, the Estimated Average Requirement for total vitamin A is 500–550 μg RE/d for men and 450 μg RE/d for women, and that for vitamin C is 55 mg/d for both sexes. The Adequate Intake of vitamin E is 8–9 mg/d for men and 8 mg/d for women[25]. Therefore, mean intakes of vitamins A and C in the present study samples were higher than the Estimated Average Requirement except for slightly lower vitamin A in Kyowa men. Mean intake of vitamin E was lower than the Adequate Intake among men and women in both communities.

Mean daily intakes of vitamins C among Americans according to the National Health and Nutrition Examination Survey (NHANES) in 1999–2000[26] were 107 mg among men aged 40–59 years, 110 mg among men aged ≥60 years, 91 mg among women aged 40–59 years and 99 mg among women aged ≥60 years. The respective intakes of vitamin E were 10.4 mg, 9.2 mg, 9.1 mg and 7.6 mg. Mean intakes of vitamin A could not be compared with the US data because of different methods of calculation. That report and the present findings suggest that the mean intake of vitamin C around 2000 was similar for men and higher for women, and that the mean intake of vitamin E was lower for both sexes of the Japanese samples than for the US samples.

The strength of the present study lay in the 24 h dietary recall method used in the surveys, with a sample large enough to statistically estimate sex-specific long-term trends. However, our study has several limitations. First, we evaluated nutrient intakes only for raw foods because there was no systematic database available to assess nutrient loss by cooking. Since the survival proportion of vitamins C in vegetables following cooking is approximately 50–90 %[22],

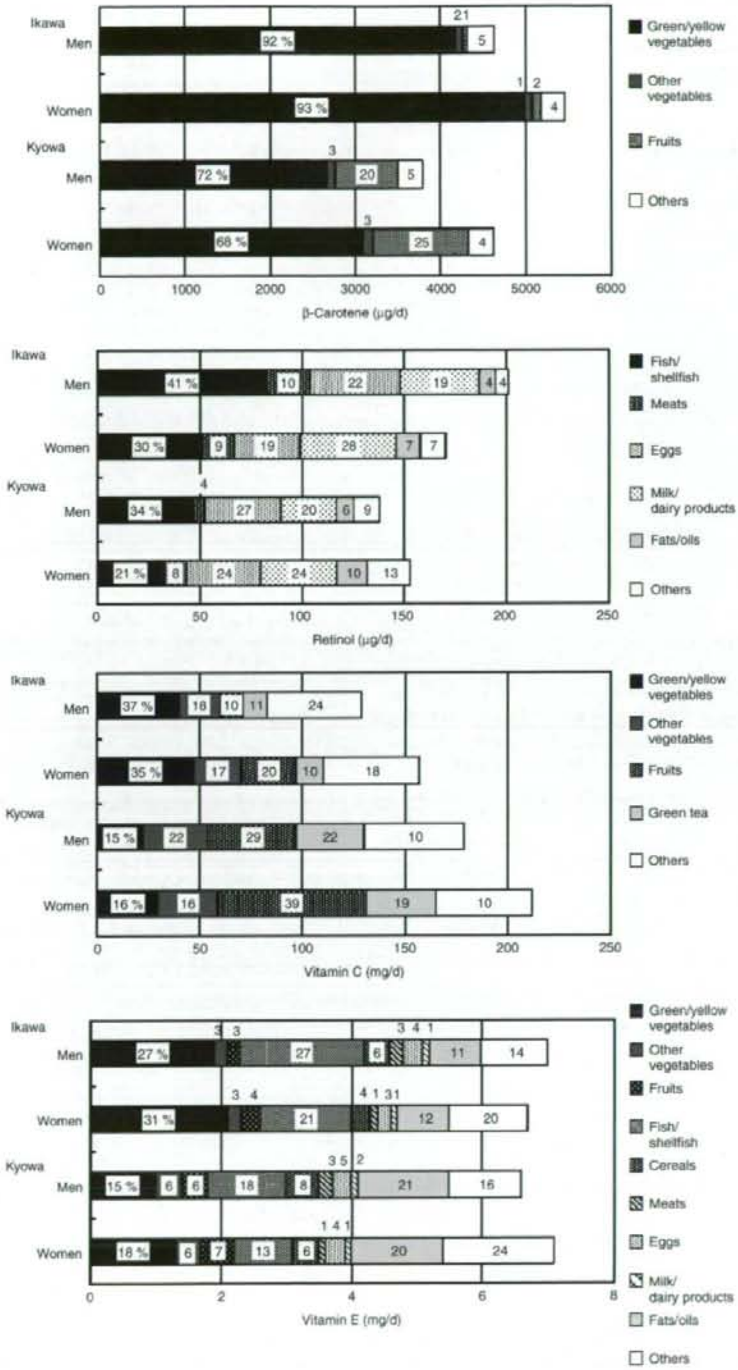

Fig. 1 Sex-specific age-adjusted mean dietary intakes of β-carotene, retinol, vitamin C and vitamin E by food group, in men and women aged 40–69 years in Ikawa and Kyowa, Japan, in the latest survey period (1998–2000 in Ikawa, 1998–2001 in Kyowa). The numbers in bars are the proportions of the vitamin intakes by food group

dietary intake of vitamin C may be overestimated systematically in the present study. Second, we did not have data on vitamin supplements in addition to dietary intake. However, this limitation is unlikely to have a large impact on the prediction of risk trends for CVD because the use of vitamin supplements may be low in these communities as vitamin supplements have been available for purchase in convenience stores only since 2004.

In summary, we investigated long-term trends in dietary intakes of vitamins A, C and E among Japanese middle-aged adults in two rural communities. Increases occurred for vitamins A, C and E between the 1970s and the 1990s except for decreased vitamin C among Kyowa men. The lower mean intake of vitamin E than the Adequate Intake should be considered a potential public health issue for the prevention of CVD.

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References

1. Witztum JL (1994) The oxidation hypothesis of atherosclerosis. *Lancet* **344**, 793–795.
2. Marchioli R (1999) Antioxidant vitamins and prevention of cardiovascular disease: laboratory, epidemiological and clinical trial data. *Pharmacol Res* **40**, 227–238.
3. Hennekens CH, Gaziano JM, Manson JE & Buring JE (1995) Antioxidant vitamin–cardiovascular disease hypothesis is still promising, but still unproven: the need for randomized trials. *Am J Clin Nutr* **62**, 1377–1380.
4. Edes TE & Gysbers DS (1993) Carcinogen-induced tissue vitamin A depletion. Potential protective advantages of β-carotene. *Ann N Y Acad Sci* **686**, 203–212.
5. Chew BP & Park JS (2004) Carotenoid action on the immune response. *J Nutr* **134**, 257–261.
6. Kohlmeier L, Simonsen N & Mottus K (1995) Dietary modifiers of carcinogenesis. *Environ Health Perspect* **103**, 177–184.
7. Valko M, Izakovic M, Mazur M, Rhodes CJ & Telser J (2004) Role of oxygen radicals in DNA damage and cancer incidence. *Mol Cell Biochem* **266**, 37–56.
8. Yoshikawa T & Kokura S (2003) Free radical and cancer prevention. *Igaku no Ayumi* **204**, 20–23.
9. Ito Y, Wakai K, Suzuki K *et al.* (2003) Serum carotenoids and mortality from lung cancer: a case-control study nested in the Japan Collaborative Cohort (JACC) study. *Cancer Sci* **94**, 57–63.
10. Ito Y, Wakai K, Suzuki K *et al.* (2005) Lung cancer mortality and serum levels of carotenoids, retinol, tocopherols, and folic acid in men and women: a case–control study nested in the JACC Study. *J Epidemiol* **15**, 140–149.
11. Wakai K, Suzuki K, Ito Y *et al.* (2005) Serum carotenoids, retinol, and tocopherols, and colorectal cancer risk in a Japanese cohort: effect modification by sex for carotenoids. *Nutr Cancer* **51**, 13–24.
12. Trout DL (1991) Vitamin C and cardiovascular risk factors. *Am J Clin Nutr* **53**, 322S–325S.
13. Yokoyama T, Date C, Kokubo Y, Yoshiike N, Matsumura Y & Tanaka H (2000) Serum vitamin C concentration was inversely associated with subsequent 20-year incidence of stroke in a Japanese rural community. The Shibata study. *Stroke* **31**, 2287–2294.
14. Gale CR, Martyn CN, Winter PD & Cooper C (1995) Vitamin C and risk of death from stroke and coronary heart disease in cohort of elderly people. *BMJ* **310**, 1563–1566.
15. Stampfer MJ & Rimm EB (1995) Epidemiologic evidence for vitamin E in prevention of cardiovascular disease. *Am J Clin Nutr* **62**, 1365–1369.
16. Voko Z, Hollander M, Hofman A, Koudstaal PJ & Breteler MM (2003) Dietary antioxidants and the risk of ischemic stroke: the Rotterdam Study. *Neurology* **61**, 1273–1275.
17. Dagenais GR, Marchioli R, Yusuf S & Tognoni G (2000) β-Carotene, vitamin C, and vitamin E and cardiovascular diseases. *Curr Cardiol Rep* **2**, 293–299.
18. Gaziano JM (2004) Vitamin E and cardiovascular disease: observational studies. *Ann N Y Acad Sci* **1031**, 280–291.
19. Miller ER 3rd, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ & Guallar E (2005) Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med* **142**, 37–46.
20. Lee IM, Cook NR, Gaziano JM, Gordon D, Ridker PM, Manson JE, Hennekens CH & Buring JE (2005) Vitamin E in the primary prevention of cardiovascular disease and cancer: the Women's Health Study: a randomized controlled trial. *JAMA* **294**, 56–65.
21. Blot WJ, Li JY, Taylor PR *et al.* (1993) Nutrition intervention trials in Linxian, China: supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population. *J Natl Cancer Inst* **85**, 1483–1492.
22. Japanese Science and Technology Agency (2006) *Standard Tables of Food Composition in Japan*, 5th revised ed. Tokyo: National Printing Bureau.
23. Ministry of Health, Labour and Welfare (1977) *Annual Report of the National Health and Nutrition Survey in Japan, 1974*. Tokyo: Daiichi Shuppan.
24. Ministry of Health, Labour and Welfare (2003) *Annual Report of the National Health and Nutrition Survey in Japan, 2001*. Tokyo: Daiichi Shuppan.
25. Ministry of Health, Labour and Welfare (2005) *Dietary Reference Intakes for Japanese, 2005*. Tokyo: Daiichi Shuppan.
26. Ervin RB, Wright JD, Wang CY & Kennedy-Stephenson J (2004) Dietary intake of fats and fatty acids for the United States population: 1999–2000. *Adv Data* **348**, 1–6.

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RESEARCH

The joint impact on being overweight of self reported behaviours of eating quickly and eating until full: cross sectional survey

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ABSTRACT

Objective To examine whether eating until full or eating quickly or combinations of these eating behaviours are associated with being overweight.

Design and participants Cross sectional survey.

Setting Two communities in Japan.

Participants 3287 adults (1122 men, 2165 women) aged 30-69 who participated in surveys on cardiovascular risk from 2003 to 2006.

Main outcome measures Body mass index (overweight ≥25.0) and the dietary habits of eating until full (lifestyle questionnaire) and speed of eating (validated brief self administered questionnaire).

Results 571 (50.9%) men and 1265 (58.4%) women self reported eating until full, and 523 (45.6%) men and 785 (36.3%) women self reported eating quickly. For both sexes the highest age adjusted mean values for height, weight, body mass index, and total energy intake were in the eating until full and eating quickly group compared with the not eating until full and not eating quickly group. The multivariable adjusted odds ratio of being overweight for eating until full was 2.00 (95% confidence interval 1.53 to 2.62) for men and 1.92 (1.53 to 2.40) for women and for eating quickly was 1.84 (1.42 to 2.38) for men and 2.09 (1.69 to 2.59) for women. The multivariable odds ratio of being overweight with both eating behaviours compared with neither was 3.13 (2.20 to 4.45) for men and 3.21 (2.41 to 4.29) for women.

Conclusion Eating until full and eating quickly are associated with being overweight in Japanese men and women, and these eating behaviours combined may have a substantial impact on being overweight.

INTRODUCTION

Obesity or being overweight is an important risk factor for lifestyle related diseases such as cancer, cardiovascular diseases, and diabetes.[1] In recent years the prevalence of overweight and obesity has increased both worldwide and among Japanese men.[2] Weight gain is caused by energy intake in excess of energy expenditure.[3,4] Eating quickly, gorging, and binge eating have been associated with total energy intake,[5-7] and eating quickly and binge eating have been associated with satiety[8,9] and insulin resistance[10,11] All these eating behaviours may lead to being overweight or obese.[12-14] In addition, the positive association of eating quickly with body mass index was observed independent of total energy intake.[15,16]

Eating until full refers to eating a large quantity of food in one meal and is unrelated to eating disorders, whereas gorging is characterised by few meals but a large quantity consumed during one meal[5,13] and binge eating by the ingestion of abnormally large quantities of food many times a day.[17]

We examined whether eating until full and eating quickly are associated with being overweight in a population based sample of adults in Japan. We also examined the combined effect of eating until full and speed of eating on being overweight.

METHODS

We carried out a cross sectional study of 4140 adults (1496 men, 2644 women) aged 30 to 69 in two Japanese communities who participated in surveys on cardiovascular risk from 2003 to 2006 under the Japan health law. The surveys were carried out in Ikawa, a rural community in the north east of Japan, and Yao, a suburb in the south west.

Overall, 3650 (88.2%) participants responded to self administered questionnaires on diet history and 489 (12%) refused. Overweight and body mass index were similar between the two groups.

We excluded participants with a history of cardiovascular diseases (n=308), excessively high (>4000 kcal) or low (<500 kcal) total reported daily energy intake (n=20), and lacking data related to eating until full or speed of eating (n=35). The data for the remaining 3287 participants (1122 men, 2165 women) were used for the analyses.

Measurements

To avoid measurement bias we used standardised methods to carry out the surveys, the details of which are described elsewhere.[18 19] We measured the participants' height without footwear and weight in light clothing and calculated their body mass index (weight (kg)/(height (m)^2). For the purposes of the analysis we considered a body mass index of 25.0 or more as indicating overweight. We also interviewed participants to ascertain data on smoking status, the number of cigarettes smoked daily, occupation, and the use of regular physical exercise for 15 minutes or more a week.

Dietary assessments

We used a validated, self administered, brief questionnaire on diet history to assess the participants' dietary habits during the previous month.[20-22] The participants were asked whether they usually eat until full (yes or no) and speed of eating was self reported according to one of five qualitative categories: very slow, slow, medium, fast, and very fast. Owing to small numbers of participants in the very fast category we combined the very fast and fast categories into the category for eating quickly. We validated the self reported speed of eating as used previously.[15] Self reported speed of eating showed a high level of agreement with speed of eating as reported by a friend: the percentages of exact and adjunct categories of answers (for example, very fast and fast were regarded as agreed) were 46% and 47%, respectively.[15] After we had combined the categories for very fast and fast and also combined the categories for medium, slow, and very slow, the percentage of agreement was reasonably good (75.3%), with a moderate κ statistics (0.35). We tested the repeatability for self reporting eating until full and eating quickly (very fast and fast combined) by repeating the questionnaire survey after one year in a subsample of the participants (1062 men, 1816 women). The κ statistics for eating until full were 0.60 in men and 0.63 in women, and for eating quickly were 0.63 in men and 0.67 in women.

Table 1 | Characteristics of participants according to combination of eating until full and eating quickly. Values are means (standard errors) unless stated otherwise

Characteristics	Not eating until full, not eating quickly	Eating until full, not eating quickly	Not eating until full, eating quickly	Eating until full, eating quickly	Total
Men:	n=352	n=258	n=199	n=313	n=1122
Mean (SD) age (years)	58.1 (10.0)	54.8 (10.3)	57.0 (9.7)	51.4 (11.3)	55.3 (10.7)
Height (cm)	164.8 (0.3)	165.8 (0.4)	165.9 (0.4)	166.6 (0.3)	165.7 (0.2)
Weight (kg)	63.1 (0.5)	66.8 (0.6)	64.9 (0.7)	69.6 (0.5)	66.1 (0.3)
Body mass index (kg/m^2)	23.2 (0.2)	24.3 (0.2)	23.6 (0.2)	25.0 (0.2)	24.0 (0.1)
Total energy intake (kcal)	2190 (30)	2296 (35)	2143 (40)	2296 (32)	2236 (17)
Total protein intake (% energy)	14.1 (0.1)	13.8 (0.2)	14.2 (0.2)	13.7 (0.1)	13.9 (0.1)
Total fat intake (% energy)	23.2 (0.3)	22.6 (0.3)	23.0 (0.4)	22.7 (0.3)	22.9 (0.2)
Carbohydrate intake (% energy)	53.2 (0.4)	53.2 (0.5)	53.2 (0.6)	53.8 (0.5)	53.4 (0.2)
Total dietary fibre intake (g/1000 kcal)	5.5 (0.1)	5.4 (0.1)	5.6 (0.1)	5.4 (0.1)	5.5 (0.0)
Alcohol intake (% energy)	7.7 (0.4)	8.6 (0.5)	7.7 (0.6)	7.9 (0.5)	8.0 (0.2)
Overweight (%)	23.1	33.1	30.2	48.7	33.8
Current smoker (%)	51.0	46.7	52.6	40.6	47.4
Desk worker (%)	10.5	11.8	9.4	10.3	10.5
Regular physical activity (%)	35.6	32.7	36.5	36.3	35.3
Women:	n=668	n=712	n=232	n=553	n=2165
Mean (SD) age (years)	54.6 (11.0)	51.2 (11.0)	53.2 (11.0)	50.9 (10.9)	52.4 (11.1)
Height (cm)	153.5 (0.2)	153.9 (0.2)	154.1 (0.3)	154.7 (0.2)	154.0 (0.1)
Weight (kg)	51.6 (0.3)	53.7 (0.3)	53.4 (0.5)	57.5 (0.3)	54.0 (0.2)
Body mass index (kg/m^2)	21.9 (0.1)	22.7 (0.1)	22.5 (0.2)	24.0 (0.1)	22.8 (0.1)
Total energy intake (kcal)	1693 (17)	1812 (17)	1719 (29)	1840 (19)	1773 (10)
Total protein intake (% energy)	15.7 (0.1)	15.2 (0.1)	15.4 (0.2)	15.4 (0.1)	15.4 (0.1)
Total fat intake (% energy)	27.6 (0.2)	27.0 (0.2)	27.5 (0.3)	27.3 (0.2)	27.3 (0.1)
Carbohydrate intake (% energy)	53.9 (0.3)	55.0 (0.3)	54.7 (0.4)	55.0 (0.3)	54.6 (0.1)
Total dietary fibre intake (g/1000 kcal)	6.9 (0.1)	6.7 (0.1)	7.1 (0.1)	6.8 (0.1)	6.8 (0.0)
Alcohol intake (% energy)	1.4 (0.2)	1.4 (0.1)	1.1 (0.3)	1.0 (0.2)	1.3 (0.1)
Overweight (%)	14.0	19.9	19.9	34.3	21.8
Current smoker (%)	10.5	8.5	11.2	10.7	10.0
Desk worker (%)	4.0	5.5	5.8	6.2	5.2
Regular physical activity (%)	39.0	35.5	41.7	38.9	38.1

All values are adjusted for age except for number of overweight, current smoker, desk worker, and engaging in regular physical activity.

Table 2 | Age adjusted and multivariable adjusted odds ratios and 95% confidence intervals for overweight according to eating until full and eating quickly

Variable	Eating until full	Eating quickly
Men (n=1122):	n=571	n=512
No (%) overweight	234 (41.0)	210 (41.0)
Age adjusted odds ratio	2.04 (1.57 to 2.64)	1.85 (1.44 to 2.38)
Multivariable odds ratio*	2.00 (1.53 to 2.62)	1.84 (1.42 to 2.38)
Women (n=2165):	n=1265	n=785
No (%) overweight	324 (25.6)	233 (29.7)
Age adjusted odds ratio	1.93 (1.54 to 2.40)	2.11 (1.71 to 2.60)
Multivariable odds ratio*	1.92 (1.53 to 2.40)	2.09 (1.69 to 2.59)

*Adjusted for age; smoking status; regular physical activity; occupation; intake of total energy, total dietary fibre, and alcohol; and survey area.

Statistical analysis

We calculated age adjusted mean values for participants' characteristics using analysis of covariance and age adjusted proportions by using logistic regression according to the combination of eating until full and eating quickly.

We calculated odds ratios and 95% confidence intervals by using the logistic regression model for age adjusted odds ratios and multivariable adjusted odds ratios. The multivariable adjustment included age (years), total energy intake (kcal/day), total fibre and alcohol intake (g/day), smoking status (non-smoker; former smoker; and 1-20, 21-40, and ≥41 cigarettes consumed daily), occupation (desk worker, service business, manual labour, unemployed), regular physical activity (yes or no), and survey area (Ikawa or Yao).

We also tried to determine whether there was a supra-additive association (additive interaction) between eating until full and eating quickly. The relative excess risk due to interaction is the excess risk as a result of joint exposure. In terms of the model coefficients, the relative excess risk due to interaction is calculated as exponent$(\beta_1+\beta_2+\beta_3)$−exponent$(\beta_1)$ −exponent(β_2)+1 where $\beta 1$, $\beta 2$, and $\beta 3$ are the coefficients from the model for specified levels of eating until full and eating quickly, as well as their interaction. Thus, the relative excess risk due to interaction equals the odds ratio(eating until full +eating quickly)−odds ratio(eating until full)−odds ratio(eating quickly)+1. We divided the statistic by the square root of its estimated variance to test the hypothesis that the relative excess risk due to interaction equalled zero with a z test (normal distribution) approximation.[23 24] This increase in excess risk due to interaction of the two categories as a percentage of the increase in risk as a result of joint exposure (relative excess risk due to interaction percentage) is then expressed as (relative excess risk due to interaction/ [odds ratio(eating until full+eating quickly)−1])×100. The percentage relative excess risk due to interaction is defined as the proportion of disease burden caused by two factors that can be attributed to their interaction. We also calculated the attributable proportion due to interaction=relative excess risk due to interaction/odds ratio(eating until full+eating quickly)×100—that is, the proportion of overweight among those both eating until full and eating quickly that is attributable to interaction.

Probability values for statistical tests were two tailed and we regarded $P<0.05$ as statistically significant. We used the SAS statistical package version 9.1 for the analyses.

RESULTS

Table 1 shows the baseline characteristics of the participants. The mean (standard deviation) age of participants was 55.3 (10.7) for men and 52.4 (11.1) for women, with 379 (33.8%) men and 472 (21.8%) women being overweight. Overall, 571 (50.9%) men and 1265 (58.4%) women reported eating until full and 523 (45.6%) men and 785 (36.3%) women reported eating quickly (very fast and fast categories combined). For both sexes the eating until full and eating quickly group had the highest age adjusted mean values for height, weight, body mass index, and total energy intake than did the group with neither of these eating behaviours.

Table 3 | Age adjusted and multivariable adjusted odds ratios and 95% confidence intervals for overweight according to combinations of eating until full and eating quickly

Variable	Not eating until full, not eating quickly	Eating until full, not eating quickly	Not eating until full, eating quickly	Eating until full, eating quickly	RERI (RERI%)*
Men (n=1122):	n=352	n=258	n=199	n=313	
No (%) overweight	84 (23.8)	85 (32.9)	61 (30.7)	149 (47.6)	—
Age adjusted odds ratio	1.00	1.64 (1.14 to 2.35)	1.43 (0.97 to 2.11)	3.17 (2.25 to 4.47)	1.10 (50.7)
Multivariable odds ratio†	1.00	1.61 (1.11 to 2.32)	1.42 (0.96 to 2.11)	3.13 (2.20 to 4.45)	1.10 (51.6)
Women (n=2165):	n=668	n=712	n=232	n=553	
No (%) overweight	100 (15.0)	138 (19.4)	47 (20.3)	186 (33.6)	—
Age adjusted odds ratio	1.00	1.50 (1.13 to 2.00)	1.51 (1.02 to 2.22)	3.23 (2.44 to 4.28)	1.22 (54.9)
Multivariable odds ratio†	1.00	1.48 (1.10 to 1.98)	1.47 (0.99 to 2.17)	3.21 (2.41 to 4.29)	1.27 (57.4)

RERI=relative excess risk due to interaction.
*P<0.05 (z test).
†Adjusted for age; smoking status; regular physical activity; occupation; intake of total energy, total dietary fibre, and alcohol; and survey area.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Eating quickly, independent of total energy intake and other confounders, is associated with overweight

WHAT THIS STUDY ADDS

Both eating quickly and eating until full were associated with being overweight, independent of total energy intake and other confounders

These eating behaviours combined may have a substantial impact on being overweight

The eating until full group had higher age adjusted odds ratios for overweight than the not eating until full group for both men and women. The odds ratios were not changed substantially by further adjustment for intake of total energy, total fibre, and alcohol; smoking status; physical activity; and survey area: 2.00 (95% confidence interval 1.53 to 2.62) for men and 1.92 (1.53 to 2.40) for women. The eating quickly group had higher age adjusted odds ratios for overweight than did the not eating quickly group for both sexes. The multivariable adjusted odds ratios for overweight for the eating quickly group was 1.84 (1.42 to 2.38) for men and 2.09 (1.69 to 2.59) for women (table 2).

The multivariable adjusted odds ratio for overweight for the eating until full and eating quickly group compared with the group with neither of these eating behaviours was 3.13 (2.20 to 4.45) for men and 3.21 (2.41 to 4.29) for women (table 3). On the basis of the multivariable adjusted model, the relative excess risk due to interaction for men was 1.10, indicating an excess burden of being overweight of 51.6% (percentage relative excess risk due to interaction, $P<0.05$) for eating until full and eating quickly, and for women was 1.27, indicating an excess burden of being overweight of 57.4% (percentage relative excess risk due to interaction, $P<0.01$; table 3). The attributable proportion due to interaction was 35.1% for men and 39.6% for women.

DISCUSSION

Eating until full and eating quickly were significantly associated with overweight in Japanese men and women after adjustment for total energy intake and other potential confounding factors. The combination of the two eating behaviours had a supra-additive effect (additive interaction) on being overweight.

Eating quickly is positively associated with body mass index and increased body weight among Japanese[15 16] and Western populations.[12] The questionnaire for evaluation of speed of eating used in the present study was the same as the one used in previous studies,[15 16] and the findings of the present and previous studies showed essentially the same trends. One study examined associations between the speed of eating and body mass index in Japanese women aged 18; the speed of eating (very slow, slow, medium, fast, and very fast) was found to be significantly and positively associated with body mass index.[15] Another study also examined associations between the speed of eating and body mass index but in Japanese men and women aged 35-69 years.[16] Furthermore, the speed of eating was positively associated with the homeostasis model assessment of insulin resistance for middle aged Japanese men and women without diabetes, especially for those who were not obese.[10] Speed of eating was significantly and positively correlated with total energy intake, but the odds ratio for overweight did not change substantially after adjustment for total energy intake and other confounding variables. Therefore the effect of speed of eating may be unrelated to that of total energy intake.

One study investigated whether gorging was associated with overweight or obesity, but the epidemiological evidence was at best weak.[13] Moreover, the present study observed that the combination of eating until full and eating quickly was strongly associated with being overweight.

The strength of our study is that we analysed the association of eating behaviour patterns with overweight using population based data for a large number of participants. The study does, however, have several potential limitations. Firstly, eating patterns were self reported and we did not determine the validity for self reporting of eating until full. The participants who reported eating until full, however, had higher total energy intake than the other participants, including those who reported gorging[5] and binge eating, which supports the validity of the questionnaire.[7] Secondly, we assessed eating behaviours as simplistic dichotomous outcomes. The validity and reproducibility of eating quickly and the reproducibility of eating until full were, however, reasonably good, and these eating behaviours as simplistic dichotomous outcomes were significantly associated with being overweight. Thirdly, we cannot deny the possibility that other potential confounding factors, such as educational history, may have had an effect on the observed associations. Fourthly, the cross sectional nature of the study indicates that the observed association between these eating behaviours and overweight does not necessarily indicate causality. It is unlikely, however, that people who are obese then change their eating habits. A cohort study of firefighters over seven years showed that eating quickly was associated with weight gain.[12]

In conclusion, eating until full and eating quickly were associated with being overweight in Japanese men and women, and the combination of the two eating behaviours may have a substantial impact on being overweight. As it is difficult to estimate these causal effects in a cross sectional study, prospective cohort and intervention studies will be needed to validate these associations between eating behaviour patterns and being overweight.

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Contributors: KM analysed and interpreted the data, drafted the manuscript, and provided statistical expertise. YK, SN, MK, and SS acquired the data and critically revised the manuscript. SS, TO, KM, HN, AK, MK, TO, HI, MN, YI, and HI conceived and designed the study, acquired and interpreted the data, and critically revised the manuscript. HI is guarantor for the paper.

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1 Kopelman P. Health risks associated with overweight and obesity. *Obes Rev* 2007;(suppl 1):13-7.
2 Ministry of Health, Labor and Welfare. *Nutrition status based on the national nutrition survey in Japan*. Tokyo: Daiichi Shuppan, 2007. [In Japanese.]
3 Shiwaku K, Anuurad E, Enkhmaa B, Nogi A, Kitajima K, Shimono K, et al. Overweight Japanese with body mass indexes of 23.0-24.9 have higher risks for obesity-associated disorders: a comparison of Japanese and Mongolians. *Int J Obes* 2004;28:152-8.
4 Das SK, Gilhooly CH, Golden JK, Pittas AG, Fuss PJ, Cheatham RA, et al. Long-term effects of 2 energy-restricted diets differing in glycemic load on dietary adherence, body composition, and metabolism in CALERIE: a 1-y randomized controlled trial. *Am J Clin Nutr* 2007;85:1023-30.
5 Drummond SE, Crombie NE, Cursiter MC, Kirk TR. Evidence that eating frequency is inversely related to body weight status in male, but not female, non-obese adults reporting valid dietary intakes. *Int J Obes* 1998;22:105-12.
6 Camell S, Wardle J. Measuring behavioural susceptibility to obesity: validation of the child eating behaviour questionnaire. *Appetite* 2007;48:104-13.
7 Raymond NC, Neumeyer B, Warren CS, Lee SS, Peterson CB. Energy intake patterns in obese women with binge eating disorder. *Obes Res* 2003;11:869-79.
8 Sakata T, Yoshimatsu H, Masaki T, Tsuda K. Anti-obesity actions of mastication driven by histamine neurons in rats. *Exp Biol Med* 2003;228:1106-10.
9 Guertin TL. Eating behavior of bulimics, self-identified binge eaters, and non-eating-disordered individuals: what differentiates these populations? *Clin Psychol Rev* 1999;19:1-23.
10 Otsuka R, Tamakoshi K, Yatsuya H, Wada K, Matsushita K, Ouyang P, et al. Eating fast leads to insulin resistance: findings in middle-aged Japanese men and women. *Prev Med* 2008;46:154-9.
11 De Zwaan M. Binge eating disorder and obesity. *Int J Obes* 2001;25:S51-5.
12 Gerace TA, George VA. Predictors of weight increases over 7 years in fire fighters and paramedics. *Prev Med* 1996;25:593-600.
13 Bellisle F, McDevitt R, Prentice AM. Meal frequency and energy balance. *Br J Nutr* 1997;77:S57-70.
14 Hill AJ. Obesity and eating disorders. *Obes Rev* 2007;(suppl 1):151-5.
15 Sasaki S, Katagiri A, Tsuji T, Shimoda T, Amano K. Self-reported rate of eating correlates with body mass index in 18-y-old Japanese women. *Int J Obes* 2003;27:1405-10.
16 Otsuka R, Tamakoshi K, Yatsuya H, Murata C, Sekiya A, Wada K, et al. Eating fast leads to obesity: findings based on self-administered questionnaires among middle-aged Japanese men and women. *J Epidemiol* 2006;16:117-24.
17 American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*, 4th ed. Washington, DC: American Psychiatric Association, 1994.
18 Iso H, Sato S, Kitamura A, Imano H, Kiyama M, Yamagishi K, et al. Metabolic syndrome and the risk of ischemic heart disease and stroke among Japanese men and women. *Stroke* 2007;38:1744-51.
19 Shimamoto T, Komachi Y, Inada H, Doi M, Iso H, Sato S, et al. Trends for coronary heart disease and stroke and their risk factors in Japan. *Circulation* 1989;79:503-15.
20 Sasaki S. Development and evaluation of dietary assessment methods using biomarkers and diet history questionnaires for individuals. In: *Research for evaluation methods of nutrition and dietary lifestyle programs held on Healthy Japan 21 (head investigator: Tanaka H)*. Summary report. Tokyo: Ministry of Health, Labor, and Welfare. 2004:10-44. [In Japanese.]
21 Sasaki S, Yanagibori R, Amano K. Self-administered diet history questionnaire developed for health education: a relative validation of the test-version by comparison with 3-day diet record in women. *J Epidemiol* 1998;8:203-15.
22 Sasaki S, Ushio F, Amano K, Morihara M, Todoriki O, Uehara Y, et al. Serum biomarker-based validation of a self-administered diet history questionnaire for Japanese participants. *J Nutr Sci Vitaminol (Tokyo)* 2000;46:285-96.
23 Rice JA. *Mathematical statistics and data analysis*, 2nd ed. Belmont, CA: Duxbury, 1995:149-54.
24 Assmann SF, Hosmer DW, Lemeshow S, Mundt KA. Confidence intervals for measures of interaction. *Epidemiology* 1996;7:286-90.

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Original Article

Body Fat Distribution and the Risk of Hypertension and Diabetes among Japanese Men and Women

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To identify anthropometrical indices of body fat distribution for predicting the risk of hypertension and diabetes, a population-based prospective study was designed. Subjects in two communities (n=2,422 and 3,195), who were free of hypertension and diabetes, respectively, were followed-up. The area and gender-specific risk of hypertension and diabetes were compared among tertiles of body mass index (BMI) and body fat distribution, including waist circumference (WC), waist-to-hip ratio (WHR), waist-to-height ratio (WHtR), and subscapular skinfold-thickness (SSF). During the 10-year follow-up for hypertension and diabetes, the incident cases of hypertension were 72 for Yao men, 125 for Kyowa men, 160 for Yao women and 193 for Kyowa women and those of diabetes were 27, 64, 37 and 77, respectively. One SD differences in BMI and WC were associated with 1.2 to1.6-fold higher risk of hypertension, and that of SSF was associated with 1.4 to 1.6-fold higher risk of diabetes for both men and women in Yao and for women, but not men, in Kyowa. One SD differences of BMI, WC and WHtR were also associated with 1.4 to 2.0-fold higher risk of diabetes for Yao and Kyowa women. In conclusion, the significant predictors for hypertension were BMI and WC and those for diabetes were BMI and SSF in both genders in both communities, except for men in Kyowa. WC and WHtR were also predictors for diabetes in women but not in men. (*Hypertens Res* 2008; 31: 851–857)

***Key Words*: hypertension, diabetes, body mass index, waist circumference, waist-to-height ratio**

Introduction

Cardiovascular disease mortality has been reported as the top-3 cause of deaths in Japan since 1958 (*1*). It is well known that the prevention and control of hypertension and diabetes could substantially reduce the risk of cardiovascular disease (*2*). Thus, it is important from the view of public health and clinical practice to find a simple and valid measurement to predict the risk of hypertension and diabetes. At present, cross-sectional studies have shown that waist circumference (WC), waist-to-hip ratio (WHR), waist-to-height ratio (WHtR) and

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body mass index (BMI) are associated with the prevalence of hypertension and diabetes (*3–12*). However, the results have not been consistent between genders and among various ethnic groups (*3–12*). In Japan, cross-sectional studies have shown that WHtR was a stronger correlate for these cardiovascular risk factors than BMI and WC (*3, 4*). A recent prospective study in the United States has reported that WC is a better predictor for the risk of diabetes than WHR and BMI (*13*). However, no prospective study has been undertaken to study systematically the association of WC, WHR, WHtR and subscapular skinfold thickness (SSF) with hypertension and diabetes in Asian populations.

To obtain better measures for the prediction of the risk of hypertension and diabetes for men and women in Asian communities, we examined gender and population-specific relationships between anthropometric measurements (BMI, WC, WHR, WHtR, SSF), and the risk of hypertension and diabetes in two populations in Japan.

Methods

Study Populations

The surveyed population included residents in two communities (aged 40–69 years) who participated in cardiovascular risk surveys between 1988 and 1993 in Minami-Takayasu, a southwest urban suburb, a district of Yao City of Osaka Prefecture, or between 1990 and 1993 in Kyowa, a rural community of Ibaraki Prefecture. After exclusion of persons with hypertension (n=1,314) or diabetes (n=314), and 353 persons who did not undergo anthropometric measurements at baseline, a total of 3,214 study subjects (Kyowa: 549 men and 992 women; Yao: 585 men and 1,088 women) and 4,214 study subjects (Kyowa: 763 men and 1,374 women; Yao: 700 men and 1,377 women) who were free of hypertension and diabetes at baseline, respectively, were followed. These subjects were followed between 1997 and 2001. The follow-up rate was 75.4% (n=2,422) for hypertension and 75.6% (n=3,195) for diabetes. The average follow-up period was 10.4 years (10.0 years for men and 10.6 years for women) for hypertension and 10.4 years (10.1 years for men and 10.6 years for women) for diabetes. The study protocol was approved by the Human Ethics Review Committee of the University of Tsukuba.

Measurement

Height in stocking feet and weight in light clothing were measured. BMI was calculated as weight (kg) divided by the square of the height (m^2). Subscapular skinfold thickness was measured to the nearest mm using keys calipers by trained physician epidemiologists with standard methods. Trained observers also measured WC and hip circumference in subjects in a standing position and breathing normally at the level of the umbilicus and at the symphysis pubis at the maximum protrusion of the hips, respectively, to the nearest 1 cm using a tape measure. These measurements were used to calculate WHR and WHtR.

Blood pressures were measured by trained technicians and/or physician epidemiologists with standardized methods, using mercury sphygmomanometers on the right arm of seated participants after at least 5 min of rest. Blood pressure was measured twice for the subjects with systolic blood pressure (SBP) of ≥140 mmHg, and/or diastolic blood pressure (DBP) of ≥90 mmHg. Hypertension was defined as SBP of ≥160 mmHg and/or DBP of ≥95 mmHg and/or current treatment with antihypertensive medication at the baseline and annual follow-up surveys.

Blood was drawn from seated participants into a plain, siliconized glass tube, and serum was separated. Serum glucose was measured by the hexokinase method. Diabetes was defined as a fasting glucose level of ≥126 mg/dL and/or a non-fasting glucose level of ≥200 mg/dL and/or use of medication for diabetes at the baseline and annual follow-up surveys.

An interview was conducted to ascertain the alcohol intake per day, the number of cigarettes smoked per day, use of medication for diabetes mellitus and hypertension, and past history of stroke and coronary heart disease. Persons who smoked ≥1 cigarette per day were defined as current smokers, and those who had not smoked for ≥3 months were defined as ex-smokers.

Statistical Analysis

The gender and population-specific area and gender-specific risks of hypertension and diabetes were compared among tertiles of BMI and body fat distribution including measurements of WC, WHtR, WHR and SSF. The odds ratio (OR) of hypertension and diabetes and their respective 95% confidence intervals (95% CI) were calculated with reference to the first tertile of each of these measurements, using the logistic regression model. We adjusted for age, alcohol intake (for men: never, former, current <23, 23–45, ≥46 g/d ethanol; for women: non-drinker and current drinker), and smoking status (for men: never, former, current 1–19, ≥20 cigarettes per day; for women: non-smoker and current smoker). Furthermore, we also adjusted baseline SBP for hypertension analysis and baseline glucose level and fasting status (yes or no) for diabetes analysis. The increased risks of hypertension and diabetes associated with a 1 SD difference of BMI and body fat distribution measurements were examined by using the logistic regression model, adjusted for age and other confounding variables. All statistical analyses were conducted using SAS, version 8.0 (SAS Japan Inc., Tokyo, Japan), and the statistical testing was two-tailed.

Results

During the average 10.4-year follow-up, we documented 550

Table 1. Gender and Population–Specific Means±SD and Proportions of Risk Characteristics and Anthropometric Measures among the Japanese Men and Women in Two Communities for Examining the Risk of Hypertension

	Men		Women	
	Yao	Kyowa	Yao	Kyowa
n	389	519	911	971
Age	56±6	56±9	56±7‡	54±9
Alcohol intake, g/d	32±20	32±22	9±9	9±11
Smoking, %	45	52	7†	4
Systolic blood pressure, mmHg	117±12‡	128±12	111±13‡	125±13
Diastolic blood pressure, mmHg	73±8‡	77±8	69±8‡	74±9
Glucose, mmol/L	6.27±1.49‡	6.97±2.27	5.91±1.09‡	6.26±1.61
Body mass index, kg/m²	22.8±2.6†	23.2±2.7	22.6±2.8‡	23.3±2.9
Waist circumference, cm	82.7±7.6	82.9±8.0	81.6±8.9‡	79.9±9.0
Waist-to-height ratio	0.50±0.05*	0.51±0.05	0.54±0.06	0.53±0.06
Waist-to-hip ratio	0.92±0.05	0.91±0.06	0.91±0.07‡	0.87±0.07
Subscapular skinfold thickness, mm	14.4±5.8	14.6±5.6	18.2±6.6‡	21.5±7.8

Data are means±SD. Differences from the rural population: $^*p<0.05$, $^\dagger p<0.01$, $^\ddagger p<0.0001$.

incident cases of hypertension (2.2%) and 205 incident cases of diabetes (0.6%).

Table 1 shows the gender- and population-specific means±SD and proportions of risk characteristics and anthropometric parameters in the subjects for examining risk of hypertension. The mean levels of SBP, DBP and glucose were higher in the Kyowa than in the Yao population for both genders. The proportion of current smokers was higher among Kyowa men than Yao men, while the opposite trend was observed for women. There was no difference in mean alcohol intake between the two populations for either gender. The mean BMI was higher in the Kyowa population than the Yao population for both genders. The mean value of WHtR for Kyowa men was higher than that for Yao men. The mean values of WC and WHR were lower among Kyowa women than Yao women, while the mean SSF was higher among Kyowa women than Yao women. Similar trends were observed for the risk of diabetes (data not shown).

The incidence of hypertension was 72 for Yao men (2.2%), 125 for Kyowa men (2.8%), 160 for Yao women (2.0%) and 193 for Kyowa women (2.1%) (Table 2). For Yao men, the multivariable OR of hypertension for the highest *vs.* lowest tertiles of anthropometric measures was statistically significant for BMI (OR [95% CI]=2.28 [1.12–4.65], $p=0.02$), and marginally significant for WC (OR [95% CI]=1.88 [0.90–3.92], $p=0.09$). One SD differences of BMI, WC, WHtR, WHR and SSF were significantly associated with 1.3 to 1.6-fold higher risk of hypertension. The multivariable OR of hypertension in the highest *vs.* lowest tertiles of anthropometric measures and those associated with 1 SD difference of anthropometric measures were not statistically significant for Kyowa men. For Yao women, the multivariate OR for the highest *vs.* lowest tertiles of anthropometric measures was statistically significant for BMI (OR [95% CI]=1.68 [1.05–2.68], $p=0.03$) and marginally significant for WC (OR [95% CI]=1.60 [0.98–2.62], $p=0.06$). One SD differences of BMI and WC were marginally significantly or significantly associated with 1.2-fold higher risk of hypertension. For Kyowa women, the risk of hypertension increased with higher tertiles in most of the anthropometric parameters: the multivariable OR of hypertension in the highest *vs.* lowest tertiles of anthropometric measures was statistically significant for BMI (OR [95% CI]=1.81 [1.16–2.84], $p=0.001$), WHtR (OR [95% CI]=1.59 [1.05–2.39], $p=0.03$), and SSF (OR [95% CI]=1.60 [1.04–2.46], $p=0.03$), and marginally significant for WC (OR [95% CI]=1.45 [0.96–2.19], $p=0.08$), and WHR (OR [95% CI]=1.48 [0.96–2.30)], $p=0.08$). One SD differences of BMI, WC, WHtR, and SSF were significantly associated with 1.2 to 1.3-fold higher risk of hypertension.

The risk of hypertension for subjects with BMI ≥27.0 kg/m² compared to those with BMI<22.0 kg/m² was examined; the multivariate OR (95% CI) was 2.83 (0.96–8.31; $p=0.06$) for Yao men, 2.32 (1.14–4.73; $p=0.02$) for Yao women and 2.42 (1.33–4.40; $p=0.004$) for Kyowa women, but no significant association was observed for Kyowa men (data not shown).

The incidence of diabetes was 27 for Yao men (0.7%), 64 for Kyowa men (1.0%), 37 for Yao women (0.4%) and 77 for Kyowa women (0.6%) (Table 3). For Yao men, the multivariable OR of diabetes for the highest *vs.* lowest tertiles of anthropometric measures was significant for BMI (OR [95% CI]=3.24 [1.08–9.71], $p=0.04$), but not for the other anthropometric measures. One SD difference of SSF was marginally significantly associated with 1.4-fold higher risk of diabetes. The multivariable OR of diabetes in highest *vs.* lowest tertiles of anthropometric measures and those associated with 1 SD difference of anthropometric measures was not statistically significant for Kyowa men. However, for Kyowa women, the multivariable OR of diabetes for the highest *vs.* lowest tertiles of anthropometric measures was statistically

Table 2. Multivariable-Adjusted Odds Ratio for Hypertension According to Anthropometric Measures among Japanese Men and Women in Two Communities

	Men							
	Yao				Kyowa			
	No. of case (n=72)	No. at risk (n=325)	Multivariable OR (95% CI)	OR (95% CI) changed per 1 SD	No. of case (n=125)	No. at risk (n=452)	Multivariable OR (95% CI)	OR (95% CI) changed per 1 SD
BMI								
T1 (15.3–22.0)	22	114	1.00		38	145	1.00	
T2 (22.0–24.1)	20	114	0.89 (0.43–1.85)	1.52 (1.12–2.05)‡	29	145	0.67 (0.37–1.22)	1.10 (0.88–1.37)
T3 (24.1–33.2)	30	97	2.28 (1.12–4.65)†		58	162	1.33 (0.78–2.28)	
Waist circumference								
T1 (60–79)	16	93	1.00		33	147	1.00	
T2 (80–86)	26	122	1.33 (0.63–2.81)	1.56 (1.14–2.14)‡	44	159	1.21 (0.69–2.11)	1.04 (0.83–1.29)
T3 (87–111)	30	110	1.88 (0.90–3.92)*		48	146	1.44 (0.82–2.53)	
Waist-to-height ratio								
T1 (0.38–0.49)	19	101	1.00		36	169	1.00	
T2 (0.49–0.53)	28	137	1.01 (0.50–2.03)	1.56 (1.11–2.19)†	34	111	1.51 (0.83–2.73)	1.09 (0.86–1.39)
T3 (0.53–0.66)	25	87	1.76 (0.84–3.70)		55	172	1.50 (0.89–2.55)	
Waist-to-hip ratio								
T1 (0.75–0.89)	21	98	1.00		37	161	1.00	
T2 (0.89–0.94)	23	118	0.91 (0.45–1.86)	1.38 (1.04–1.84)†	50	147	1.44 (0.83–2.50)	0.90 (0.73–1.10)
T3 (0.94–1.09)	28	109	1.22 (0.61–2.43)		38	144	1.04 (0.59–1.83)	
Subscapular skinfold thickness								
T1 (5.0–11.0)	22	102	1.00		35	145	1.00	
T2 (12.0–16.0)	25	129	0.97 (0.48–1.97)	1.34 (1.02–1.77)†	43	161	1.14 (0.65–2.00)	1.13 (0.90–1.42)
T3 (17.0–45.0)	25	94	1.40 (0.67–2.91)		47	146	1.51 (0.85–2.68)	

	Womem							
	Yao				Kyowa			
	No. of case (n=160)	No. at risk (n=772)	Multivariable OR (95% CI)	OR (95% CI) changed per 1 SD	No. of case (n=193)	No. at risk (n=873)	Multivariable OR (95% CI)	OR (95% CI) changed per 1 SD
BMI								
T1 (15.2–21.5)	46	298	1.00		37	250	1.00	
T2 (21.5–24.0)	55	248	1.64 (1.02–2.61)†	1.20 (0.99–1.45)*	59	301	1.16 (0.72–1.87)	1.29 (1.09–1.54)‡
T3 (24.0–36.8)	59	226	1.68 (1.05–2.68)†		97	322	1.81 (1.16–2.84)‡	
Waist circumference								
T1 (57–76)	32	225	1.00		60	357	1.00	
T2 (77–84)	51	257	1.28 (0.77–2.15)	1.21 (1.00–1.47)†	57	248	1.25 (0.81–1.92)	1.23 (1.03–1.47)†
T3 (85–110)	77	290	1.60 (0.98–2.62)*		76	268	1.45 (0.96–2.19)*	
Waist-to-height ratio								
T1 (0.38–0.50)	35	228	1.00		58	351	1.00	
T2 (0.50–0.56)	56	281	1.16 (0.71–1.91)	1.14 (0.94–1.38)	42	222	0.96 (0.60–1.53)	1.28 (1.08–1.53)‡
T3 (0.56–0.75)	69	263	1.40 (0.86–2.29)		93	300	1.59 (1.05–2.39)†	
Waist-to-hip ratio								
T1 (0.68–0.85)	29	182	1.00		66	368	1.00	
T2 (0.85–0.92)	44	256	1.04 (0.61–1.80)	1.11 (0.92–1.32)	66	299	1.12 (0.75–1.69)	1.16 (0.97–1.39)
T3 (0.92–1.15)	87	334	1.40 (0.84–2.31)		61	206	1.48 (0.96–2.30)*	
Subscapular skinfold thickness								
T1 (5.0–16.0)	60	337	1.00		42	245	1.00	
T2 (17.0–22.0)	54	257	1.05 (0.68–1.63)	1.16 (0.94–1.42)	43	267	0.73 (0.44–1.20)	1.27 (1.08–1.49)‡
T3 (23.0–60.0)	46	178	1.34 (0.83–2.15)		108	361	1.60 (1.04–2.46)†	

*$p<0.1$, †$p<0.05$, ‡$p<0.01$. OR, odds ratio; 95% CI, 95% confidence interval. Multivariate-adjusted: age (years), baseline systolic blood pressure levels (mmHg), alcohol intake (never, former, current <23, 23–45, ≥46 g/d ethanol for men; non-drinker and current-drinker for women) and smoking status (never, former, current 1–19 and ≥20 cigarettes per day for men; non-smoker and current smoker for women).

Table 3. Multivariable-Adjusted Odds Ratio for Diabetes According to Anthropometric Measures among Japanese Men and Women in Two Communities

	Men							
	Yao				Kyowa			
	No. of case (n=27)	No. at risk (n=392)	Multivariable OR (95% CI)	OR (95% CI) changed per 1 SD	No. of case (n=64)	No. at risk (n=628)	Multivariable OR (95% CI)	OR (95% CI) changed per 1 SD
BMI								
T1 (15.3–22.3)	6	137	1.00		23	205	1.00	
T2 (22.3–24.4)	7	140	1.16 (0.35–3.82)	1.33 (0.90–1.97)	16	197	0.74 (0.36–1.51)	1.08 (0.82–1.43)
T3 (24.4–34.5)	14	115	3.24 (1.08–9.71)†		25	226	1.22 (0.63–2.34)	
Waist circumference								
T1 (60–80)	5	129	1.00		16	215	1.00	
T2 (81–87)	11	139	2.65 (0.81–8.65)	1.39 (0.90–2.13)	22	216	1.56 (0.76–3.22)	1.15 (0.87–1.51)
T3 (88–112)	11	124	2.10 (0.65–6.79)		26	197	1.71 (0.85–3.42)	
Waist-to-height ratio								
T1 (0.38–0.49)	4	130	1.00		17	209	1.00	
T2 (0.49–0.54)	13	150	3.56 (1.01–12.56)†	1.27 (0.81–2.00)	20	191	1.22 (0.59–2.54)	1.12 (0.83–1.50)
T3 (0.54–0.67)	10	112	3.09 (0.84–11.44)*		27	228	1.30 (0.66–2.56)	
Waist-to-hip ratio								
T1 (0.71–0.90)	7	131	1.00		16	202	1.00	
T2 (0.90–0.94)	8	137	1.01 (0.33–3.10)	1.19 (0.78–1.82)	22	213	1.22 (0.59–2.51)	1.04 (0.82–1.34)
T3 (0.94–1.09)	12	124	1.70 (0.61–4.73)		26	213	1.34 (0.66–2.70)	
Subscapular skinfold thickness								
T1 (5.0–11.0)	4	114	1.00		18	181	1.00	
T2 (12.0–16.0)	12	156	2.81 (0.82–9.67)	1.35 (0.95–1.93)*	24	220	1.19 (0.59–2.40)	1.10 (0.83–1.46)
T3 (17.0–40.0)	11	122	3.01 (0.84–10.77)*		22	227	1.13 (0.55–2.32)	

	Women							
	Yao				Kyowa			
	No. of case (n=37)	No. at risk (n=970)	Multivariable OR (95% CI)	OR (95% CI) changed per 1 SD	No. of case (n=77)	No. at risk (n=1,205)	Multivariable OR (95% CI)	OR (95% CI) changed per 1 SD
BMI								
T1 (15.2–21.8)	8	386	1.00		17	339	1.00	
T2 (21.9–24.4)	10	317	1.44 (0.54–3.81)	2.00 (1.48–2.70)‡	16	406	0.81 (0.39–1.68)	1.53 (1.21–1.93)‡
T3 (24.4–36.8)	19	267	3.34 (1.40–7.95)‡		44	460	1.64 (0.89–3.03)	
Waist circumference								
T1 (57–77)	8	302	1.00		15	454	1.00	
T2 (78–85)	11	322	1.32 (0.51–3.42)	1.67 (1.19–2.35)‡	21	354	1.58 (0.78–3.19)	1.68 (1.31–2.16)‡
T3 (86–120)	18	346	2.07 (0.85–5.06)		41	397	2.83 (1.49–5.39)‡	
Waist-to-height ratio								
T1 (0.38–0.51)	11	307	1.00		16	406	1.00	
T2 (0.51–0.57)	11	358	0.82 (0.34–1.97)	1.59 (1.14–2.22)‡	16	376	0.96 (0.46–2.01)	1.46 (1.16–1.84)‡
T3 (0.57–0.81)	15	305	1.39 (0.59–3.28)		45	423	2.26 (1.19–4.29)†	
Waist-to-hip ratio								
T1 (0.68–0.86)	7	246	1.00		14	449	1.00	
T2 (0.86–0.93)	14	321	1.43 (0.55–3.69)	1.26 (0.89–1.78)	25	414	1.90 (0.95–3.90)*	1.56 (1.21–2.02)‡
T3 (0.93–1.15)	16	403	1.46 (0.56–3.82)		38	342	3.21 (1.63–6.30)‡	
Subscapular skinfold thickness								
T1 (5.0–16.0)	6	399	1.00		13	316	1.00	
T2 (17.0–23.0)	17	351	3.10 (1.19–8.09)†	1.61 (1.15–2.27)‡	23	391	1.44 (0.69–2.98)	1.38 (1.10–1.73)‡
T3 (24.0–60.0)	14	220	3.58 (1.33–9.64)†		41	498	2.06 (1.05–4.04)†	

$^{*}p<0.1$, $^{\dagger}p<0.05$, $^{\ddagger}p<0.01$. OR, odds ratio; 95% CI, 95% confidence interval. Multivariate-adjusted: age (years), baseline glucose levels (mmol/L), fasting status (yes or no), alcohol intake (never, former, current <23, 23–45, ≥46 g/d ethanol for men; non-drinker and current-drinker for women) and smoking status (never, former, current 1–19 and ≥20 cigarettes per day for men; non-smoker and current smoker for women).

significant for WC (OR [95% CI]=2.83 [1.49–5.39], $p=0.002$), WHtR (OR [95% CI]=2.26 [1.19–4.29], $p=0.01$), WHR (OR [95% CI]=3.21 [1.63–6.30], $p<0.001$) and SSF (OR [95% CI]=2.06 [1.05–4.04], $p=0.04$), and 1 SD differences of BMI, WC, WHtR, WHR and SSF were significantly associated with 1.4 to 1.7-fold higher risk of diabetes. For Yao women, the multivariable OR of diabetes for the highest *vs.* lowest tertiles of anthropometric measures was statistically significant for BMI (OR [95% CI]=3.34 [1.40–7.95], $p=0.007$) and SSF (OR [95% CI]=3.58 [1.33–9.64], $p=0.01$). One SD difference of BMI was significantly associated with 2-fold, and that of WC, WHtR and SSF was significantly associated with 1.3 to 1.7-fold higher risk of diabetes.

The risk of diabetes for subjects with BMI ≥27.0 kg/m² compared to those with BMI<22.0 kg/m² was also examined; the multivariate OR (95% CI) was 3.24 (1.08–9.71; $p=0.04$) for Yao men and 3.34 (1.40–7.95; $p=0.007$) for Yao women. However, no significant association was observed in either Kyowa men or women (data not shown).

Discussion

In the present follow-up study, increased BMI and WC were positively associated with risk of hypertension in men and women in the city of Yao in Osaka Prefecture and in women in the rural community of Kyowa in Ibaraki Prefecture, Japan. In Yao men and women, and Kyowa women, BMI and SSF were associated with risk of diabetes. WC and WHtR were also associated with risk of diabetes in Yao and Kyowa women, but not in men.

Previous cross-sectional studies have indicated that BMI, WC, and WHR or WHtR were equally correlated with the prevalence of hypertension in both genders (*7, 8, 11, 14*), while other studies showed that WC was the best single correlate for hypertension (*10, 12*). Many prospective studies have shown that BMI, a measure of overall obesity, is associated with hypertension (*15–17*), while other follow-up studies have shown that WC, WHtR and WHR, measures of abdominal adiposity, were significantly associated with the risk of hypertension (*18*). Our results were consistent with the findings from those studies that both overall obesity and abdominal adiposity were associated with hypertension.

Previous cross-sectional studies showed that WHtR (*3, 4, 8*), WHR (*11*) and WC (*19*) were associated with the prevalence of diabetes in both genders. Follow-up studies in Germany and the United States found that overall obesity measured by BMI and abdominal adiposity measured by WC and WHR are useful in predicting the risk of diabetes (*3, 20*), while another 6-year follow-up study in the United States showed that WHR and the waist-to-thigh ratio were better measures for diabetes than BMI in both genders (*21*). In the present study, BMI and SSF were marginally significant or significant indicator for risk of diabetes in both populations and both genders, with the exception of men in Kyowa, and WC and WHtR were also significant indicators for the risk of diabetes in women. Our finding for women agrees with the results from a study of Pima Indians showing that BMI, WC, WHR and waist-to-thigh ratio were equally good predictors for the risk of diabetes (*22*), and also with the results from the MONICA/KORA Augsburg Study showing that BMI and WC were equally good predictors for the risk of diabetes (*20*).

One strength of the present study was that the incidence of hypertension and diabetes was ascertained by repeated standardized measurements of blood pressure and blood glucose levels. The anthropometrics measurements were conducted according to a standard protocol by trained technicians. We had good reproducibility and validity for the measurements. For example, the Spearman correlation coefficients of SSF, measured 1 year apart for the same subject ranged from 0.7 to 0.9, as shown in a previous study (*23*). In that study, SSF was correlated with central fat mass estimated by dual-energy X-ray absorptiometry scanning for men ($r=0.80$) and women ($r=0.82$) (*23*). These study characteristics allowed us to examine carefully the relationships of anthropometrics measures with established and modifiable cardiovascular risk factors, such as hypertension and diabetes.

The reason for the lack of significant association between anthropometric measures and risks of hypertension and diabetes in Kyowa men was uncertain. We may have had limited statistical power to detect real associations and/or residual confounders of the associations. We adjusted for selected cardiovascular risk factors, but we could not exclude the possible influence of other risk factors, such as lifestyle and psychosocial factors.

In summary, the significant predictors for hypertension were BMI and WC and those for diabetes were BMI and SSF in both populations and genders, with the exception of men in Kyowa. WC and WHtR were also predictors for diabetes in women but not in men.

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References

1. Health and Welfare Statistics Association: Kokumin Eisei no Doukou 2005. *Kousei no Shihyou* (*J Health Welfare Stat*) 2005; **52**: 378–379 (in Japanese).
2. Black HR: Cardiovascular risk factors, in Zaret BL, Moser M, Cohen LS (eds): Yale University School of Medicine Heart Book. New York, Hearst Books, 1992, pp 23–35.
3. Hsieh SD, Yoshinaga H, Muto T: Waist-to-height ratio, a simple and practical index for assessing central fat distribution and metabolic risk in Japanese men and women. *Int J Obes* 2003; **27**: 610–616.
4. Hsieh SD, Muto T: The superiority of weight-to-height ratio as an anthropometric index to evaluate clustering of coro-

nary risk factors among non-obese men and women. *Prev Med* 2005; **40**: 216–220.
5. Kawada T: Body mass index is a good predictor of hypertension and hyperlipemia in a rural Japanese population. *Int J Obes* 2002; **26**: 725–729.
6. Ho SC, Chen YM, Woo JLF, Leung SSF, Lam TH, Janus ED: Association between simple anthropometric indices and cardiovascular risk factors. *Int J Obes* 2001; **25**: 1689–1697.
7. Ko GTC, Chan JCN, Woo J, *et al*: Simple anthropometric indexes and cardiovascular risk factors in Chinese. *Int J Obes* 1997; **21**: 995–1001.
8. Huang KC, Lin WY, Lee LT, *et al*: Four anthropometric indices and cardiovascular risk factors in Taiwan. *Int J Obes* 2002; **26**: 1060–1068.
9. Onat A, Sansoy V, Uysal O: Waist circumference and waist-to-hip ratio in Turkish adults: interrelation with other risk factors and association with cardiovascular disease. *Int J Cardiol* 1999; **70**: 43–50.
10. Zhu SK, Wang ZM, Heshka S, Heo M, Faith MS, Heymsfield SB: Waist circumference and obesity-associated risk factors among whites in the third National Health and Nutrition Examination Survey: clinical action thresholds. *Am J Clin Nutr* 2002; **76**: 743–749.
11. Dalton M, Cameron AJ, Zimmet PZ, *et al*: Waist circumference, waist-hip ratio and body mass index and their correlation with cardiovascular disease risk factors in Australian adults. *J Intern Med* 2003; **254**: 555–563.
12. Dobbelsteyn CJ, Joffres MR, MacLean DR, Flowerdew G, The Canadian Heart Health Surveys Research Group: A comparative evaluation of waist circumference, waist-to-hip ratio and body mass index as indicators of cardiovascular risk factors. The Canadian Heart Health Surveys. *Int J Obes* 2001; **25**: 652–661.
13. Wang Y, Rimm EB, Stampfer MJ, Willett WC, Hu FB: Comparison of abdominal adiposity and overall obesity in predicting risk of type 2 diabetes among men. *Am J Clin Nutr* 2005; **81**: 555–563.
14. Harris MM, Stevens J, Thomas N, Schreiner, Folsom AR: Association of fat distribution and obesity with hypertension in a bi-ethnic population: the ARIC Study. *Obes Res* 2000; **8**: 516–524.
15. Huang Z, Willet WC, Manson JE, *et al*: Body weight, weight change, and risk for hypertension in women. *Ann Intern Med* 1998; **128**: 81–88.
16. Jousilahti P, Tuomilehto J, Vartiainen E, Pekkanen J, Puska P: Body weight, cardiovascular risk factors, and coronary mortality. *Circulation* 1996; **93**: 1372–1379.
17. Wilson PWF, D'Agostino RB, Sullivan L, Parise H, Kannel WB: Overweight and obesity as determinants of cardiovascular risk. The Framingham Experience. *Arch Intern Med* 2002; **162**: 1867–1872.
18. Fuchs FD, Gus M, Moreira LB, *et al*: Anthropometric indices and the incidence of hypertension: a comparison analysis. *Obes Res* 2005; **13**: 1515–1517.
19. Wildman RP, Gu D, Reynolds K, Duan X, Wu X, He J: Are waist circumference and body mass index independently associated with cardiovascular disease risk in Chinese adults? *Am J Clin Nutr* 2005; **82**: 1195–1202.
20. Meisinger C, Döring A, Thorand B, Heier M, Löwel H: Body fat distribution and risk of diabetes in the general population: are there differences between men and women? The MONICA/KORA Augsburg Cohort Study. *Am J Clin Nutr* 2006; **84**: 483–489.
21. Snijder MB, Dekker JM, Visser M, *et al*: Association of hip and thigh circumferences independent of waist circumference with the incidence of type 2 diabetes: Hoorn Study. *Am J Clin Nutr* 2003; **77**: 1192–1197.
22. Tulloch-Reid MK, Hanson RL, William DE, Knowler WC, Looker HC: Do measures of body fat distribution provide information on the risk of type 2 diabetes in addition to measures of general obesity? *Diabetes Care* 2003; **26**: 2556–2561.
23. Ketel IJG, Volman MNM, Seidell JC, Stehouwer CDA, Twisk JW, Lambalk CB: Superiority of skinfold measurements and waist over waist-to-hip ratio for determination of body fat distribution in a population-based cohort of Caucasian Dutch adults. *Eur J Endocrinol* 2007; **156**: 655–661.

Trends in the Incidence of Coronary Heart Disease and Stroke and Their Risk Factors in Japan, 1964 to 2003

The Akita-Osaka Study

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A continuous decline in mortality and morbidity from coronary heart disease (CHD) has been documented in the U.S. (1–4). This decline is accompanied by a reduction in serum total cholesterol levels, which has been attributed to improvements in medical care and community-based prevention strategies (2,5,6). In Asia, there is concern that the incidence of CHD may be increasing as the result of socioeconomic development and a growing westernization of lifestyles, including greater availability of high-calorie and high-fat foods, as well as widespread sedentary work patterns coupled with high mental stress (7,8). Although an increased incidence of CHD has not been demonstrated yet by long-term community-based studies, there have been signs of a developing epidemic of CHD in several Asian countries (9–12).

For example, in Japan, a highly developed country in Asia, total cholesterol levels and obesity have increased substantially during the past several decades, partly as the result of the spread of western lifestyles (13). Despite this increase in total cholesterol levels, the mortality from CHD has been declining since 1970 among Japanese men and women (14), and CHD mortality in Japan remains approximately one-fourth of that in the U.S. (15). However, in Tokyo and Osaka (16), the largest metropolitan areas where Westernized lifestyles are more common, CHD mortality has been greater and has declined less than the overall numbers for Japan. We hypothesized that the incidence of CHD has increased in urban communities of Japan compared with rural areas. In this report, we conducted a systematic examination of 40-year trends in the incidence of CHD and stroke as well as in the prevalence of cardiovascular risk factors among middle-aged residents in urban and rural communities in Japan. Our findings may be a harbinger of future trends in CHD in the developing countries of Asia.

Methods

The survey populations were residents of the Minami-Takayasu district of Yao City (an urban community in Osaka Prefecture, 250 miles west of Tokyo, with a total census population of 23,552 in 2000) and Ikawa (a rural community in Akita Prefecture, 290 miles northeast of Tokyo, with a total census population of 6,116 in 2000). The target populations for this study were residents ages 40 to 69 years. This criterion resulted in a study population of 9,549 people in the urban community and 2,671 in the rural community. According to 24-h dietary recall surveys taken from 1988 to 1995, men ages 40 to 59 years in the urban community had greater intakes of fat and cholesterol and a lower intake of sodium than those in the rural community (fat intake: 22% vs. 19% of total energy; cholesterol intake: 415 mg/day vs. 387 mg/day; and salt intake: 13 g/day vs. 14g/day, respectively) (17).

For all the residents, cardiovascular disease (CVD) end points were ascertained from death certificates, national insurance claims, reports by local physicians, reports by public health nurses and health volunteers, and annual cardiovascular risk surveys. For a supplemental information source, we also mailed an annual questionnaire to all the households in the urban community to determine the incidence of CVD. To ascertain the diagnosis of CVD for living cases, physicians participating in this study obtained medical histories and reviewed medical records from local clinics and hospitals. In the case of deaths, histories were obtained from the families and medical records were reviewed.

The criteria for CHD and stroke have been described in detail elsewhere (9). In brief, the indication for definite myocardial infarction (MI) was typical severe chest pain (lasting at least 30 min and with no definite nonischemic cause) accompanied by new, abnormal, and persistent Q or QS waves; consistent changes in cardiac enzyme levels; or both. If the electrocardiographic and enzyme levels were nondiagnostic or not obtainable, but the patient had typical chest pain, a diagnosis of possible MI was made. In this report, definite and possible infarctions have been combined and categorized as MI. Sudden cardiac death was defined as death within 1 h of symptom onset, a witnessed cardiac arrest, or abrupt collapse preceded by not more than 1 h of symptoms. We defined CHD as MI or sudden cardiac death.

Starting in 1980, we expanded clinical data collected among the study populations to include percutaneous coronary interventions for angiographically documented severe stenosis accompanied by atypical chest pain. Stroke was defined as a constellation of neurological deficits that were sudden or rapid in onset that lasted at least 24 h or until death. For long-term comparability of CHD and stroke incidence, we have used these classical criteria consistently. Final diagnoses of CHD and stroke were made by a panel of 4 study physician epidemiologists, 1 of whom was involved in the diagnostic process throughout the study to avoid the misclassification of diagnoses.

Age-adjusted annual incidence rates for CHD and stroke were calculated from the number of new cases per 100,000 persons during the periods 1964 to 1971, 1972 to 1979, 1980 to 1987, 1988 to 1995, and 1996 to 2003 in both communities. Cases of recurrent CHD and stroke were excluded.

Cardiovascular risk factors were ascertained among a sample of residents during each of the 5 survey periods, 1964 to 1966 (1963 to 1966 for the rural community), 1976 to 1979, 1984 to 1987, 1992 to 1995, and 2000 to 2003. The participants in the risk factor surveys were recruited from all residents who were 40 years old or older in both communities, and the surveys were conducted for the purpose of promoting primary prevention of CVD. The respective participation rates for the urban and rural census population within the target age group were 93% and 87% during 1964 to 1966, 37% and 81% during 1976 to 1979, 31% and 84% during 1984 to 1987, 28% and 68% during 1992 to 1995, and 24% and 61% during 2000 to 2003. The participation rates in the latter 4 periods were lower in an urban population than in a rural population probably because urban residents had more opportunities to undergo medical check-ups other than our risk factor surveys.

The methodological details of risk factor examinations were reported previously (18). The definition of each risk factor was as follows. Hypertension was defined as a systolic blood pressure ≥140 mm Hg, a diastolic blood pressure ≥90 mm Hg, or use of an antihypertensive medication. High total cholesterol was defined as a total cholesterol level of 5.18 mmol/l (200 mg/dl) or more, or use of a lipid-lowering medication. High serum triglyceride (TG) levels were defined as a fasting level ≥1.69 mmol/l (150 mg/dl) or a nonfasting TG level ≥2.82 mmol/l (250 mg/dl). High blood glucose was defined as a fasting glucose level of ≥6.11 mmol/l (110 mg/dl), a nonfasting glucose level of ≥7.77 mmol/l (140 mg/dl), or the use of medication for diabetes. This study was approved by the human ethics review committee of Osaka Medical Center for Health Science and Promotion.

To calculate the age-adjusted incidence, we employed the direct standardization method using the age distribution of national model population in 1985. Linear trends in incidence rates were examined with the chi-square test. Age-adjusted means of risk factors were estimated with analysis of covariance and age-adjusted prevalences with the direct method of standardization.

The significance of risk factor trends was examined for continuous variables by using regression analysis for repeated measures (19), with the 5 periods represented as 1965.0, 1977.5, 1985.5, 1993.5, and 2001.5, and for discrete variables by using the chi-square test for trend.

Differences in means or proportions were examined with the analysis of covariance or chi-square test. All statistical analyses were performed using the SAS System for Windows (Version 9.1, SAS Institute, Cary, North Carolina).

Results

The age-adjusted incidence of CHD among urban men (Table 1) showed an insignificant increase from 1964 to 1971 to 1972 to 1979, followed by a tendency to decline until 1980 to 1987. However, the age-adjusted incidence of CHD started

Table 1 Age-Adjusted Annual Incidence of Coronary Heart Disease and Stroke per 100,000 Persons Among 40- to 69-Year-Old Men and Women During 5 Survey Periods From 1964 to 1971 to 1996 to 2003 in a Japanese Urban Community

	1964–1971	1972–1979	1980–1987	1988–1995	1996–2003	p for Trend
Men						
No. at risk	1,367	2,074	3,135	4,164	4,656	
Coronary heart disease						
No. of cases	6	13	12	27	41	
Age-adjusted incidence	54 (11–97)	90 (45–136)	52 (24–80)	83 (52–114)	100 (68–132)	0.13
Myocardial infarction						
No. of cases	5	12	10	25	37	
Age-adjusted incidence	45 (5–85)	83 (40–127)	42 (16–67)	76 (47–106)	90 (59–120)	0.13
Sudden cardiac death						
No. of cases	1	1	2	2	4	
Age-adjusted incidence	—	—	10 (0–23)	7 (0–15)	10 (0–21)	0.85
Coronary intervention						
No. of cases	—	—	1	7	12	
Age-adjusted incidence	—	—	—	23 (7–40)	27 (10–43)	0.011
Coronary heart disease and coronary intervention						
No. of cases	—	—	13	34	53	
Age-adjusted incidence	—	—	56 (27–85)	106 (71–141)	127 (91–163)	0.008
Stroke						
No. of cases	30	49	51	71	50	
Age-adjusted incidence	268 (172–364)	319 (234–404)	242 (182–302)	230 (179–281)	118 (84–153)*	<0.001
Women						
No. at risk	1,517	2,302	3,244	4,364	4,893	
Coronary heart disease						
No. of cases	4	4	8	12	8	
Age-adjusted incidence	33 (1–66)	22 (1–44)	36 (13–59)	37 (17–57)	18 (5–32)	0.53
Myocardial infarction						
No. of cases	3	2	6	11	6	
Age-adjusted incidence	25 (0–53)	10 (0–25)	27 (7–47)	34 (15–53)	14 (2–26)	0.98
Sudden cardiac death						
No. of cases	1	2	2	1	2	
Age-adjusted incidence	—	12 (0–27)	9 (0–21)	—	4 (0–11)	0.37
Coronary intervention						
No. of cases	—	—	0	1	2	
Age-adjusted incidence	—	—	—	—	4 (0–11)	0.35
Coronary heart disease and coronary intervention						
No. of cases	4	4	8	13	10	
Age-adjusted incidence	33 (1–66)	22 (1–44)	36 (13–59)	40 (19–61)	23 (8–37)	0.85
Stroke						
No. of cases	15	39	37	27	34	
Age-adjusted incidence	125 (62–187)	213 (147–279)	161 (113–210)	83 (53–113)†	80 (52–108)	<0.001

Numbers at risk in 1964–1971, 1972–1979, 1980–1987, 1988–1995, and 1996–2003 are based on the average numbers of the census population in 1965 and 1970, in 1975, the average in 1980 and 1985, in 1990, and in 2000, respectively. Numbers in parentheses show 95% confidence interval. *$p < 0.001$. †$p < 0.01$ (level compared with the immediately preceding period). Age-adjusted incidence was not calculated in case of the small number of subjects.