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Title

Impact of Obesity on Incident Hypertension Independent of Weight Gain among Non-hypertensive Japanese: The Ibaraki Prefectural Health Study (IPHS)

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Abstract

Objective: The aim of this study was to examine the association between body mass index (BMI) and risk of incident hypertension among Japanese men and women who are middle-aged and older.

Design: Prospective, population-based cohort study.

Subjects: A total of 68 205 non-hypertensive adults (18 336 men and 49 869 women) aged 40-79 years who completed health check-ups in the Ibaraki prefecture, Japan, in 1993 were followed-up through 2006. To exclude the impact of BMI change during the follow-up period, a time-dependent covariate Cox proportional hazards model was used to compute the hazard ratios (HRs) of incident hypertension according to BMI categories. Incident hypertension was defined as a systolic blood pressure (BP) of ≥ 140 mmHg, a diastolic BP of ≥ 90 mmHg, and/or hypertensive medication use.

Results: A total of 30 982 adults (45.4%) developed hypertension (9 331 men and 21 651 women) during a mean of 3.9 years of follow-up. Compared with a BMI of < 19.0, time-dependent covariates adjusted HRs (95% confidence interval [CI]) for hypertension among participants with a BMI of ≥ 25.0 were 1.42 (1.17-1.73) for men aged 40 to 59 years, 1.34 (1.19-1.51) for men aged 60 to 79 years, 1.47 (1.33-1.62) for women aged 40 to 59 years**,** and 1.29 (1.18-1.41) for women aged 60 to 79 years.

Conclusion: The baseline BMI is associated with future risk for incident hypertension even after accounting for weight change during the follow-up period. Weight loss may be recommended to non-hypertensive obese adults to prevent the development of hypertension.

Introduction

Hypertension is a major cause of cardiovascular disease [1]. Currently, approximately 45% of Japanese adults are considered hypertensive [2], defined as systolic blood pressure (SBP) ≥ 140 mmHg, diastolic blood pressure (DBP) ≥ 90 mmHg or treatment with an antihypertensive drug. Many prospective cohort studies have consistently shown that the higher the BMI, the greater the likelihood of developing hypertension [3-11]. Some prospective cohort studies have reported that long-term weight gain was associated with a risk of hypertension among hypotensive or high-normal blood pressure patients [12-15]. Moreover, many intervention studies have also shown that weight loss reduced blood pressure [16-18]. These results could lead to a hypothesis that the association between baseline BMI and the risk of hypertension are due to weight gain during the follow-up period. If this hypothesis were true, non-hypertensive obese individuals would not be required to lose weight to prevent incident hypertension. To clarify whether weight loss should be recommended for non-hypertensive obese people to prevent incident hypertension, a large cohort study that accounts for weight change is warranted. The purpose of this study was to clarify the association between long-term weight stability and the risk of incident hypertension in a large community-based cohort of men and women who are middle-aged and older.

Methods

Study population

The study population comprised 194 333 individuals (63 865 men and 130 468 women) aged 40-79 years living in the Ibaraki Prefecture, Japan. The population participated in community-based annual health checkups beginning in 1993 (Ibaraki Prefectural Health Study). These health checkups were conducted by local governments in accordance with the Japan Health Laws. Data were collected by the Ibaraki prefectural government from local governments after depersonalizing them to ensure anonymity. We excluded 3 080 individuals (738 men and 2 342 women) with incomplete data and 94 153 individuals (35 647 men and 58 506 women) with a SBP of ≥ 140 mmHg and/or a DBP of ≥ 90 mmHg or antihypertensive medication use. We further excluded 28 895 individuals (9 144 men and 19 751 women) who did not participate in the 1994 survey, thereby ensuring that the participants were followed for at least one year.

Ultimately, the study subjects consisted of 68 205 individuals (18 336 men and 49 869 women). These participants were followed up by annual examinations until hypertension had been diagnosed or until the end of 2006. Blood pressure was measured at annual follow-up examinations. Participants who did not undergo annual checkups during the follow-up periods were censored on the date of their latest checkup. The protocol for this cohort study was approved by the Ibaraki Epidemiology Study Union Ethics Review Committee.

Assessment of body mass index, blood pressure, and other covariates

Height in stockinged feet and weight in light clothing were measured at baseline. BMI was calculated as weight in kilograms divided by the height in meters squared. BP was measured from the right arm of seated participants who had rested for more than 5 minutes by trained observers using standard mercury sphygmomanometers during examinations that occurred

between 1993 and 2004 and by an automated sphygmomanometer between 2005 and 2006. When the SBP was greater than 150 mmHg or DBP was greater than 90 mmHg, a second measurement was performed after several deep breaths, and the lower values, which were almost always observed after the second measurement, were used for analyses.

Blood samples were drawn from seated participants into two polyethylene terephthalate tubes: one with an accelerator and the other with sodium fluoride and ethylenediaminetetraacetic acid. Overnight fasting (≥ 8 hours) was not required. The blood glucose level was measured by the glucose oxidase electrode method with a GA1140 device (Kyoto Daiichi Kagaku, Kyoto, Japan) during examinations that occurred between 1993 and 1996, by the enzyme method with a H7170 device (Hitachi, Tokyo, Japan) between 1997 and 2003, and with a H7700 device (Hitachi, Tokyo, Japan) between 1994 and 2006. Participants were considered diabetic if they had a fasting plasma glucose level of at least 6.1 mmol/L or a non-fasting glucose level of at least 7.8 mmol/L, or if they were being treated for diabetes mellitus. Serum total cholesterol and serum triglyceride levels were measured by the enzyme method with a RX-30 device (Nihon Denshi, Tokyo, Japan) between 1993 and 1995, with a H7350 device (Hitachi, Tokyo, Japan) between 1996 and 2003, and with a H7700 device between 2004 and 2006. High-density lipoprotein (HDL) cholesterol levels were measured by the phosphotungstic acid magnesium method with a MTP-32 device (Corona Electric, Ibaraki, Japan) between 1993 and 1995, by the selective inhibition method with a H7350 device between 1996 and 2003, and with a H7700 device between 2004 and 2006. The laboratory participated in external standardization and successfully met the criteria for precision accuracy for the measurement of blood samples by the Japan Medical Association, the Japanese Association of Medical Technologists, and the Japan Society of Health Evaluation and Promotion. An interview was conducted to ascertain medical history, smoking status (never, ex-, current < 20 cigarettes/day, and ≥ 20 cigarettes/day), and alcohol intake (non-,

sometimes, < 66 g/day, and ≥ 66 g/day).

Endpoint determination

Incident hypertension was defined as SBP of ≥ 140 mmHg, DBP of ≥ 90 mmHg, and/or when treatment for hypertension was initiated.

Statistical analysis

Participants were classified into the following 7 categories with regard to their BMI: < 19.0, 19.0-20.9, 21.0-22.9, 23.0-24.9, 25.0-26.9, 27.0-29.9, or ≥ 30.0 kg/m^2. Baseline participant characteristics were compared according to BMI categories using chi-squared tests for categorical variables and analysis of variance for continuous variables. Hazard ratios (HRs) with 95% confidence intervals (CIs) for incident hypertension relative to BMI categories were calculated with a reference of < 19.0 kg/m^2 using a Cox proportional hazards regression model [19]. The analyses were stratified by sex and age groups (40-59 and 60-79 years).

Three multivariable-adjusted models were used. In Model 1, covariates included age (years), SBP (mmHg), DBP (mmHg), fasting status (yes or no), total cholesterol level (mmol/L), HDL cholesterol level (mmol/L), log-transformed triglyceride level (mmol/L), lipid medication use (yes or no), blood glucose status (normal: < 6.1 mmol/L during fasting or < 7.8 mmol/L during non-fasting; border: 6.1-7.0 mmol/L during fasting or 7.8-11.1 mmol/L during non-fasting; hyperglycemia: ≥ 7.0 mmol/L during fasting or ≥ 11.1 mmol/L during non-fasting), smoking status (never, ex-, current < 20 cigarettes/day, or ≥ 20 cigarettes/day), and alcohol intake (non-, sometimes, < 66 g/day, or ≥ 66 g/day). In Model 2, the changes in BMI, total cholesterol level (mmol/L), HDL cholesterol level (mmol/L), and log-transformed triglyceride level (mmol/L) from baseline to the end of follow-up were added as covariates to Model 1. In Model 3, time-dependent variables of BMI and covariates

in Model 1 were used with a time-dependent Cox hazard model, which was used for adjusting the change in the variable from the baseline to the final year of follow-up [20]. For the secondary analysis, we excluded 34 190 participants with incomplete data and 16,370 participants with a SBP of ≥ 140 mmHg and/or a DBP of ≥ 90 mmHg or antihypertensive medication use at a 5-year follow-up. The remaining 17 645 qualified participants were classified into the following 4 categories with regard to their baseline BMI and BMI 5 years later: (a) BMI of less than 25 kg/m^2 at baseline and BMI of less than 25 kg/m^2 at a 5-year follow-up (-/-); (b) BMI of 25 kg/m^2 or more at baseline and BMI of less than 25 kg/m^2 at a 5-year follow-up (+/-); (c) BMI of less than 25 kg/m^2 at baseline and BMI of 25 kg/m^2 or more at a 5-year follow-up (-/+); and (d) BMI of 25 kg/m^2 or more at baseline and BMI of 25 kg/m^2 or more at a 5-year follow-up (+/+). We calculated HRs for incident hypertension to consider long-term changes of their weights.

All statistical analyses were conducted using SAS, version 9.1 (SAS Institute, Inc., Cary, North Carolina).

Results

Sex-stratified baseline characteristics according to BMI categories are shown in Table 1. All covariates, except for blood glucose status, diabetic medication use and smoking status in men and lipid medication use in women, were associated with BMI in both sexes. A higher BMI was linked with higher SBP and DBP at baseline in both sexes.

Of the 68 205 adults (18 336 men and 49 869 women), 30 982 (45.4%) developed hypertension (9 331 men and 21 651 women) during a mean follow-up of 3.9 years (3.4 years for men and 4.1 years for women). Table 2 shows sex- and age-stratified HRs for hypertension according to the baseline BMI categories. In men aged 40-59 years, compared with a baseline BMI < 19.0 kg/m^2, the multivariate HRs of BMI ≥ 25.0 kg/m^2 was significantly higher in Model 1 and Model 2. In men aged 60-79 years, compared with a baseline BMI < 19.0 kg/m^2, the multivariate HRs of BMI ≥ 19.0 kg/m^2 was significantly higher in Model 1 and the multivariate HRs of BMI ≥ 23.0 kg/m^2 was significantly higher in Model 2. In both age groups among men, time-dependent covariates adjustment HRs (BMI ≥ 25.0 kg/m^2: 1.42, ≥ 30.0 kg/m^2: 1.77 in aged 40-59 years; BMI ≥ 25.0 kg/m^2: 1.34, ≥ 30.0 kg/m^2: 1.68 in aged 60-79 years) showed a trend similar to Model 1 and Model 2.

In women aged 40-59 years, compared with a baseline BMI < 19.0 kg/m^2, the multivariate HRs of BMI ≥ 21.0 kg/m^2 was significantly higher in Model 1 and of BMI ≥ 23.0 kg/m^2 was significantly higher in Model 2.

In women aged 60-79 years, compared with a baseline BMI < 19.0 kg/m^2, the multivariate HRs of BMI ≥ 21.0 kg/m^2 was significantly higher in Model 1 and 25.0-26.9 kg/m^2 of BMI was significantly higher in Model 2. In both age groups among women, time-dependent covariates adjustment HRs (BMI ≥ 25.0 kg/m^2: 1.53, ≥ 30.0 kg/m^2: 2.07 in age 40-59 years; BMI ≥ 25.0 kg/m^2: 1.47, ≥ 30.0 kg/m^2: 1.91 in age 60-79 years) showed a trend similar to Model 1 and Model 2.

Figure 1 represents HRs for hypertension according to the BMI categories at baseline and at a 5-year follow-up. Among all non-hypertensive participants at baseline and at a 5-year follow-up, compared with the -/- group, the age-adjusted HRs (95% CI) of +/-, -/+, and +/+ were 1.12 (1.03-1.41), 1.69 (1.47-1.94), and 1.67 (1.53-1.82), respectively. The multivariate HRs of +/-, -/+, and +/+ were 1.12 (1.03-1.41), 1.69 (1.47-1.94), and 1.67 (1.53-1.82), respectively.

Discussion

To the best of our knowledge, the results of the present large prospective study showed that stable obesity in non-hypertensive individuals was significantly associated with an increased risk of incident hypertension among men and women who are middle-aged and older.

Previous studies that examined the relationship between BMI and hypertension reported results consistent with the present study. Many cross-sectional studies showed a dose-dependent relationship between BMI and the prevalence of hypertension in Caucasian [5, 21] and Asian [3, 13, 22] populations. Kawada [3] reported that the odds ratios for hypertension against the lowest quartile of BMI (separated by 20, 25 and 28) were 1.7, 3.6, and 7.2, respectively, with 95% CIs of 1.2-2.3, 2.5-5.2 and 4.7-11.0, respectively, among middle-aged men and women (5 346 men and 11 525 women, aged 40-59). Prospective studies [4, 12, 23] also showed similar results to the present study. The Physicians' Health Study (13 563 healthy and non-hypertensive men in U.S.) [4] showed that the HRs (95% CIs) of developing hypertension for men with a BMI of 22.4-23.6, 23.7-24.7, 24.8-26.4, and >26.4 kg/m^2 were 1.20 (1.09-1.32), 1.31 (1.19-1.44), 1.56 (1.42-1.72), and 1.85 (1.69-2.03), respectively (*P* for the trend, < 0.001), compared with participants who had the lowest BMI quintile (< 22.4 kg/m^2). A cohort study of U.S. female nurses (82 473 women, aged 30-55) [12] showed that the multivariate HRs (95% CIs) of developing hypertension for women with a BMI of 22.0-22.9, 24.0-24.9, 26.0-27.9, and > 31.0 kg/m^2 were 1.57 (1.44-1.72), 2.15 (1.97-2.35), 3.33 (3.06-3.62), and 6.31 (5.80-6.87), respectively (*P* for the trend, < 0.001), compared with women who had the lowest BMI decile (< 20.0 kg/m^2), and an increase in BMI of 1 kg/m^2 was associated with a 12 % increased risk for incident hypertension. These results suggested a strong association between higher BMI and increased risk of incident hypertension in men and women.

We also examined the effect of 5-year changes in BMI category (BMI less than, or equal or

more than 25 kg/m^2) on incident hypertension. The HRs of non-obese people at a 5-years follow-up, despite obesity at baseline, was not significant compared with non-obese people at both baseline and at a 5-years follow-up. In contrast, the HRs of obese individuals at a 5-year follow-up, despite non-obesity at baseline, was significantly higher compared with non-obese people at both baseline and at a 5-years follow-up. The effect of change in BMI on blood pressure has already been examined in some studies [12-18]. A systematic review [24] of lifestyle intervention studies reported differences ranging from -11 to + 4 kg for weight, -7 to + 2.2 mmHg for DBP and -13 to + 6.1 mmHg for SBP. It is suggested that SBP differences were equal to a ratio of 1 kg to every 1 mmHg. These studies suggest the efficacy of weight loss for the hypertensive obese population. The present study further represented the efficacy of weight loss for the non-hypertensive obese population to prevent incident hypertension. Williams [25] examined the relationship between long-term stable individuals' BMI (change less than ± 0.4 kg/m^2) and the cumulative incidence of hypertension and showed that the odds ratio of each kg/m^2 increment in baseline BMI was 1.19 (95% CIs: 1.14-1.24) in men and 1.11 (95% CIs: 1.02-1.20) in women. Matsuo et al [26] reported in a cohort study of 5 201 Japanese middle-aged male employees using of a time-dependent Cox proportional hazard model for analysis that the HRs (95% CIs) of stable BMI of 25.0-26.9, 27.0-29.9, and ≥ 30.0 kg/m^2 were 1.11 (0.93-1.32), 1.34 (1.09-1.65) and 1.49 (1.09-2.04), respectively, compared with men who had a BMI of 23.0-24.9 kg/m^2. These results are consistent with our results, although Williams calculated the BMI with a self-reported weight and cumulative incidence of hypertension at 2 points (baseline and 7 years later), and Matsuo et al. studied middle-aged male employees.

The exact mechanism by which stable adiposity raises BP is uncertain. However, a likely explanation is that obesity-associated hypertension appears to be due to inadequate vasodilatation in the setting of increased blood volume and cardiac output. A defect in control

of vascular resistance has been attributed to enhanced activity of the sympathetic nervous system, abnormal rennin-angiotensin-aldosterone relations, and insulin resistance [27-31]. The peripheral vascular resistance is increased by adipocytokines (e.g., leptin, TNF-α, RBP4) [32-34].

The study has several strengths. First, the effect of weight change during the follow-up period was taken into account to investigate the association between long-term weight stability and future incident risk for hypertension, while many previous epidemiological studies did not account for these factors. Second, the present study had a large cohort for which gender, age and BMI stratification analysis was possible. In addition, all blood samples in each year were measured by the same device, reagents, and quality control programs [35].

However, there are several limitations. First, the participation rate for the follow-up examinations was approximately 40%, but the mean SBP and DBP did not differ between individuals who were and were not followed up. In this context, the potential selection bias may have been small. Second, the instrument used to measure the blood pressure was switched from the standard mercury sphygmomanometer to an automatic sphygmomanometer following 2005. The BP determined by means of an automated sphygmomanometer method was compared with those determined by a standard mercury sphygmomanometer method, using 18 859 samples (non-medication participants) in 2004 and 2005. Comparability between BP measured using the 2 sphygmomanometers was acceptable (SBP: $r = 0.69$, DBP: $r = 0.55$, $P < 0.05$, respectively). Third, we could not assess the potential confounding variables such as fat distribution, physical activity, nutritional status (e.g., sodium intake), and family history of hypertension.

In conclusion, the baseline BMI is associated with a future incident risk for hypertension, even after accounting for weight change during the follow-up period. Weight loss may be recommended for obese non-hypertensive individuals to prevention incident hypertension

among men and women who are middle-aged and older.

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Conflict of interest

The authors declare no conflict of interest.

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Figure legend

Figure 1

Abbreviations: HRs, hazard ratios; CIs, confidence intervals. Age-adjusted HRs with 95% confidence intervals were adjusted for age (years) in 1998 and sex. Multivariate HRs with 95% confidence intervals were adjusted for possible confounders measured in 1998: age (years), sex, systolic blood pressure (mmHg), diastolic blood pressure (mmHg), fasting status (yes or no), total cholesterol level (mmol/liter), high density lipoprotein cholesterol level (mmol/liter), log-transformed triglyceride level (mmol/liter), lipid medication use (yes or no), blood glucose status (normal, border, hyperglycemia), diabetic medication use (yes or no), smoking status (never, ex-, < 20 cigarettes/day, or $\geq$ 20 cigarettes/day), and alcohol intake (never, sometimes, < 66 g/day, or $\geq$ 66 g/day). Bold values showed statistical significance ($P < 0.05$).

Table 1. Baseline characteristics of participants by body mass index (BMI) categories

Gender and baseline variables	Body mass index, kg/m^2														*P*-value
	< 19.0		19.0 - 20.9		21.0 - 22.9		23.0 - 24.9		25.0 - 26.9		27.0 - 29.9		> 30.0		
Men (n = 18 336)															
No. of subjects	1 545		3 476		4 934		4 544		2 598		1 085		154		
Age, years	63.5	(9.5)	60.5	(10.2)	58.8	(10.3)	57.7	(10.2)	56.5	(10.0)	56.6	(9.8)	55.3	(10.0)	<.001
Change in body mass index, kg/m^2	0.0	(1.1)	0.1	(1.2)	0.0	(1.2)	-0.1	(1.3)	-0.2	(1.3)	-0.4	(1.5)	-0.7	(1.5)	<.001
Systolic blood pressure, mmHg	119.9	(11.4)	121.7	(10.8)	122.7	(10.2)	124.0	(9.5)	124.4	(9.4)	125.4	(9.2)	126.2	(8.8)	<.001
Diastolic blood pressure, mmHg	71.9	(8.4)	73.1	(8.0)	74.1	(7.9)	75.4	(7.3)	75.9	(7.4)	76.6	(7.1)	78.1	(7.8)	<.001
Total cholesterol, mmol/liter	4.7	(0.8)	4.8	(0.8)	5.0	(0.8)	5.1	(0.9)	5.2	(0.8)	5.2	(0.9)	5.2	(0.9)	<.001
HDL cholesterol, mmol/liter	1.6	(0.4)	1.5	(0.4)	1.4	(0.4)	1.3	(0.3)	1.2	(0.3)	1.1	(0.3)	1.1	(0.3)	<.001
Triacylglycerol, mmol/liter	1.1	(0.5)	1.2	(0.7)	1.5	(0.8)	1.8	(1.0)	2.0	(1.2)	2.2	(1.3)	2.2	(1.0)	<.001
Lipid medication use, %	3.2		2.8		2.6		3.1		3.2		3.1		2.6		<.001
Diabetic medication use, %	0.4		0.8		1.0		1.3		1.2		1.4		2.6		0.177
Blood glucose status, %															0.866
Normal	81.9		83.9		84.3		84.6		81.9		82.0		83.8		
Border	13.6		12.4		12.0		11.4		13.5		12.7		9.7		
Hyperglycemia	4.5		3.7		3.7		4.0		4.5		5.3		6.5		
Smoking status, %															0.116
Never	19.4		20.6		22.4		25.1		24.1		23.3		25.3		
Ex	23.4		23.3		27.0		28.1		29.5		33.9		27.9		
Current															
< 20 cigarettes/day	22.8		18.7		15.3		12.3		11.5		9.8		9.7		
≥ 20 cigarettes/day	34.4		37.4		35.3		34.4		34.9		33.0		37.0		
Alcohol intake, %															<.001
Never	48.5		40.6		37.2		36.6		37.6		38.2		51.3		
Sometimes	11.5		13.2		13.6		15.1		15.9		18.8		17.5		
Everyday															
< 66 g/day	36.6		41.9		44.0		43.4		41.4		37.1		25.3		
≥ 66 g/day	3.4		4.3		5.1		5.0		5.1		5.8		5.8		

Table 1. Baseline characteristics of participants by body mass index (BMI) categories (continued)

Gender and baseline variables	Body mass index, kg/m^2														*P*-value
	< 19.0		19.0 - 20.9		21.0 - 22.9		23.0 - 24.9		25.0 - 26.9		27.0 - 29.9		> 30.0		
Women (n = 49 869)															
No. of subjects	3 796		9 391		13 824		11 887		6 781		3 434		756		
Age, years	56.8	(10.9)	54.1	(10.1)	54.4	(9.7)	55.1	(9.5)	56.0	(9.4)	56.1	(9.4)	55.4	(9.2)	<.001
Change in body mass index, kg/m^2	0.2	(1.2)	0.1	(1.2)	0.0	(1.3)	-0.1	(1.4)	-0.2	(1.5)	-0.3	(1.6)	-0.6	(2.0)	<.001
Systolic blood pressure, mmHg	117.6	(11.9)	118.5	(11.5)	120.0	(11.1)	121.3	(10.7)	122.7	(10.2)	123.8	(9.8)	124.7	(8.9)	<.001
Diastolic blood pressure, mmHg	70.0	(8.5)	70.9	(8.3)	72.1	(8.1)	73.3	(7.9)	74.3	(7.6)	75.3	(7.5)	76.7	(7.4)	<.001
Total cholesterol, mmol/liter	5.1	(0.9)	5.2	(0.9)	5.3	(0.9)	5.4	(0.9)	5.4	(0.9)	5.5	(0.9)	5.5	(0.9)	<.001
HDL cholesterol, mmol/liter	1.7	(0.4)	1.6	(0.4)	1.5	(0.4)	1.4	(0.3)	1.4	(0.3)	1.3	(0.3)	1.3	(0.3)	<.001
Triacylglycerol, mmol/liter	1.0	(0.5)	1.2	(0.6)	1.3	(0.7)	1.5	(0.9)	1.6	(0.9)	1.8	(1.0)	1.9	(1.0)	<.001
Lipid medication use, %	1.7		1.5		2.3		2.9		3.3		3.1		3.2		0.367
Diabetic medication use, %	0.9		1.0		1.5		1.2		1.6		1.8		2.2		<.001
Blood glucose status, %															<.001
Normal	91.1		92.5		92.6		91.8		90.0		89.1		87.0		
Border	7.5		6.1		6.1		6.3		8.0		8.4		9.7		
Hyperglycemia	1.3		1.4		1.3		1.9		1.9		2.6		3.3		
Smoking status, %															<.001
Never	92.6		94.7		94.7		95.2		94.9		94.5		92.2		
Ex	0.6		0.5		0.7		0.5		0.6		0.9		0.9		
Current															
< 20 cigarettes/day	4.7		3.4		3.2		2.8		2.9		3.0		3.6		
≥ 20 cigarettes/day	2.1		1.5		1.5		1.5		1.6		1.6		3.3		
Alcohol intake, %															<.001
Never	90.9		88.7		89.0		89.6		90.2		90.7		90.7		
Sometimes	5.2		6.9		7.2		6.8		6.5		6.0		5.4		
Everyday															
< 66 g/day	3.9		4.2		3.7		3.5		3.3		3.1		3.4		
≥ 66 g/day	-		0.1		0.1		0.1		0.0		0.2		0.4		

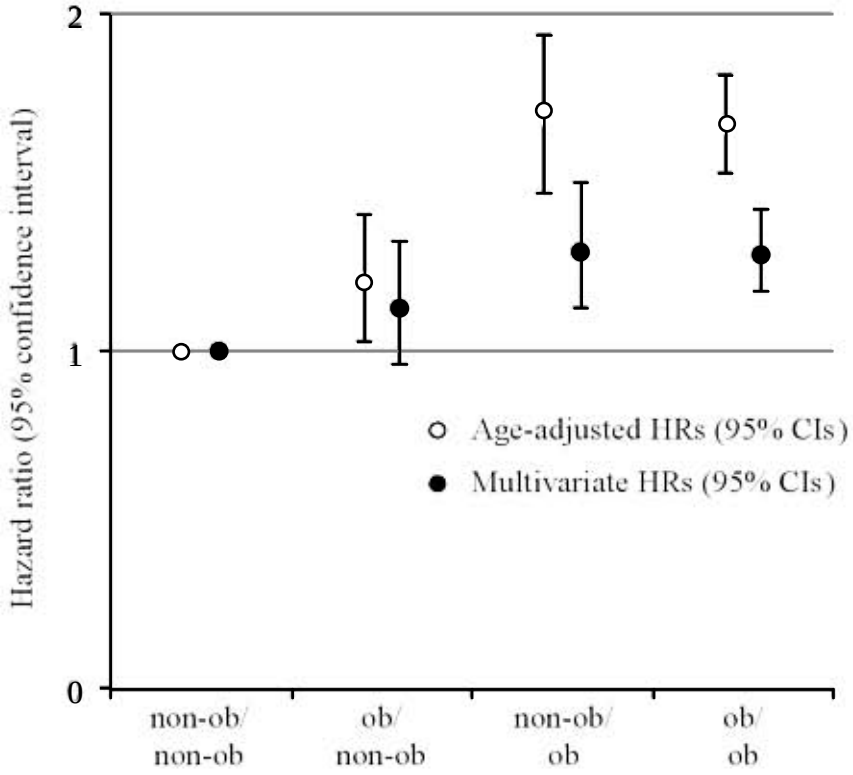
HDL = high-density lipoprotein. The means (SD) are shown for continuous variables: age, fasting and non-fasting blood glucose, systolic and diastolic blood pressure, total cholesterol, HDL cholesterol, and triglycerides. SI conversion factors: blood glucose values were converted to mmol/L by multiply by 0.05551; cholesterols values were converted to mmol/L by multiply by 0.02586; triglycerides values were converted to mmol/L by multiply by 0.01129.

Table 2. The effect of hazard ratios on hypertension within each of seven BMI categories

	Baseline BMI categories (kg/cm^2)						
	< 19.0	19.0 - 20.9	21.0 - 22.9	23.0 - 24.9	25.0 - 26.9	27.0 - 29.9	> 30.0
Men, age 40-59 years (n = 8 540)							
No. of person-years	1 590	5 713	9 042	8 267	4 964	1 952	285
No. of hypertension cases	127	434	882	1 048	740	351	61
Incidence rates per 1 000 person-years	80	76	98	127	149	180	214
Age-adjusted HRs (95% CIs)	1.00	1.01 (0.83-1.23)	**1.26 (1.05-1.52)**	**1.57 (1.31-1.89)**	**1.81 (1.50-2.19)**	**2.12 (1.73-2.60)**	**2.48 (1.83-3.36)**
Model 1† HRs (95% CIs)	1.00	0.90 (0.74-1.09)	1.05 (0.87-1.27)	1.19 (0.98-1.44)	**1.36 (1.16-1.66)**	**1.52 (1.23-1.89)**	**1.75 (1.28-2.40)**
Model 2‡ HRs (95% CIs)	1.00	1.01 (0.59-1.73)	0.97 (0.58-1.65)	1.10 (0.64-1.88)	**1.82 (1.04-3.16)**	**1.83 (1.00-3.35)**	2.37 (0.91-6.17)
Model 3§ HRs (95% CIs)	1.00	0.95 (0.78-1.15)	1.13 (0.94-1.36)	**1.24 (1.03-1.50)**	**1.42 (1.17-1.73)**	**1.60 (1.30-1.97)**	**1.77 (1.29-2.41)**
Men, age 60-79 years (n = 9 796)							
No. of person-years	3 831	6 982	8 334	6 582	2 937	1 075	101
No. of hypertension cases	517	1 177	1 566	1 366	710	314	38
Incidence rates per 1 000 person-years	135	169	188	208	242	292	376
Age-adjusted HRs (95% CIs)	1.00	**1.25 (1.13-1.38)**	**1.38 (1.25-1.52)**	**1.51 (1.36-1.67)**	**1.67 (1.49-1.87)**	**1.94 (1.69-2.24)**	**2.24 (1.61-3.11)**
Model 1† HRs (95% CIs)	1.00	**1.15 (1.03-1.27)**	**1.20 (1.09-1.33)**	**1.26 (1.13-1.41)**	**1.35 (1.20-1.53)**	**1.54 (1.32-1.78)**	**1.68 (1.20-2.35)**
Model 2‡ HRs (95% CIs)	1.00	1.01 (0.71-1.44)	1.24 (0.88-1.75)	**1.48 (1.03-2.13)**	1.52 (0.98-2.37)	**2.01 (1.11-3.64)**	N/A
Model 3§ HRs (95% CIs)	1.00	**1.11 (1.00-1.22)**	**1.17 (1.06-1.29)**	**1.26 (1.14-1.40)**	**1.34 (1.19-1.51)**	**1.48 (1.28-1.72)**	**1.68 (1.21-2.35)**
Women, age 40-59 years (n = 32 133)							
No. of person-years	10 877	32 781	45 716	34 389	16 754	7 410	1 402
No. of hypertension cases	496	1 682	2 975	2 969	1 940	1 001	265
Incidence rates per 1 000 person-years	46	51	65	86	116	135	189
Age-adjusted HRs (95% CIs)	1.00	**1.15 (1.04-1.27)**	**1.40 (1.27-1.54)**	**1.76 (1.60-1.94)**	**2.25 (2.04-2.49)**	**2.56 (2.30-2.86)**	**3.32 (2.86-3.86)**
Model 1† HRs (95% CIs)	1.00	1.04 (0.94-1.15)	**1.15 (1.05-1.27)**	**1.33 (1.20-1.46)**	**1.58 (1.43-1.75)**	**1.65 (1.48-1.84)**	**1.90 (1.63-2.22)**
Model 2‡ HRs (95% CIs)	1.00	1.12 (0.90-1.14)	1.23 (0.99-1.53)	**1.59 (1.28-1.98)**	**1.67 (1.32-2.11)**	**1.99 (1.52-2.60)**	**1.86 (1.16-2.98)**
Model 3§ HRs (95% CIs)	1.00	0.98 (0.89-1.08)	**1.12 (1.02-1.23)**	**1.27 (1.16-1.39)**	**1.47 (1.33-1.62)**	**1.55 (1.39-1.73)**	**1.91 (1.66-2.21)**
Women, age 60-79 years (n = 17 736)							
No. of person-years	5 535	10 525	15 260	12 907	7 673	3 611	598
No. of hypertension cases	790	1 591	2 580	2 569	1 663	940	190
Incidence rates per 1 000 person-years	143	151	169	199	217	260	318
Age-adjusted HRs (95% CIs)	1.00	**1.11 (1.02-1.21)**	**1.24 (1.14-1.34)**	**1.42 (1.31-1.54)**	**1.53 (1.40-1.66)**	**1.77 (1.61-1.95)**	**2.07 (1.77-2.43)**
Model 1† HRs (95% CIs)	1.00	1.04 (0.95-1.13)	**1.09 (1.01-1.19)**	**1.21 (1.11-1.31)**	**1.25 (1.15-1.37)**	**1.39 (1.26-1.54)**	**1.61 (1.37-1.90)**
Model 2‡ HRs (95% CIs)	1.00	1.04 (0.80-1.35)	1.16 (0.90-1.49)	1.25 (0.96-1.62)	**1.35 (1.02-1.80)**	1.20 (0.84-1.70)	1.66 (0.82-3.38)
Model 3§ HRs (95% CIs)	1.00	1.06 (0.98-1.16)	**1.10 (1.02-1.19)**	**1.22 (1.12-1.32)**	**1.29 (1.18-1.41)**	**1.40 (1.27-1.54)**	**1.72 (1.47-2.01)**

Abbreviations: HRs, hazard ratios; CIs, confidence intervals; N/A, data was not available.
†Adjusted for age (years), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), fasting status (yes or no), total cholesterol level (mmol/liter), high density lipoprotein cholesterol level (mmol/liter), log-transformed triglyceride level (mmol/liter), lipid medication use (yes or no), blood glucose status (normal, border, hyperglycemia), diabetic medication use (yes or no), smoking status (never, ex-, < 20 cigarettes/day, or ≥ 20 cigarettes/day), and alcohol intake (never, sometimes, < 66 g/day, or ≥ 66 g/day).
‡Addition of BMI (kg/m^2), total cholesterol level (mmol/liter), high-density lipoprotein cholesterol level (mmol/liter), and log-transformed triglyceride level (mmol/liter) change values (the endpoint minus the baseline) to Model 1 for adjustment.
§Adjusted for time-dependent covariates: age (years), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), fasting status (yes or no), total cholesterol level (mmol/liter), high density lipoprotein cholesterol level (mmol/liter), log-transformed triglyceride level (mmol/liter), lipid medication use (yes or no), blood glucose status (normal, border, hyperglycemia), diabetic medication use (yes or no), smoking status (never, ex-, < 20 cigarettes/day, or ≥ 20 cigarettes/day), and alcohol intake (never, sometimes, < 66 g/day, or ≥ 66 g/day).
Bold values showed statistical significance ($P < 0.05$).

Figure 1



No. of subjects	14 055	740	676	2 174
No. of hypertension cases	2 877	165	165	662