Trends in the proportions of stroke subtypes and coronary heart disease in the Japanese men and women from 1995–2009

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Abstract

Background: The limited evidence on trends in the proportions of stroke subtypes and coronary heart disease in Japan.

Methods and results: Stroke and coronary heart disease registrations from three periods including 1995 to 1999, 2000 to 2004, and 2005 to 2009 were examined for residents aged 55 to 74 years for each period who were admitted with acute cardiovascular disease. Subjects who experienced an onset of stroke, or coronary heart disease, or moved at the beginning of each period were excluded. There were 3,181 cases of strokes and 768 cases of coronary heart disease in 1995 to 2009. The age-adjusted proportion of intraparenchymal hemorrhage was 34%, 25%, and 24% ($p = 0.02$) for men, and 27%, 29%, and 30% ($p = 0.41$) for women; ischemic stroke was 57%, 68%, and 73% ($p = 0.002$) for men, and 46%, 52%, and 58% ($p = 0.02$) for women; and embolic infarction was 23%, 31%, and 32% ($p < 0.001$) for men, and 21%, 23%, and 30% ($p = 0.009$) for women, respectively. The proportions of sudden cardiac death and myocardial infarction among total coronary heart disease did not change during the three periods for either sex.

Conclusions: Between 1995–1999 and 2005–2009, the proportion of intraparenchymal hemorrhage among all types of stroke decreased for men, while the proportions of ischemic stroke among all types of stroke and embolic infarction among ischemic stroke increased for both men and women.

1. Introduction

Past epidemiologic studies have indicated that the proportion of hemorrhagic stroke among all types of stroke was higher in Asians than in Americans and Europeans [1-4]. For ischemic stroke subtypes, the proportion of large-artery occlusive infarction in Americans [5] was much greater than that in Japanese (61% versus 25%–26%) [4]. The higher proportions of hemorrhagic stroke and lower proportions of large-artery occlusive infarction in Japanese may be explained in part by the higher prevalence of hypertension [6], and lower serum total cholesterol levels [7] from 1980 to 2000 in Japan. In addition, the proportions of hemorrhagic and ischemic strokes did not change substantially from 1992 to 2002 among Japanese people age ≥40 years [4]. On the other hand, from 1964 to 2003, the incidence of stroke declined substantially for Japanese men and women, while the incidence of coronary heart disease increased for urban men, but not for rural men and women aged 40–69 years [8]. Similarly, the Hisayama study reported that from 1961 to 2000, the incidence of stroke declined, while the incidence of coronary heart disease was unchanged for both sexes aged ≥40 years [1].

We investigated the proportion of stroke subtypes among all types of stroke, sudden cardiac death (SCD), and myocardial infarction among coronary heart disease in a large Japanese cohort from the Japan Public Health Center-basedprospective (JPHC) study.

2. Methods

2.1 Surveyed Populations

The JPHC study was conducted in 1990 to 1994 with a population aged 40 to 69 at 11 public health center areas throughout Japan. There were a total of 140,420 registered residents in the JPHC study from the baseline survey [9].

In this study, all types of stroke and coronary heart disease registrations were examined from 1995 to 2009 with residents aged 55 to 74 years for each year (40 to 69 years at baseline survey). We excluded subjects who experienced an onset of stroke, or coronary heart disease at the beseline survey. The study protocol was approved by the human ethics review committees of the National Cancer Center, Osaka University Graduate School of Medicine and each registered hospital.

2.2 Confirmation of Stroke and Coronary Heart Disease Incidence

The objective of the present study was to determine the incidence of stroke and coronary heart disease. A total of 78 hospitals were registered in the sampling areas of the JPHC cohort. They were all major hospitals where acute stroke and coronary heart disease cases would be admitted. At each hospital, all medical records of stroke and coronary heart disease events were reviewed by hospital physicians, public health center physicians, or research physicians who were blind to the baseline data, using the standard format of registration. Stroke and coronary heart disease events were regis-

tered if they occurred after the return of the baseline questionnaire or after January 1, 2010. To complete the review of fatal stroke and coronary heart disease cases, we also conducted a systematic search of death certificates and medical records at the registered hospitals. These records were reviewed by a panel of physician epidemiologists.

Stroke was confirmed based on medical records and meeting the criteria of the National Survey of Stroke [10], which requires a constellation of neurological deficits of sudden or rapid onset lasting at least 24 hours or until death. Strokes were classified as ischemic stroke (lacunar, large-artery occlusive, embolic, and unclassified infarctions), and hemorrhagic stroke (intracerebral or subarachnoid hemorrhage), primarily based on computed tomography (CT), magnetic resonance imaging (MRI) or autopsy findings [11]. Infarcts ≤1.5 cm in diameter at the based ganglion and/or pons on brain imaging were classified as lacunar infarction, while infarcts >1.5 cm involving cortical areas were classified as large-artery occlusive infarction [11,12]. The definition of embolic infarction required the same criteria as ischemic infarction, plus either a source of possible cerebral emboli in a vessel or the presence of an embolus in the brain, or medical record evidence of a possible source of embolus. A stroke case diagnosed clinically but showing no lesions on CT, MRI, or autopsy was classified as a stroke of undetermined type.

Coronary heart disease was defined as myocardial infarction and SCD. Incidence of myocardial infarction and SCD were confirmed in the medical records according to the criteria of the MONICA (Multinational MONItoring of trends and determinants in CArdiovascular disease) project [13], which required evidence from electrocardiograms, cardiac enzymes, and/or autopsy. Based on a combination of all findings available for review, we classified diagnoses as "definite myocardial infarction" and "possible myocardial infarction". The definite and possible myocardial infarction were combined and presented as myocardial infarction. In the absence of a diagnosis for myocardial infarction, deaths that occurred within one hour from onset or within one hour of having been observed alive and symptom-free were regarded as SCD. We excluded candidate cases if they survived for over one hour after symptom onset, or if there was another apparent cause of death, such as stroke, cancer, or accident.

2.3 Statistical Analyses

For the analysis, all types of stroke and coronary heart disease registrations were examined from three periods including 1995 to 1999, 2000 to 2004, and 2005 to 2009 with residents aged 55 to 74 years for each period. We excluded subjects who experienced an onset of stroke, or coronary heart disease, or moved at the beginning of each

period. The sex-specific age-adjusted incidence of stroke and its subtypes, and coronary heart disease were tested by the Poisson regression analysis in each period. We also tested the age-adjusted linear trends in all types of stroke and coronary heart disease incidence, the proportions of stroke subtypes among all types of stroke or ischemic stroke, and SCD among total coronary heart disease across the three study periods using the Poisson regression analysis. All *p* values for statistical tests were two-tailed and a *p* value <0.05 was considered statistically significant. We used SAS (version 9.3) for all statistical analyses.

3. Results

A total census population consisted of 23,902 men and 27,826 women in 1995 to 1999, 26,898 men and 31,247 women in 2000 to 2004, and 30,408 men and 35,054 women in 2005 to 2009. Participants were aged 55 to 74 years. All participants were divided into 5-year age groups between 40 and 69 years at baseline survey (Figure 1).

Table 1 shows the crude number at risk, and incidence of all types of stroke and coronary heart disease in the survey periods. There were 3,181 cases (1,902 men and 1,279 women) of all stroke incidences, including 892 cases in 1995 to 1999, 1,092 cases in 2000 to 2004, and 1,197 cases in 2005 to 2009. For coronary heart disease, there were 238 cases from 1995 to 1999, 252 cases from 2000 to 2004, and 278 cases from 2005 to 2009. The number of stroke and coronary heart disease incidents was the lowest among women aged 55 to 59 years in each study period.

Table 2 shows the incidence of stroke and coronary heart disease, proportion of stroke subtypes among all types of stroke, and proportions of SCD and myocardial infarction among total coronary heart disease. The age-adjusted incidence of coronary heart disease during the three periods, and the incidence of stroke between 2000–2004 and 2005–2009 trend to decreased for both sexes. The age-adjusted incidence of stroke was 470, 497, and 460 per 100,000 individuals per year ($p = 0.61$) for men, and 282, 279, and 241 per 100,000 individuals per years ($p = 0.02$) for women, respectively. The corresponding age-adjusted incidence of coronary heart disease was 156, 136, and 121 per 100,000 individuals per years ($p = 0.05$) for men, and 43, 39, and 30 per 100,000 individuals per years ($p = 0.01$) for women, respectively.

The proportion of intraparenchymal hemorrhage for men and subarachnoid hemorrhage for both sexes among all types of stroke declined, while the proportion of ischemic stroke among all types of stroke increased for both sexes throughout the three periods. However, this trend did not reach statistical significance for subarachnoid hemorrhage. The age-adjusted proportion of intraparenchymal hemorrhage was 34%, 25%, and 24% ($p = 0.02$) for men, and 27%, 29%, and 30% ($p = 0.41$) for women, respectively; subarachnoid hemorrhage was 8%, 6%, and 3% ($p = 0.08$) for men, and 25%, 18%, and 12% ($p = 0.06$) for women, respectively; and ischemic stroke was 57%, 68%, and 73% ($p = 0.002$) for men, and 46%, 52%, and 58% ($p = 0.02$) for women, respectively. The proportions of SCD and myocardial infarction among coronary heart disease did not change during the three periods for either sex.

We also examined the proportions of ischemic stroke subtypes among ischemic stroke across the three study periods, as shown in Table 3. The proportion of embolic infarction among ischemic stroke increased for both sexes. The age-adjusted proportion of embolic infarction within ischemic stroke was 23%, 31%, and 32% ($p < 0.001$) for men, and 21%, 23%, and 30% ($p = 0.009$) for women, respectively. The corresponding proportion of large-artery occlusive infarction was 20%, 19%, and 21% ($p = 0.10$) for men, and 16%, 20%, and 21% ($p = 0.09$) for women, respectively. The proportions of lacunar infarction among ischemic stroke did not change during the three study periods.

4. Discussion

The incidence of stroke and coronary heart disease treend to decreased for Japanese men and women aged 55 to 74 years from 1995 to 2009, which was consistent with the findings from previous studies [8, 14]. A Japanese community-based study showed that the incidence of coronary heart disease decreased by 45% for women, but increased by 15% for men, and the incidence of stroke decreased by 72% for men and 66% for women aged 40–69 years from 1964 to 2003 [8]. A meta-analysis of 119 studies with 16.8 million cases of stroke reported that the age-standardized incidence of stroke decreased by 53% in Japanese between 1990 and 2010 [14].

The reduced proportion of intraparenchymal hemorrhage among all types of stroke may be due to decreased blood pressure levels and increased total cholesterol levels in the past two decades in Japan [7, 8]. Mean systolic blood pressure levels decreased by 6.7% for men and 7.2% for women from 1963 to 2003 among Japanese aged 40–69 years [8], while the mean serum total cholesterol levels increased by 7.3% for men and 8.7% for women from 1980 to 2000 among those aged ≥30 years [7], reaching the same levels as from US men and women aged ≥20 years in 2000 [15].

Furthermore, the declining trend for the proportion of subarachnoid hemorrhage among all types of stroke may be due to the wide use of clipping for unruptured aneurysms in Japan. Since 1988, hospital-based health check-ups have been conducted for unruptured aneurysms using CT or MRI [16]. Thirty seven percent of patients with ruptured and unruptured aneurysms underwent clipping for unruptured aneurysms in

Japan according to a study of 369 core neurosurgical training centers [17]. The risk of regrowth of completely clipped aneurisms was lower than the risk of de novo aneurysm formation during the mean 9.3-year follow-up of 412 patients who underwent clipping of cerebral aneurysms; the annual rate was 0.26% versus 0.89% [18].

The proportions of ischemic stroke among all types of stroke, in particular, large-artery occlusive infarction and embolic infarction among ischemic stroke increased for both sexes. However, this trend of borderline statistical significance for large-artery occlusive infarction. The Atherosclerosis Risk in Communities Study (ARIC) indicated that total cholesterol levels were positively associated with the risk of large-artery occlusive infarction among 14,448 men and women aged 45–64 years: multivariable HR=1.13 (1.02–1.26) per 1-SD (41mg/dL) of total cholesterol levels [5]. The JPHC study of 33,469 men and women aged 40–69 years reported that a 1mmol/L (39mg/dL) increment of total cholesterol levels was associated with a 1.30 (1.04–1.63) higher risk of large-artery occlusive infarction [12]. A recent hospital-based study of 3,950 consecutive stroke patients reported that the proportion of embolic infarction among ischemic stroke increased from 26% to 56% in the 2000 to 2012 period [19]. The increased proportions of large-artery occlusive infarction and embolic infarction in Japanese men and women paralleled the trends for risk factors i.e., the increased prevalence of high total cholesterol (total cholesterol ≥5.69 mmol/L, 14% to 31% for men and 25% to 45% for women) and diabetes mellitus (4% to 10% for men and 2% to 4% for women) between 1981–1985 and 2001–2005 [20].

We also observed that the proportion of SCD among total coronary heart disease trended to decrease for men. The potential risk factors of SCD, such as overweight, hypertension, current smoking, and heavy drinking decreased from 1981 to 2005 for Japanese men aged 30–84 years [20]. Furthermore, the number of patients transported to emergency rooms by ambulance increased by 60% from 1995 to 2009 [21] may have contributed to the decrease in SCD.

The strengths of this study include the large population size with a small follow-up loss and that more than 98% of stroke incidence was confirmed by the findings of CT, MRI, or autopsy. The major study limitation was that the subjects were limited to the cohort participants. However, both the incidence of and mortality from each stroke subtype declined between 1995–1999 and 2005–2009.

In conclusion, between 1995–1999 and 2005–2009, the proportion of intraparenchymal hemorrhage among all types of stroke decreased for men, while the proportions of ischemic stroke among all types of stroke and embolic infarction among ischemic stroke increased for both men and women.

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Disclosure

The authors declared no conflict of interest.

5. References

[1] M. Kubo, Y. Kiyohara, I. Kato, Y. Tanizaki, H. Arima, K. Tanaka, et al. Trends in the incidence, mortality, and survival rate of cardiovascular disease in a Japanese community: the Hisayama study, Stroke 34 (2003) 2349 –2354.

[2] Korean Neurological Association. Epidemiology of cerebrovascular disease in Korea—a collaborative study, 1989 –1990, J. Korean. Med. Sci 8 (1993) 281-289.

[3] B. Jiang, W.Z. Wang, H. Chen, Z. Hong, Q.D. Yang, S.P. Wu, et al. Incidence and trends of stroke and its subtypes in China: results from three large cities, Stroke 37 (2006) 63-68.

[4] A. Kitamura, Y. Nakagawa, M. Sato, H. Iso, S. Sato, H. Imano, et al. Proportions of stroke subtypes among men and women > or =40 years of age in an urban Japanese city in 1992, 1997, and 2002, Stroke 37 (2006) 1374-1378.

[5] T. Ohira, E. Shahar, L.E. Chambless, W.D. Rosamond, T.H. Mosley, A.R. Folsom. Risk factors for ischemic stroke subtypes: the Atherosclerosis Risk in Communities study, Stroke 37 (2006) 2493-2498.

[6] The Ministry of Health, Labour and Welfare. A Report of The Fifth National Survey of Cardiovascular Diseases (in Japanese), Tokyo. Japan: Chuohoki Syuppan (2003) 45-190.

[7] National Survey on Circulatory Disorders in 1980, 1990, and 2000. Tokyo, Japan: Ministry of Health, Labor and Welfare; 1983, 1993 and 2003. (in Japanese)

[8] A. Kitamura, S. Sato, M, Kiyama, H. Imano, H, Iso, T, Okada, et al. Trends in the incidence of coronary heart disease and stroke and their risk factors in Japan, 1964 to 2003: the Akita-Osaka study, J. Am. Coll. Cardiol 52 (2008) 71–79.

[9] S. Tsugane, N. Sawada. The JPHC study: design and some findings on the typical Japanese diet, Jpn. J. Clin. Oncol 44 (2014) 777-782.

[10] A.E. Walker, M. Robins, F.D. Weinfeld. The National Survey of Stroke. Clinical findings, Stroke 12 (1981) I13-I44.

[11] H. Iso, K. Rexrode, C.H. Hennekens. Application of computer tomography-oriented criteria for stroke subtype classification in a prospective study, Ann. Epidemiol 10 (2000) 81-87.

[12] R. Cui, H. Iso, K. Yamagishi, I. Saito, Y. Kokubo, M. Inoue, et al. High serum total cholesterol levels is a risk factor of ischemic stroke for general Japanese population: The JPHC study, Atherosclerosis 221 (2012) 565-569.

[13] H. Tunstall-Pedoe, K. Kuulasmaa, P. Amouyel, D. Arveiler, A.M. Rajakangas, A. Pajak. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents, Circulation 90 (1994) 583-612.

[14] R.V. Krishnamurthi, V.L. Feigin, M.H. Forouzanfar, G.A. Mensah, M. Connor, D.A. Bennett, et al. Global and regional burden of first-ever ischaemic and haemorrhagic stroke during 1990-2010: findings from the Global Burden of Disease Study 2010, Lancet. Glob. Health 1 (2013) e259-e281.

[15] E.S. Ford, A.H. Mokdad, W.H. Giles, G.A. Mensah. Serum Total Cholesterol Concentrations and Awareness, Treatment, and Control of Hypercholesterolemia Among US Adults: Findings From the National Health and Nutrition Examination Survey, 1999 to 2000, Circulation 107 (2003) 2185-2189.

[16] The Japan Brain Dock Society. The health guideline by 2014. http://jbds.jp/guideline.html. (accessed 1 April 2015).

[17] N. Hattori, Y. Katayama, T. Abe; Japan Neurosurgical Society. Case volume does not correlate with outcome after cerebral aneurysm clipping: a nationwide study in Japan, Neurol. Med. Chir (Tokyo) 47 (2007) 95-100.

[18] K. Tsutsumi, K. Ueki, A. Morita, M. Usui, T. Kirino. Risk of aneurysm recurrence in patients with clipped cerebral aneurysms: results of long-term follow-up angiography, Stroke 32 (2001) 1191-1194.

[19] C. Bogiatzi, D.G. Hackam, A.I. McLeod, J.D. Spence. Secular trends in ischemic stroke subtypes and stroke risk factors, Stroke 45 (2014) 3208-13.

[20] M. Maruyama, T. Ohira, H. Imano, A. Kitamura, M. Kiyama, T. Okada, et al. Trends in sudden cardiac death and its risk factors in Japan from 1981 to 2005: the Circulatory Risk in Communities Study (CIRCS), BMJ Open 2 (2012) e000573.

[21] Fire and disaster management agency. Current state of emergency rescue in Japan 2014. http://www.fdma.go.jp/neuter/topics/kyukyukyujo_genkyo/h26/01_kyukyu.pdf. (accessed 24 Dec 2014).

Figure legend

Figure 1. All participants were divided into 5-year age groups between 40 and 69 years at baseline survey.

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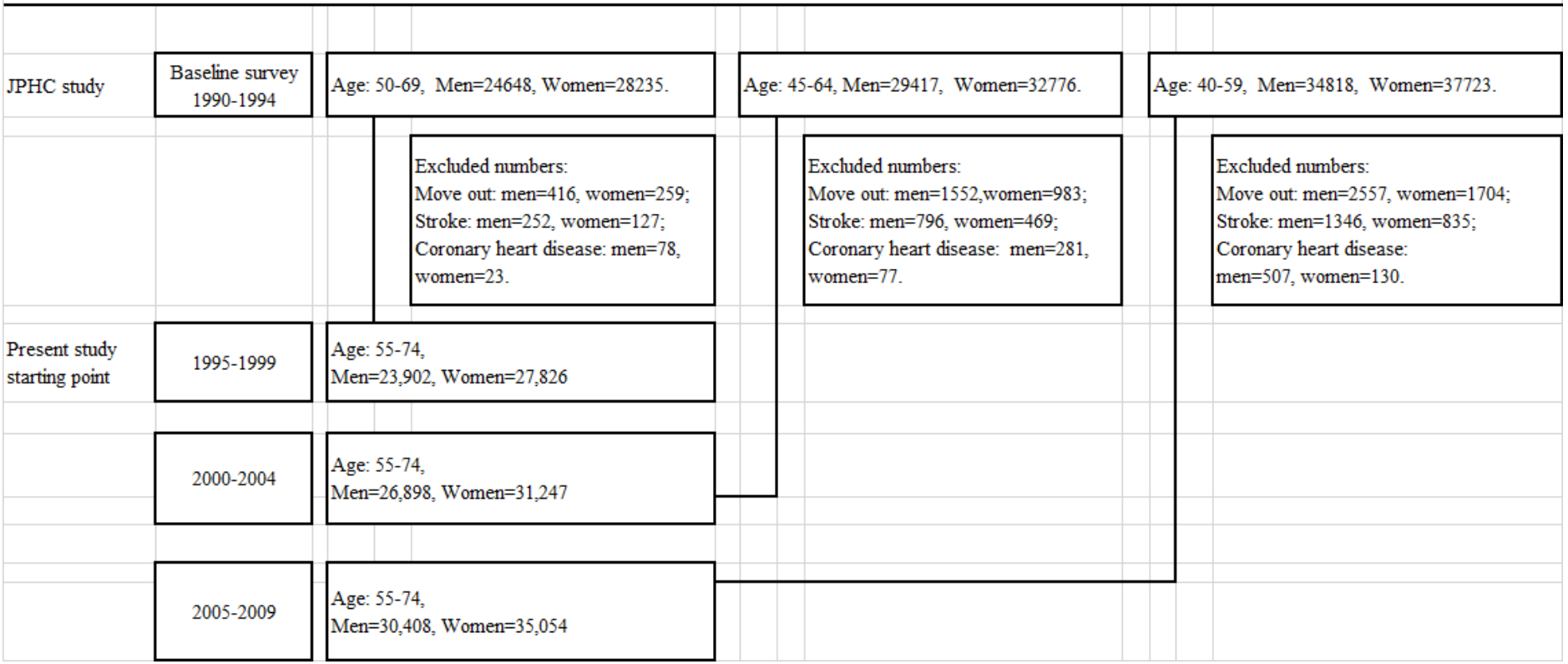

Table 1. The number of incident stroke and coronary heart disease in 1995-1999, 2000-2004 and 2005-2009 among Japanese aged 55 to 74 years.

		1995-1999			2000-2004			2005-2009		
	Age	No. at risk	No. of cases	Proportion, %	No. at risk	No. of cases	Proportion, %	No. at risk	No. of cases	Proportion, %
Men										
Total stroke	55-59	8119	117	22.4	7659	120	18.3	8815	119	16.4
	60-64	8670	190	36.4	7624	163	24.8	7210	148	20.5
	65-69	3927	113	21.7	8054	251	38.3	7114	181	25.0
	70-74	3186	102	19.5	3561	122	18.6	7269	276	38.1
	55-74	23902	522	100	26898	656	100	30408	724	100
Coronary heart disease	55-59	8119	47	26.3	7659	37	19.8	8815	37	17.5
	60-64	8670	62	34.6	7624	55	29.4	7210	31	14.7
	65-69	3927	46	25.7	8054	60	32.1	7114	64	30.3
	70-74	3186	24	13.4	3561	35	18.7	7269	79	37.5
	55-74	23902	179	100	26898	187	100.0	30408	211	100.0
Women										
Total stroke	55-59	9354	65	17.6	8437	75	17.2	9294	64	13.6
	60-64	9635	134	36.2	9020	108	24.8	8116	81	17.1
	65-69	4696	69	18.6	9408	155	35.5	8658	116	24.5
	70-74	4141	102	27.6	4382	98	22.5	8986	212	44.8
	55-74	27826	370	100	31247	436	100	35054	473	100
Coronary heart disease	55-59	9354	8	13.6	8437	8	12.3	9294	4	6.0
	60-64	9635	20	33.9	9020	9	13.8	8116	8	11.9
	65-69	4696	14	23.7	9408	31	47.7	8658	17	25.4
	70-74	4141	17	28.8	4382	17	26.2	8986	38	56.7
	55-74	27826	59	100.0	31247	65	100.0	35054	67	100.0

Table 2. Age-adjusted proportions (95%CI) and annual incidence of stroke and coronary heart disease among Japanese aged 55 to 74 years during 3 survey periods.

	1995-1999			2000-2004			2005-2009			P for trend
	Cases, n	Incidence rate*	Proportion, %	Cases, n	Incidence rate*	Proportion, %	Cases, n	Incidence rate*	Proportion, %	
Men										
Total stroke	522	470	100.0	656	497	100.0	724	460	100.0	
Intraparenchymal hemorrhage	155	135	34(30-38)	164	124	25(22-29)	196	129	24(20-27)	0.02
Subarachnoid hemorrhage	32	26	8(6-10)	41	30	6(5-8)	35	22	3(2-5)	0.08
Ischemic stroke	332	300	57(53-62)	446	332	68(64-71)	493	301	73(69-77)	0.002
Unclassified infaction	3	-	-	5	-	-	0	-	-	
Coronary heart disease	179	156	100.0	187	136	100.0	211	121	100.0	
Sudden cardiac death	32	29	17(11-22)	31	23	17(11-22)	25	15	13(8-18)	0.19
Myocardial infarction	147	131	83(78-89)	156	119	83(78-89)	186	120	87(82-92)	0.50
Women										
Total stroke	370	282	100.0	436	279	100.0	473	241	100.0	
Intraparenchymal hemorrhage	95	72	27(22-32)	125	81	29(24-33)	145	62	30(25-34)	0.41
Subarachnoid hemorrhage	80	60	25(21-30)	81	53	18(15-22)	71	39	12(9-16)	0.06
Ischemic stroke	188	141	46(40-51)	227	141	52(48-57)	256	123	58(53-63)	0.02
Unclassified infaction	7	5	2(-3, 7)	3	2	-	1	0.6	-	
Coronary heart disease	59	43	100.0	65	39	100.0	67	30	100.0	
Sudden cardiac death	8	6	17(7-27)	12	8	18(9-27)	13	6	17(8-26)	0.84
Myocardial infarction	51	37	83(73-93)	53	31	82(73-91)	54	24	83(74-93)	0.59

*Incidence rate is per 100,000 individuals per year.
P for trend is compared to proportions during 3 survey periods.

Table 3 Age-adjusted proportions (95%CI) and annual incidence of ischemic stroke subtypes among Japanese aged 55 to 74 years during 3 survey periods

	1995-1999			2000-2004			2005-2009			P for trend
	Cases, n	Incidence rate*	Proportion, %	Cases, n	Incidence rate*	Proportion, %	Cases, n	Incidence rate*	Proportion, %	
Men										
Ischemic stroke	332	296	100.0	446	324	100.0	493	230	100	
Lacunar infarction	169	153	54(48-59)	214	161	48(43-53)	235	147	46(41-51)	0.38
Large-artery occlusive infaction	68	61	20(16-25)	85	62	19(15-23)	103	61	21(17-25)	0.10
Embolic infaction	82	74	23(18-28)	140	103	31(27-36)	152	90	32(28-36)	<0.001
Unclassified infaction	13	11	3(2-6)	7	5	2(1-3)	3	1	-	
Women										
Ischemic stroke	188	140	100.0	227	139	100.0	256	116	100	
Lacunar infarction	112	85	61(53-68)	127	79	56(49-62)	132	64	51(44-57)	0.83
Large-artery occlusive infaction	30	23	16(11-23)	46	29	20(15-25)	55	26	21(16-26)	0.09
Embolic infaction	43	32	21(14-28)	53	32	23(18-29)	73	34	30(24-36)	0.009
Unclassified infaction	3	2	1(-0.1, 2)	1	-	-	-	0	-	-

*Incidence rate is per 100,000 individuals per year.
P for trend is compared to proportions during 3 survey periods.971