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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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).

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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.

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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 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).

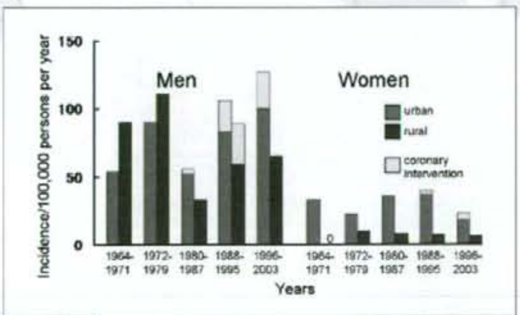

Figure 1 **Trends for Age-Adjusted Incidence of CHD**

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.

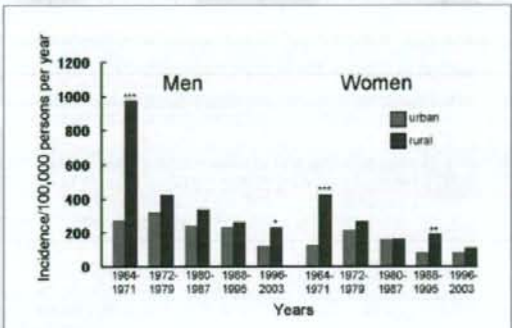

Figure 2 **Trends for Age-Adjusted Incidence of Stroke**

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.

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-

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/m²)	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/m²)	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.

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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