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to increase again thereafter (p for trend = 0.045, between 1980 to 1987 and 1996 to 2003). For CHD combined with coronary intervention, the increase between 1980 to 1987 and 1996 to 2003 was even more evident (p for trend = 0.008).

To determine cohort effects qualitatively, we calculated the age-specific incidence of CHD in each study period. The later cohorts tended to have a greater incidence of CHD among urban men; the CHD incidence rates among

Table 2 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 Rural Community

	1964–1971	1972–1979	1980–1987	1988–1995	1996–2003	p for Trend
Men						
No. at risk	946	1,063	1,131	1,281	1,294	
Coronary heart disease						
No. of cases	7	9	3	6	8	
Age-adjusted incidence	90 (23–158)	111 (40–181)	33 (4–71)	59 (12–106)	65 (16–114)	0.30
Myocardial infarction						
No. of cases	5	5	2	5	6	
Age-adjusted incidence	64 (7–121)	62 (9–115)	21 (0–50)	48 (5–90)	51 (8–94)	0.59
Sudden cardiac death						
No. of cases	2	4	1	1	2	
Age-adjusted incidence	26 (0–63)	49 (2–96)	—	—	14 (0–37)	0.12
Coronary intervention						
No. of cases	—	—	0	3	0	
Age-adjusted incidence	—	—	—	30 (0–64)	—	—
Coronary heart disease and coronary intervention						
No. of cases	7	9	3	9	8	
Age-adjusted incidence	90 (23–158)	111 (40–181)	33 (0–71)	89 (32–147)	65 (16–114)	0.50
Stroke						
No. of cases	75	36	32	30	28	
Age-adjusted incidence	974 (761–1,188)	421 (285–557)*	333 (216–451)	261 (163–359)	231 (139–323)	<0.001
Women						
No. at risk	1,103	1,228	1,315	1,415	1,377	—
Coronary heart disease						
No. of cases	0	1	1	1	1	
Age-adjusted incidence	0	—	—	—	—	—
Myocardial infarction						
No. of cases	0	1	1	1	1	
Age-adjusted incidence	—	—	—	—	—	—
Sudden cardiac death						
No. of cases	0	0	0	0	0	
Age-adjusted incidence	—	—	—	—	—	—
Coronary intervention						
No. of cases	—	—	0	0	0	
Age-adjusted incidence	—	—	—	—	—	—
Coronary heart disease and coronary intervention						
No. of cases	0	1	1	1	1	
Age-adjusted incidence	0	—	—	—	—	—
Stroke						
No. of cases	37	27	19	26	12	
Age-adjusted incidence	424 (290–557)	264 (163–364)	162 (86–239)	189 (110–269)	106 (45–166)	<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 of 1965 and 1970, in 1975, the average of 1980 and 1985, in 1990, and in 2000, respectively. Numbers in parentheses show 95% confidence interval. Age-adjusted incidence was not calculated in case of the small number of subjects.
*p < 0.001 (level compared with the immediately preceding period).

men ages 40 to 49 years in 1972 to 1979, 50 to 59 years in 1980 to 1987, and 60 to 69 years in 1988 to 1995 were 0, 62, and 108 per 100,000, respectively. The respective incidence rates among urban men ages 40 to 49 years in 1980 to 1987, 50 to 59 years in 1988 to 1995, and 60 to 69 years in 1996 to 2003 were 31, 154, and 186 per 100,000. The incidence of stroke for urban men increased slightly from 1964 to 1971 to 1972 to 1979, and subsequently decreased. Among urban women, the age-adjusted incidence of CHD remained relatively low over time. The trend in the incidence of stroke among urban women was similar to that observed in urban men.

For rural men, the age-adjusted incidence of CHD tended to decrease between the periods from 1972 to 1979 and 1980 to 1987 and demonstrated no consistent change during subsequent periods (Table 2). The incidence of stroke for rural men declined dramatically between 1964 to 1971 and 1972 to 1979, and this decline continued until 1996 to 2003. Rural women showed few occurrences of CHD throughout the 5 survey periods. In addition, the downward trend of the incidence of stroke for rural women was identical to that for rural men.

Comparisons of the age-adjusted incidence of CHD and coronary intervention in urban and rural communities are shown in Figure 1. The CHD incidence tended to be greater among rural than urban men between 1964 to 1971

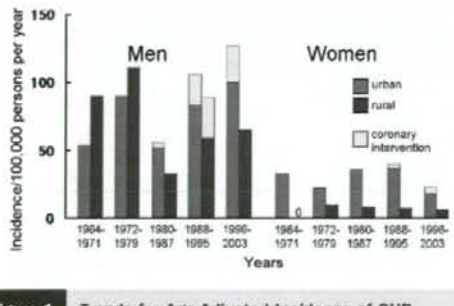

Figure 1 Trends for Age-Adjusted Incidence of CHD

The incidence of CHD tended to be greater among rural than urban men between 1964 to 1971 and 1972 to 1979, although this trend was reversed from the period of 1980 to 1987 as a result of the increase in CHD among urban men between 1980 to 1987 and 1996 to 2003. For CHD combined with coronary intervention, the increasing trend in CHD among urban men from 1980 to 1987 was more evident. The CHD incidence tended to be greater among urban than rural women over time. CHD = coronary heart disease.

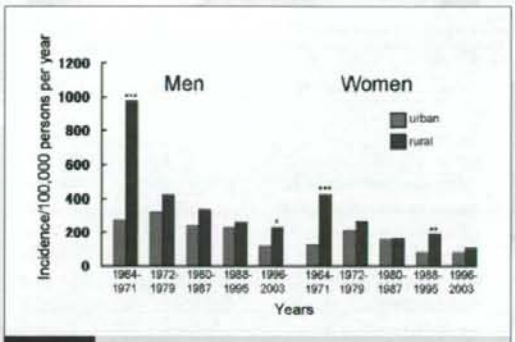

Figure 2 Trends for Age-Adjusted Incidence of Stroke

During 1964 to 1971, stroke incidence was significantly greater among rural men and women than urban ones, but the incidence of stroke in the rural community decreased substantially between 1964 to 1971 and 1972 to 1979 and, therefore, the urban-rural difference has become smaller since 1972 to 1979. *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$ for differences between urban and rural communities.

and 1972 to 1979, although this trend was reversed from the period of 1980 to 1987. The incidence of CHD tended to be greater among urban than rural women over time, although none of the differences was statistically significant. During 1964 to 1971, stroke incidence was significantly greater among rural men and women than urban ones, but the urban-rural difference has become smaller since 1972 to 1979 (Fig. 2).

The mean systolic blood pressure of urban men showed no difference between the periods 1964 to 1966 and 1976 to 1979, then decreased from 1976 to 1979 to 1984 to 1987 and did not show any further decrease thereafter (Table 3). Mean diastolic blood pressure increased between the periods 1984 to 1987 and 1992 to 1995 and remained level during 2000 to 2003. The prevalence of antihypertensive medication use increased significantly between 1964 to 1966 and 1976 to 1979 but did not change thereafter. The prevalence of hypertension declined from 1976 to 1979 to 1984 to 1987, but then increased from 1984 to 1987 to 2000 to 2003. Mean body mass index (BMI) showed significantly upward linear trends from 1976 to 1979 to 2000 to 2003, whereas the prevalence of current smoking and mean alcohol intake decreased with time. Mean total cholesterol levels and the prevalence of high total cholesterol showed a linear increase from 1964 to 1966 throughout 2000 to 2003. High-density lipoprotein cholesterol (HDL-

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Table 3 Age-Adjusted Cardiovascular Risk Characteristics Among 40- to 69-Year-Old Men and Women During 5 Survey Periods From 1963 to 1966 to 2000 to 2003 in a Japanese Urban Community

Mean ± SD or Number (%)	1963–1966	1976–1979	1984–1987	1992–1995	2000–2003	p for Trend
Men						
Number	994	491	755	790	730	
Age (yrs)	53 ± 8	55 ± 9*	54 ± 9	56 ± 8*	58 ± 8*	<0.001
Systolic blood pressure (mm Hg)	135 ± 18	135 ± 16	132 ± 16*	131 ± 17	132 ± 18	<0.001
Diastolic blood pressure (mm Hg)	80 ± 11	81 ± 10	80 ± 10	84 ± 11*	85 ± 11	<0.001
Antihypertensive medication	46 (5)	63 (13)*	80 (11)	86 (10)	100 (11)	<0.001
Hypertension	347 (38)	192 (39)	237 (33)†	306 (38)†	326 (41)	0.43
Body mass index (kg/m^2)	22.5 ± 2.8	22.3 ± 1.9†	22.7 ± 2.1*	23.3 ± 2.3*	23.8 ± 2.6*	<0.001
Current smokers	—	328 (67)	475 (63)	404 (51)*	338 (49)	<0.001
Alcohol intake (ethanol, g/day)	—	—	36 ± 27	33 ± 24*	31 ± 26	<0.001
Biochemical examination of blood						
Number	455	457	754	790	730	
Total cholesterol (mmol/l)	4.75 ± 0.84	4.94 ± 0.75*	5.09 ± 0.77*	5.22 ± 0.78*	5.45 ± 0.85*	<0.001
High total cholesterol	126 (28)	169 (37)‡	343 (45)†	385 (49)	444 (61)*	<0.001
High triglyceride	—	65 (14)	123 (16)	121 (15)	128 (18)	0.09
Lipid-lowering medication	—	—	3 (0.4)	15 (2)‡	30 (3)	<0.001
High blood glucose	—	—	120 (17)	192 (24)*	165 (22)	0.02
Antidiabetic medication	—	—	4 (1)	10 (1)	16 (2)	0.03
Women						
Number	1,224	940	1,515	1,720	1,594	
Age (yrs)	52 ± 8	54 ± 9*	53 ± 8†	53 ± 8	56 ± 8*	<0.001
Systolic blood pressure (mm Hg)	135 ± 17	130 ± 16*	130 ± 16	129 ± 16‡	128 ± 17†	<0.001
Diastolic blood pressure (mm Hg)	80 ± 11	79 ± 9†	78 ± 10†	80 ± 10*	80 ± 11	0.007
Antihypertensive medication	42 (4)	121 (13)*	154 (11)	152 (9)	185 (10)	<0.001
Hypertension	424 (37)	319 (33)	426 (29)†	456 (27)	493 (27)	<0.001
Body mass index (kg/m^2)	23.4 ± 3.0	22.9 ± 2.2*	22.6 ± 2.4*	22.9 ± 2.6*	22.8 ± 2.9‡	<0.001
Current smokers	—	90 (10)	153 (10)	163 (9)	151 (10)	0.93
Alcohol intake (ethanol, g/day)	—	—	13 ± 35	11 ± 27‡	12 ± 25	0.26
Biochemical examination of blood						
Number	562	857	1,513	1,720	1,594	
Total cholesterol (mmol/l)	4.94 ± 0.84	5.26 ± 0.78*	5.38 ± 0.81*	5.52 ± 0.81*	5.75 ± 0.87*	<0.001
High total cholesterol	188 (34)	454 (53)*	866 (59)‡	1,100 (65)*	1,209 (73)*	<0.001
High triglyceride	—	99 (12)	113 (9)†	127 (8)	135 (8)	<0.001
Lipid-lowering medication	—	—	16 (1)	43 (3)‡	110 (6)*	<0.001
High blood glucose	—	—	140 (10)	193 (11)	162 (9)	0.58
Antidiabetic medication	—	—	7 (0.5)	13 (0.8)	26 (1.4)	0.008

*p < 0.001, †p < 0.05, ‡p < 0.01 (level compared with the immediately preceding period).

C), which was examined only between 2000 and 2003, showed a mean value of 1.46 mmol/l (57 mg/dl; not shown in Table 3). The prevalence of high blood glucose increased between 1984 to 1987 and 1992 to 1995. The prevalence of the use of both lipid-lowering and antidiabetic medications increased with time, although it was much lower than that of antihypertensive medication.

For urban women, the prevalence of hypertension decreased, with downward trends in mean systolic blood pressure documented from 1964 to 1966 to 2000 to 2003. Their mean BMI also decreased over time. Mean total cholesterol and the prevalence of high total cholesterol showed upward trends similar to those for men, with a mean HDL-C level of 1.72 mmol/l (67 mg/dl) during 2000 to 2003. The prevalence of high TG decreased between 1976 to 1979 and 1984 to 1987. There was no significant change in the prevalence of high blood glucose between the periods 1984 to 1987 and 2000 to 2003.

Table 4 Age-Adjusted Cardiovascular Risk Characteristics Among 40- to 69-Year-old Men and Women During 5 Survey Periods From 1964 to 1966 to 2000 to 2003 in a Japanese Rural Community

Mean ± SD or Number (%)	1964–1966	1976–1979	1984–1987	1992–1995	2000–2003	p for Trend
Men						
Number	764	797	900	791	662	
Age (yrs)	53 ± 8	53 ± 9	54 ± 8	55 ± 9	57 ± 8*	<0.001
Systolic blood pressure (mm Hg)	150 ± 20	141 ± 19*	136 ± 19*	133 ± 19*	132 ± 20	<0.001
Diastolic blood pressure (mm Hg)	87 ± 12	86 ± 11†	85 ± 11‡	83 ± 11†	86 ± 12*	<0.001
Antihypertensive medication	51 (7)	189 (26)*	166 (19)*	157 (19)	147 (19)	<0.001
Hypertension	477 (64)	451 (59)	411 (46)*	347 (43)	338 (49)‡	<0.001
Body mass index (kg/m^2)	22.6 ± 2.6	23.1 ± 2.2*	22.9 ± 2.2‡	23.2 ± 2.3*	24.0 ± 2.5*	<0.001
Current smokers	—	537 (68)	579 (64)	463 (59)‡	339 (53)‡	<0.001
Alcohol intake (ethanol, g/day)	—	—	48 ± 27	43 ± 25*	41 ± 26	<0.001
Biochemical examination of blood						
Number	742	780	900	791	662	
Total cholesterol (mmol/l)	3.98 ± 0.76	4.55 ± 0.71*	4.67 ± 0.71*	4.92 ± 0.72*	5.12 ± 0.76*	<0.001
High total cholesterol	32 (4)	154 (19)*	217 (24)†	288 (37)*	315 (49)*	<0.001
High triglyceride	—	61 (9)	74 (9)	100 (13)‡	86 (14)	<0.001
Lipid-lowering medication	—	—	0 (0)	8 (1)†	22 (3)‡	<0.001
High blood glucose	—	—	176 (23)	178 (22)	159 (23)	0.90
Antidiabetic medication			14 (2)	22 (3)	37 (5)‡	0.001
Women						
Number	955	989	1,184	1,051	955	
Age (yrs)	52 ± 8	53 ± 8	54 ± 8‡	55 ± 9‡	56 ± 8‡	<0.001
Systolic blood pressure (mm Hg)	142 ± 19	135 ± 17*	132 ± 17*	129 ± 17*	129 ± 18	<0.001
Diastolic blood pressure (mm Hg)	83 ± 11	81 ± 10*	80 ± 10†	79 ± 10	81 ± 10*	<0.001
Antihypertensive medication	52 (6)	218 (24)*	205 (18)*	200 (18)	188 (17)	<0.001
Hypertension	459 (51)	424 (45)‡	430 (37)*	360 (33)	354 (34)	<0.001
Body mass index (kg/m^2)	23.1 ± 3.4	24.0 ± 2.7*	23.9 ± 2.8	23.9 ± 2.8	24.3 ± 3.2*	<0.001
Current smokers	—	26 (3)	29 (2)	19 (2)	29 (3)	0.73
Alcohol intake (ethanol, g/day)	—	—	15 ± 74	10 ± 47‡	9 ± 36	0.02
Biochemical examination of blood						
Number	933	966	1,183	1,051	955	
Total cholesterol (mmol/l)	4.14 ± 0.80	4.85 ± 0.74*	5.01 ± 0.74*	5.25 ± 0.75*	5.45 ± 0.79*	<0.001
High total cholesterol	57 (7)	314 (34)*	451 (38)‡	562 (53)*	634 (64)*	<0.001
High triglyceride	—	60 (8)	65 (6)	58 (6)	59 (6)	0.11
Lipid-lowering medication	—	—	3 (0.3)	17 (2)*	91 (9)*	<0.001
High blood glucose	—	—	100 (11)	122 (11)	121 (12)	0.63
Antidiabetic medication	—	—	21 (3)	22 (2)	26 (3)	0.92

*$p < 0.001$, †$p < 0.01$, ‡$p < 0.05$ (level compared with the immediately preceding period).

In the rural community, mean systolic blood pressure declined drastically between the periods 1963 to 1966 and 1976 to 1979 with a major increase in the prevalence of antihypertensive medication use by both men and women (Table 4). The downward trend in systolic blood pressure continued until 2000 to 2003. Mean BMI of both men and women increased over time. The prevalence of current smoking by men and mean alcohol intake by both sexes decreased with time. On the other hand, mean total cholesterol levels and the prevalence of high total cholesterol for both genders increased progressively from 1963 to 1966 through 2000 to 2003. The respective mean HDL-C levels for rural men and women in 2000 to 2003 were 1.56 mmol/l (60 mg/dl) and 1.64 mmol/l (64 mg/dl). The prevalence of high TG increased between 1984 to 1987 and 1992 to 1995 for men. The prevalence of high blood glucose among rural men and women did not change between 1984 to 1987 and 2000 to 2003.

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Discussion

We observed a significant increase in the incidence of CHD among urban Japanese middle-aged men between the periods 1980 to 1987 and 1996 to 2003, whereas the CHD incidence decreased slightly between that recorded in the 1972 to 1979 and 1980 to 1987 periods, perhaps in part because of a reduction in mean systolic blood pressure and the prevalence of hypertension. Among men, the general increase in CHD from the 1980s onward may be attributable to a concurrent increase in mean total cholesterol level and BMI, followed by an increase in mean diastolic blood pressure and the prevalence of high blood glucose levels in the later periods. One countervailing trend among urban men was a continuing decline in the prevalence of smoking.

In contrast, there was no change in the incidence of CHD among either urban women or rural men and women, despite the same upward trend in total cholesterol levels and prevalence of hypercholesterolemia found among urban men. We speculate that urban women may have lower levels of several risk factors such as systolic and diastolic blood pressure, BMI, high TG, blood glucose, and smoking. Lower levels of these risk factors might offset the expected greater incidence of CHD as the result of increased levels of total cholesterol. For rural men and women, the reduction in systolic blood pressure and hypertension was greater and change in total cholesterol and prevalence of high TG were lower than for urban men, which may contribute to the lower incidence of CHD in these 2 groups.

The incidence of stroke declined significantly for men and women of both communities between 1964 to 1971 and 1996 to 2003; however, the decline in stroke incidence was much greater in the rural than the urban community, probably because of the greater decline in blood pressure levels in the rural community. This improvement in blood pressure may be attributable to an increased utilization of antihypertensive medication and a large reduction of sodium intake our group previously reported (18).

The increasing trend in CHD incidence among urban Japanese men that began in the 1980s was in direct contrast to a substantial decrease in CHD mortality and incidence in the U.S. starting in the 1970s (2–4). Nevertheless, the CHD incidence rate among urban Japanese men remains much lower than that observed in several population-based studies in the U.S. The Minnesota Heart Survey (3) of 1995, for example, showed an age-adjusted incidence of hospitalized definite MI of 272 per 100,000 and an out-of-hospital CHD death rate of 491 per 100,000, respectively, for Twin Cities male residents ages 30 to 74 years. Among 35- to 74-year-old black and white men, the ARIC (Atherosclerosis Risk in Communities) study (4) of 1996 reported rates of 470 and 390 per 100,000, respectively, for age-adjusted hospitalized MI. Although there were differences in time, age distribution, and diagnostic criteria, the most recent incidence of CHD among urban Japanese men in our study was 100 per 100,000.

Because our laboratory has been standardized by the U.S. Centers for Disease Control-National Heart, Lung, and Blood Institute Lipid Standardization Program (20), comparisons of our data with those from NHANES (U.S. National Health and Nutrition Examination Survey) (6) are considered valid. It is interesting that recent mean total cholesterol levels of urban Japanese and Americans appear to be similar. However, total cholesterol levels may have a less atherogenic effect on urban Japanese than on their American counterparts. There are 2 reasons for this difference. The first is that urban Japanese show greater levels of HDL-C (1.46 mmol/l for men ages 40 to 69 years in our study vs. 1.19 mmol/l for men ages 50 to 59 years as reported by NHANES). The second is the lower prevalence of lipid-lowering medication usage (3% for men ages 40 to 69 years in our study, vs. 12% for men ages 40 to 59 years as reported by NHANES). This discrepancy suggests Japanese doctors see less need for patients to be on lipid-lowering therapy, and support for such clinical decision making would seem to be borne out by the low prevalence of severe hypercholesterolemia and the low incidence of CHD in Japan versus the U.S.

Our study has several limitations. First, although we used the same surveillance system for more than 40 years, the likelihood of diagnosing CHD may have increased with time as the result of improvements in diagnostic procedures, particularly the general use of cardiac enzymes since the 1980s. However, this improvement is unlikely to have had a major impact on our findings because all of the definite MIs in the present study were detected with the use of electrocardiograms, whereas none of them was confirmed based only on positive enzyme values. To avoid misclassification of the diagnoses over time, we have used the consistent ascertainment system and the same diagnostic criteria throughout all study periods.

Second, the participant rate for risk factor surveys has declined markedly in the urban community since the 1970s and in the rural community since the 1990s. Because the participants were generally more health conscious and took better care of themselves for the prevention of cardiovascular diseases, we speculate that the actual prevalence of persons having each of the risk factors is likely to be higher than our data indicate. Third, trends in HDL-C, a protective factor for CHD, could not be examined since the systematic measurement of HDL-C only started in 1996.

Conclusions

Our report is the first of a longitudinal community-based study showing a significant increase in the incidence of CHD in Asia. This finding supports the evidence that developing countries globally may face an emerging epidemic of CVD (7,8) as they adopt more Westernized diets and lifestyles, which is an important issue from the point of public health and clinical practice.

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