

# Understanding the decline of mean systolic blood pressure in Japan: an analysis of pooled data from the National Nutrition Survey, 1986–2002

Nayu Ikeda,<sup>a</sup> Emmanuela Gakidou,<sup>a</sup> Toshihiko Hasegawa<sup>b</sup> & Christopher JL Murray<sup>a</sup>

**Objective** To assess the relationships between the observed drop in mean systolic blood pressure (SBP) in Japan in 1986–2002 and the use of antihypertensive treatment and lifestyle factors.

**Methods** A nationally representative sample of 90 554 men and 101 903 women aged 20 years and over was obtained from pooled data of annual cross-sectional surveys in Japan during 1986–2002. Using two-stage least squares with an instrumental variable, we examined the association between SBP and antihypertensive medication and lifestyle factors, including body mass index (BMI), physical activity, alcohol consumption, cigarette smoking and dietary salt intake. In the surveys, regular exercise was defined as exercise for more than 30 minutes at a time more than twice a week for over 1 year. Current smoking was defined as either daily or occasional cigarette use. Current drinking was defined as an intake of more than one standard cup of Japanese sake, one large bottle of regular beer, or one double measure of whisky at a time more than three times a week. Changes in mean predicted SBP in each sex and age group between 1986 and 2002 were decomposed into the respective contributions of these explanatory variables.

**Findings** Age-specific means of predicted SBP declined during this period by 1.8 (95% confidence interval, CI: 1.2–2.5) to 3.0 (95% CI: 2.4–3.6) mmHg in men and 3.7 (95% CI: 3.4–4.1) to 5.1 (95% CI: 4.5–5.7) mmHg in women. These reductions were partly explained by the increased use of medications across all sex and age groups and decreased mean BMI in women in their 30s and 40s. The contributions of treatment effects increased with age. Elevated mean BMI in men and elderly women offset part of the decline of their mean SBP.

**Conclusion** Declining mean SBP in Japan between 1986 and 2002 was partly attributable to the increased use of antihypertensive medications, especially in the older population, and lowered mean BMI in young women. However, a substantial part of the decline was left unexplained and needs to be investigated further. A still greater decline in SBP would be expected through improvements in body weight management, salt and alcohol intake, and treatment and control of hypertension.

Bulletin of the World Health Organization 2008;86:978–988.

Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

## Introduction

Control of systolic blood pressure (SBP) is an important public health issue because elevated SBP is one of the independent risk factors for cardiovascular disease (CVD).<sup>1–3</sup> CVD is a leading contributor to the global burden of disease, accounting for 28% of 50 million deaths and 13% of 1.4 billion disability-adjusted life years in 2001.<sup>4</sup> Several prospective cohort studies revealed that lower SBP at baseline is associated with reduced CVD mortality and incidence.<sup>2,3,5</sup> It has been reported that even a decline of SBP at baseline by 2 mmHg is related to a reduction of 16-year mortality from CVD by 5%.<sup>6</sup> Effective control of SBP is thus essential for improving population health.

However, the global trend of hypertension has been worsening. The estimated global prevalence of hypertension was more than 25% among adults in the year 2000 and it is projected to rise, especially in developing countries, between 2000 and 2025.<sup>7</sup> It is also noteworthy that mean SBP in the United States of America decreased during the 1970s and 1980s, but the trend has stagnated since the 1990s.<sup>8–10</sup>

A declining trend of mean SBP has been observed in several general populations, including Japan.<sup>8,11–15</sup> Understanding why mean SBP has been decreasing in these populations is crucial for public health policy. Although population-wide and personal interventions might have been effective, the

factors that actually contributed to the decline of mean SBP have not been investigated yet, largely due to the lack of longitudinal data based on a nationally representative sample. According to two previous studies of how individual SBP is distributed in the population and how the distribution had shifted over time, changes in population-wide behaviours and environmental conditions made a larger contribution to the trend than improved treatments.<sup>16,17</sup> However, the nature of the cross-sectional survey data that were used in these studies precluded further quantification of the contributions of individual factors.

Japan has experienced a remarkable reduction in mean SBP since the late 1960s.<sup>12,13,15,18</sup> A study using published

<sup>a</sup> Institute for Health Metrics and Evaluation, University of Washington, 2301 5th Avenue, Seattle, WA 98121, United States of America.

<sup>b</sup> Department of Health Service Administration, Nippon Medical School, Tokyo, Japan.

Correspondence to Nayu Ikeda (e-mail: ikedan@u.washington.edu).

doi:10.2471/BLT.07.050195

(Submitted: 5 December 2007 – Revised version received: 19 March 2008 – Accepted: 21 March 2008 – Published online: 17 September 2008)

Table 1. Description of variables used in the regression analysis, based on data from the National Nutrition Survey, Japan, 1986–2000

Variable	Survey year	Possible values	Reference categories/ analytic strategies
Measured SBP <sup>a</sup>	1986–2002	Continuous in mmHg	
Age (years)	1986–2002	20–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75+	20–29
Measured BMI <sup>b</sup>	1986–2002	Continuous in kg/m <sup>2</sup>	Interacted with age
Regular exercise <sup>c</sup>	1986–1989	“Yes”/“No”	“No”
	1990–2002	“Unable to do for health reasons,” “Unable to do for other reasons,” “Currently doing regular exercise”	“Unable to do for health reasons” or “Unable to do for other reasons”
Current smoker <sup>c</sup>	1986–2002	“Never,” “Discontinued,” “Currently smoking”	“Never” or “Discontinued”
Current drinker <sup>c</sup>	1986–1989	“Yes”/“No”	“No”
	1990–2002	“Never or rarely,” “Discontinued,” “Currently drinking”	“Never or rarely” or “Discontinued”
Daily salt intake per capita by prefecture (g) <sup>d</sup>	1986–2002	Salt intake in grams	
Antihypertensive medication use	1986–1989	“Taking,” “Not taking”	“Not taking”
	1990–2002	“Never,” “Discontinued,” “Taking occasionally,” “Taking daily”	“Never,” “Discontinued” or “Taking occasionally”
Survey year	1986–2002	1986–2002	1986

BMI, body mass index; SBP, systolic blood pressure.

<sup>a</sup> Using a Riva-Rocci mercury manometer and no specification on cuff size, certified professionals such as medical doctors, public health nurses and registered nurses measured blood pressure in the right upper arm of seated persons after 5 minutes' rest. Systolic and diastolic blood pressures were recorded once until 1999 and twice starting in 2000. The first measurement of SBP was used for consistency of measurements in this analysis.

<sup>b</sup> Using a spring scale and a stadiometer, public health nurses measured the height and weight of participants wearing light clothes and no shoes.

<sup>c</sup> In the survey, individuals were considered to have regular exercise if they had exercised for more than 30 minutes at a time more than twice a week for over 1 year; they were considered current smokers if they smoked daily or occasionally; and they were considered current drinkers if they consumed more than one standard cup of Japanese sake, one large bottle of regular beer, or one double measure of whisky at a time more than three times a week.

<sup>d</sup> Japan has 47 prefectures (local governing units). Daily salt intake per capita at the prefecture level in each survey year was used as a reference for individual salt intake because it afforded the best available data between 1986 and 1994. Nutrition intake was recorded at the household level only, and microdata on nutrition intake were not available during this period. Data were obtained for the 1986–1994 surveys from the Health and Nutrition Information Infrastructure Database based on the NNS, available from: [http://nihn-jst.nih.go.jp:8888/nns/owa/nns\\_main\\_e.hm01a](http://nihn-jst.nih.go.jp:8888/nns/owa/nns_main_e.hm01a) [accessed on 7 February 2007]. For the 1995–2002 surveys we aggregated microdata to obtain the variable.

summary statistics attributed the decline of mean SBP between 1965 and 1980 to the improved treatment rate of CVD.<sup>15</sup> However, so far no one has examined why mean SBP further decreased since the 1980s in Japanese adults for which individual-level data on SBP and the use of antihypertensive medications are electronically available.

The objective of this study was to explore the factors linked to the decline of mean SBP and evaluate their individual contributions by using a statistical model to address potential treatment bias in cross-sectional data and thereby obtain useful information for public health policies. Pooling data of nationally representative annual surveys in Japan between the mid 1980s and the early 2000s, this study assessed the relationships between the change in mean SBP and changes in the use of antihypertensive treatment and lifestyle factors in Japanese adults.

## Methods

### Data sources

We used microdata of the National Nutrition Survey (NNS), which is a cross-sectional interview and examination survey conducted on a nationally representative sample every November by the Ministry of Health, Labour and Welfare. This survey aims at obtaining basic data on anthropometry, nutritional intake and diet, and lifestyles to establish measures for nationwide health promotion.<sup>19</sup> The methods of the NNS have been described in detail elsewhere.<sup>20</sup> Eligible respondents included all residents aged 1 year and older in 300 census tracts that were randomly selected from around 900 000 census tracts. Response rates of the NNS were estimated to be 60–70%,<sup>21</sup> and the sample was considered representative of the Japanese population.<sup>22</sup>

In the NNS, all household members were asked to participate in physi-

cal examinations at a local community centre near their residence on a specific day during the survey period. At the site of the physical examination, a medical doctor also questioned participants aged 20 years and over about their current use of antihypertensive medications, smoking and drinking habits, and physical activity. Nutritional intake was surveyed at households using a self-administered questionnaire. Household representatives weighed and recorded the quantity of each food item consumed by the household for three consecutive days until 1994 and for only one day beginning in 1995.

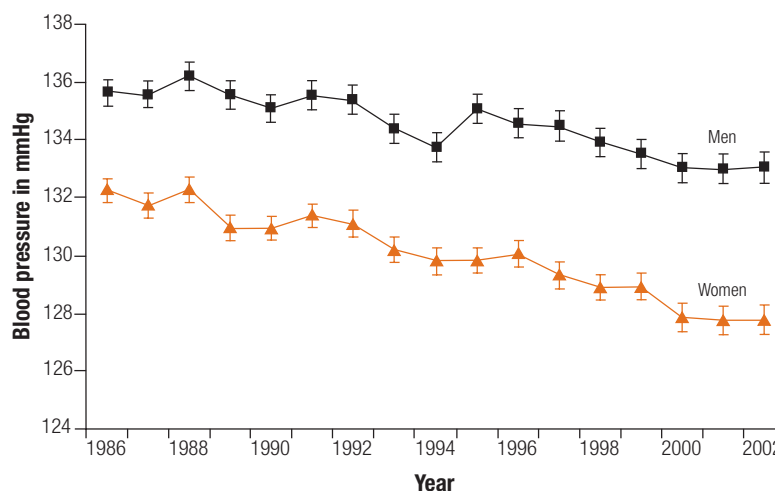
We pooled data of the NNS between 1986 and 2002 because the survey started collecting data on antihypertensive medication in 1986, and microdata were electronically available up to the survey in 2002, when this study was conducted. Table 1 lists the definitions, recoding and analytic strat-

gies for the key variables used in this analysis. We imputed missing values on these variables and created five imputed datasets for analysis using a software package for multiple imputation, Amelia II: A Program for Missing Data version 1.1–23.<sup>23</sup>

### Statistical analysis

We performed all analyses separately by sex due to different trends in the key variables. We used two-stage least squares, including an instrumental variable, to estimate parameters of interest.<sup>24</sup> This is an econometric method to correct bias and inconsistency in estimators resulting from simultaneous causality between a treatment variable and an outcome variable in non-experimental data. A simple regression of blood pressure in persons taking antihypertensive medication would incorrectly yield a positive coefficient because people who have high blood pressure are more likely to take medication. Our instrumental variable was the proportion of individuals with hypertension who were on treatment. We defined treatment as the self-reported daily use of antihypertensive medications. For each group defined by sex and prefecture of residence, we computed this instrumental variable as a single average across the period from 1986 to 2002 rather than calculating annual averages to avoid small denominators, as there were 47 prefectures in

Fig. 1. Age-standardized mean and 95% confidence interval of systolic blood pressure in the adult population over 20 years of age, by sex, based on data from the National Nutrition Survey, Japan, 1986–2002



total. In this study, individuals were considered to be hypertensive if they had an SBP of 140 mmHg or higher or reported daily use of antihypertensive medications. Although a diastolic blood pressure of 90 mmHg or over is also included in the widely-used definition of hypertension,<sup>25</sup> for simplification we did not use diastolic blood pressure in defining hypertension.

In the first stage of the two-stage least squares regression, for each individual we predicted the probability of being on treatment using the following logistic model:

$$MED_i = \alpha_1 + \beta_1 COV_i + \gamma_1 X_i + \varepsilon_{1i}$$

where MED is a binary variable for taking antihypertensive medication; COV is the instrumental variable;  $X$  is the matrix of other covariates;  $\varepsilon$  is an error term; 1 signifies the first equation; and  $i$  indexes observations. The covariates include an interaction between BMI and age; cigarette smoking; alcohol drinking; regular exercise; daily salt intake; and survey year. The variables on cigarette smoking, alcohol drinking, and regular exercise were qualitative, and

Table 2. Age-standardized means of key variables in the adult population over 20 years of age, by sex, based on data from the National Nutrition Survey, Japan, in 1986 and 2002

Variable	Men				Women			
	1986 (n = 6 612)		2002 (n = 4 278)		1986 (n = 7 224)		2002 (n = 4 897)	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
BMI (kg/m <sup>2</sup> )	22.5	22.5–22.6	23.3	23.2–23.4	22.4	22.4–22.5	22.4	22.3–22.5
Regular exercise <sup>a</sup> (%)	21.5	20.5–22.6	32.2	30.8–33.6	14.9	14.0–15.7	29.0	27.7–30.3
Current smoker <sup>b</sup> (%)	55.1	53.9–56.4	43.9	42.4–45.4	9.3	8.6–10.0	12.7	11.7–13.7
Current drinker <sup>c</sup> (%)	49.2	48.0–50.5	48.7	47.2–50.2	7.0	6.4–7.6	12.6	11.6–13.6
Daily salt intake (g)	12.1	12.1–12.2	11.8	11.7–11.8	12.1	12.1–12.1	11.7	11.7–11.8
Prevalence of hypertension (%) <sup>d</sup>	43.7	42.5–44.8	42.9	41.6–44.2	38.3	37.4–39.3	35.3	34.1–36.4
Hypertensives on treatment (%) <sup>d,e,f</sup>	29.8	27.8–31.8	39.7	36.9–42.6	36.3	33.5–39.2	48.0	44.3–51.7
Hypertensives under control (%) <sup>d,e,g</sup>	12.4	10.9–14.0	20.5	17.9–23.1	17.5	14.8–20.1	27.2	23.7–30.8

BMI, body mass index; CI, confidence interval.

<sup>a</sup> In the survey, individuals were considered to have regular exercise if they had exercised for more than 30 minutes at a time more than twice a week for over 1 year.

<sup>b</sup> In the survey, individuals were considered current smokers if they smoked daily or occasionally.

<sup>c</sup> In the survey, individuals were considered current drinkers if they consumed more than one standard cup of Japanese sake, one large bottle of regular beer, or one double measure of whisky at a time more than three times a week.

<sup>d</sup> Hypertension was defined as SBP  $\geq$  140 mmHg or daily use of antihypertensive medication.

<sup>e</sup> Out of hypertensive population.

<sup>f</sup> Treatment was defined as daily use of antihypertensive medications.

<sup>g</sup> Control was defined as SBP < 140 mmHg.

survey participants answered using dichotomous or multichotomous response categories. In the survey, individuals reported whether or not they had regular exercise, which was defined as exercising for more than 30 minutes at a time more than twice a week for over 1 year.<sup>19</sup> They were considered current smokers if they reported smoking cigarettes daily or occasionally, and current drinkers if they reported drinking alcohol, which was defined as consuming more than one standard cup of Japanese sake, one large bottle of regular beer, or one double measure of whisky at a time more than three times a week.<sup>19</sup>

In the second stage of the model, we used ordinary least squares regression to study the SBP of individuals as a function of the predicted probability of being treated and all independent variables used in the first stage except for the instrumental variable. The equation was specified as follows:

$$SBP_i = \alpha_2 + \beta_2 \text{Prob}(\text{MED})_i + \gamma_2 X_i + \varepsilon_{2i}$$

where SBP is systolic blood pressure; Prob(MED) is the predicted probability of taking antihypertensive medication; 2 signifies the second equation;  $X$  is defined as in the first equation.

Using regression estimators, we decomposed the change in mean predicted SBP by sex and age between 1986 and 2002 into contributions of the explanatory variables. For each explanatory variable, we computed

Table 3. Age-standardized mean SBP (in mmHg), by sex and use or non-use of antihypertensive medications, based on data from the National Nutrition Survey, Japan, 1986–2002

Statistics	Untreated	Treated
<b>Men</b>		
<i>n</i>	76 781	13 773
Mean SBP	133.5	140.4
95% CI	133.3–133.6	140.0–140.8
<b>Women</b>		
<i>n</i>	85 728	16 175
Mean SBP	128.7	138.4
95% CI	128.6–128.8	138.0–138.8

CI, confidence interval; SBP, systolic blood pressure.

adjusted linear predictions of SBP in 1986 and 2002, setting other variables to their means. We then used these adjusted means, standard errors and the numbers of samples to calculate means and 95% confidence intervals (CIs) for the differences noted between the beginning and end of the study period, 1986 and 2002.

We conducted all analyses in STATA/SE 9.2 (StataCorp LP, College Station, TX, United States of America). Means and standard errors calculated from the five imputed datasets were combined following King et al.<sup>26</sup> We also used CLARIFY 2.0 (Harvard University, Cambridge, MA, USA) to simulate and combine parameters of regression equations from the imputed datasets.<sup>27,28</sup> For age-standardization, we obtained the total

population by 5-year age groups from the 2000 Population Census of Japan.<sup>29</sup>

## Results

Out of a total of 259 850 respondents in the pooled dataset, we obtained a sample of 192 457 for analysis (90 554 men and 101 903 women), after excluding 64 722 respondents < 20 years and 2671 pregnant or breastfeeding women. Age-standardized mean SBP in this sample decreased between 1986 and 2002, from 135.6 mmHg (95% CI: 135.2–136.1 mmHg) to 133.0 mmHg (95% CI: 132.5–133.6 mmHg) in men, and from 132.3 mmHg (95% CI: 131.8–132.7 mmHg) to 127.8 mmHg (95% CI: 127.3–128.3 mmHg) in women (Fig. 1). Table 2 summarizes the age-standardized means and 95% confidence intervals of other key variables by sex in 1986 and 2002. Despite the declining trend of mean SBP, the age-standardized prevalence of hypertension did not show a remarkable change in either sex, reflecting the increasing proportion of hypertensive people who used antihypertensive medications daily and had a controlled SBP of less than 140 mmHg.

As expected, age-standardized mean SBP was substantially higher in the treated than in the untreated group in both sexes (Table 3). This confirms the existence of simultaneous causality or endogeneity in the data. Table 4 shows that there is no difference in age-standardized mean SBP across quintiles of treatment coverage by prefecture: this indicates that the proposed instrumental variable is exogenous and satisfies one of the two conditions of a valid instrumental variable.

Table 4. Age-standardized mean SBP (in mmHg) in the adult population over 20 years of age, by sex and quintiles of antihypertensive treatment coverage at the prefecture level, based on data from the National Nutrition Survey, Japan, 1986–2002

Statistics	Coverage quintile				
	1st	2nd	3rd	4th	5th
<b>Men<sup>a</sup></b>					
<i>n</i>	19 478	19 719	18 782	17 282	15 293
Mean SBP	135.0	134.6	134.5	134.6	134.8
95% CI	134.8–135.3	134.4–134.9	134.3–134.8	134.3–134.9	134.5–135.0
<b>Women<sup>b</sup></b>					
<i>n</i>	22 434	19 143	20 945	20 442	18 939
Mean SBP	130.7	130.1	130.0	129.9	130.5
95% CI	130.5–130.9	129.8–130.3	129.8–130.3	129.6–130.1	130.2–130.7

CI, confidence interval; SBP, systolic blood pressure.

<sup>a</sup> The coverage quintiles were, from first to fifth, 28.7–32.7%, 32.9–34.7%, 35.1–37.1%, 37.3–38.4% and 38.6–42.0%, respectively.

<sup>b</sup> The coverage quintiles were, from first to fifth, 33.1–38.9%, 39.3–40.7%, 41.0–42.5%, 42.9–44.5% and 44.8–52.7%, respectively.

In the first-stage logistic regression, the individual use of antihypertensive medications was significantly and positively associated with the proportion of individuals with hypertension who were treated in their prefecture of residence in both sexes (odds ratio, OR: 47.7, 95% CI: 22.5–100.8 in men; OR: 16.1, 95% CI: 8.9–29.2 in women). Its significant association with the endogenous variable means that it meets another condition for a valid instrumental variable. The median of predicted probability of taking medications was 0.11 (range: 0.02–0.70) in men and 0.10 (range: 0.02–0.92) in women.

In the second-stage regression of SBP, the coefficient of the probability of being treated indicates that individual SBP would significantly decline on average by 2.1 mmHg (95% CI: 1.4–2.7) and 3.3 mmHg (95% CI: 2.3–4.2) in men and women, respectively, with an increase of the probability of taking medication by 10% (Table 5). All other explanatory variables were significantly associated with SBP in both sexes, except regular exercise and cigarette smoking in women. In men, the association of regular exercise with SBP was substantially smaller than that of alcohol drinking, and the association of cigarette smoking with SBP was small too.

Table 6 provides the age-specific means of predicted SBP by sex and age group in 1986 and 2002. The means declined in all age groups in both sexes by 1.8 (95% CI: 1.2–2.5) to 3.0 (95% CI: 2.4–3.6) mmHg in men and 3.7 (95% CI: 3.4–4.1) to 5.1 (95% CI: 4.5–5.7) mmHg in women. The differences in means between 1986 and 2002 were statistically significant across all sex and age groups.

### Contributions of different factors

The decomposition of the change in age-specific mean SBP by sex between 1986 and 2002 into contributions of the explanatory variables is illustrated in Fig. 2 and Fig. 3. The contribution of increased mean probability of taking antihypertensive medications was the largest of all the contributions made by the independent variables included in the model, except in young women. The magnitude of its contribution in men ranged from –0.29 mmHg (95% CI: –0.31 to –0.27 mmHg) to –1.93 mmHg (95% CI:

Table 5. Results from the second-stage linear regression model on SBP, based on data from the National Nutrition Survey, Japan, 1986–2002

Independent variables	Men (n = 90 554)			Women (n = 101 903)		
	<i>b</i>	SE	<i>P</i> -value	<i>b</i>	SE	<i>P</i> -value
<b>BMI (kg/m<sup>2</sup>)</b>	1.36	0.07	< 0.001	1.29	0.05	< 0.001
<b>Age (years)<sup>a</sup></b>						
30–34	4.30	2.44	0.095	0.97	1.79	0.587
35–39	4.90	2.73	0.100	0.89	1.87	0.637
40–44	8.84	2.85	0.011	3.04	1.73	0.081
45–49	9.84	2.28	< 0.001	2.35	1.69	0.165
50–54	12.21	2.13	< 0.001	5.23	1.97	0.010
55–59	14.76	2.47	< 0.001	6.19	2.68	0.038
60–64	19.45	2.35	< 0.001	13.89	2.18	< 0.001
65–69	20.65	2.69	< 0.001	19.36	2.70	< 0.001
70–74	28.10	2.60	< 0.001	28.71	1.99	< 0.001
≥ 75	30.99	2.24	< 0.001	39.67	1.79	< 0.001
<b>Age (years) × BMI</b>						
30–34 × BMI	–0.05	0.11	0.626	0.07	0.08	0.428
35–39 × BMI	0.02	0.12	0.903	0.22	0.09	0.016
40–44 × BMI	–0.02	0.13	0.891	0.33	0.08	< 0.001
45–49 × BMI	0.10	0.10	0.333	0.58	0.08	< 0.001
50–54 × BMI	0.17	0.10	0.112	0.71	0.10	< 0.001
55–59 × BMI	0.26	0.12	0.037	0.89	0.14	< 0.001
60–64 × BMI	0.24	0.12	0.048	0.75	0.12	< 0.001
65–69 × BMI	0.38	0.13	0.008	0.76	0.15	< 0.001
70–74 × BMI	0.19	0.13	0.150	0.60	0.12	< 0.001
≥ 75 × BMI	0.24	0.12	0.053	0.38	0.12	0.003
<b>Regular exercise<sup>a,b</sup></b>	–0.56	0.18	0.007	–0.35	0.19	0.085
<b>Current smoker<sup>a,c</sup></b>	0.39	0.19	0.048	0.38	0.27	0.186
<b>Current drinker<sup>a,d</sup></b>	3.17	0.13	< 0.001	2.41	0.23	< 0.001
<b>Daily salt intake (g)</b>	0.43	0.08	< 0.001	0.44	0.07	< 0.001
<b>Predicted probability of treatment</b>	–20.50	3.16	< 0.001	–32.52	4.56	< 0.001
<b>Survey year, 2002<sup>a,e</sup></b>	–2.44	0.56	0.001	–3.14	0.38	< 0.001
<b>Intercept</b>	86.08	2.14	< 0.001	83.29	1.35	< 0.001
<b>F</b>	776.6		< 0.001	1 428.5		< 0.001
<b>Adjusted R-squared</b>	0.26			0.37		

*b*, regression coefficient; BMI, body mass index; SBP, systolic blood pressure; SE, standard error.

<sup>a</sup> Referent categories: 20–29 years old, no regular exercise, non/ex-smoker, non/ex-drinker.

<sup>b</sup> In the survey, individuals were considered to have regular exercise if they had exercised for more than 30 minutes at a time more than twice a week for over 1 year.

<sup>c</sup> In the survey, individuals were considered current smokers if they smoked daily or occasionally.

<sup>d</sup> In the survey, individuals were considered current drinkers if they consumed more than one standard cup of Japanese sake, one large bottle of regular beer, or one double measure of whisky at a time more than three times a week.

<sup>e</sup> 1987–2001 are omitted.

–2.19 to –1.68 mmHg) in the 20–29 year and 70–74 year age groups, respectively, and in women from –0.22 mmHg (95% CI: –0.24 to –0.20 mmHg) to –2.46 mmHg (95% CI: –2.90 to –2.03 mmHg) in the 30–34 year and 70–74 year age groups, respectively. The contribution of treatment increased with age in both sexes, reflecting a larger in-

crease in the probability of being treated among older adults.

In women in their 30s and 40s, decreased mean BMI was the major contributor to the decline of mean SBP. Portions of the SBP decline attributed to this factor were as follows for the respective age groups: –0.68 mmHg (95% CI: –1.21 to –0.16 mmHg)

in 30–34 years,  $-0.56$  mmHg (95% CI:  $-1.13$  to  $0.01$  mmHg) in 35–39 years,  $-0.93$  mmHg (95% CI:  $-1.59$  to  $-0.28$  mmHg) in 40–44 years, and  $-1.09$  mmHg (95% CI:  $-1.86$  to  $-0.33$  mmHg) in 45–49 years. However, the trend of mean BMI reversed in elderly women, with an associated increase in mean SBP of  $1.48$  mmHg (95% CI:  $0.53$ – $2.44$  mmHg) in 65–69-year-old women,  $2.04$  mmHg (95% CI:  $1.08$ – $3.00$  mmHg) in 70–74-year-old women, and  $1.09$  mmHg (95% CI:  $0.32$ – $1.85$  mmHg) in women aged 75 years and over. Mean BMI rose across all age groups in men, with an associated increase in mean SBP of up to  $2.60$  mmHg (95% CI:  $1.82$ – $3.39$  mmHg) in 70–74-year-old men.

Reduced mean daily salt intake contributed significantly to the decline of mean SBP by  $-0.4$  to  $-0.2$  mmHg in all age groups in both sexes. However, these values should be considered as a reference only, because the measure of salt intake used in this study was an aggregate at the prefecture level as described in Table 1.

Decreased prevalence of alcohol drinking contributed to the reduction of mean SBP in men in their 30s. The size of its contribution in the respective age groups is:  $-0.31$  mmHg (95% CI:  $-0.52$  to  $-0.10$  mmHg) in 30–34 years, and  $-0.22$  mmHg (95% CI:  $-0.42$  to  $-0.03$  mmHg) in 35–39 years. In contrast, the prevalence of alcohol drinking rose in men aged 70 years and over, and mean SBP increased by  $0.35$  mmHg (95% CI:  $0.10$ – $0.60$ ) in men 70–74 years and by  $0.25$  mmHg (95% CI:  $0.02$ – $0.48$ ) in men 75 years and over. The prevalence of alcohol drinking also increased in women aged under 60 years, and a concomitant rise in their mean SBP by  $0.2$  mmHg was noted.

Regular exercise contributed very little to the decline of mean SBP by less than  $0.1$  mmHg in all age groups in both sexes. This minor effect of physical activity was largely attributable to its small association with individual SBP, given that the prevalence of regular exercise increased substantially during this period.

Finally, after considering both positive and negative contributions to the decline of mean SBP, a remaining reduction of  $2.44$  mmHg in men and  $3.14$  mmHg in women was left unexplained by this model. These values

Table 6. Change in age-specific means of SBP (in mmHg) predicted from the two-stage least squares model, by sex, between 1986 and 2002, based on data from the National Nutrition Survey, Japan, 1986–2002

Age (years)	Number surveyed		Mean prediction		Difference between means* and 95% CI	
	1986	2002	1986	2002		
<b>Men</b>						
20–29	993	540	121.6	119.1	–2.5	–2.9 to –2.0
30–34	642	327	125.8	123.2	–2.6	–3.2 to –2.0
35–39	1019	330	128.1	126.2	–1.9	–2.4 to –1.4
40–44	702	321	131.5	128.9	–2.5	–3.0 to –2.0
45–49	655	356	135.0	132.1	–2.8	–3.4 to –2.3
50–54	667	476	138.0	135.3	–2.7	–3.2 to –2.2
55–59	536	415	141.8	138.9	–2.9	–3.4 to –2.3
60–64	482	418	144.5	141.8	–2.7	–3.2 to –2.1
65–69	339	383	147.6	144.6	–3.0	–3.6 to –2.4
70–74	261	324	148.1	146.3	–1.8	–2.5 to –1.2
75+	316	388	151.3	148.8	–2.5	–3.1 to –1.8
<b>Women</b>						
20–29	980	570	114.4	110.7	–3.7	–4.1 to –3.4
30–34	689	340	117.9	113.8	–4.1	–4.7 to –3.6
35–39	989	326	121.7	117.6	–4.1	–4.7 to –3.6
40–44	707	353	127.2	122.6	–4.6	–5.2 to –4.0
45–49	731	387	131.6	126.7	–4.8	–5.5 to –4.2
50–54	694	518	136.3	132.2	–4.2	–4.8 to –3.6
55–59	659	478	140.1	135.0	–5.1	–5.7 to –4.5
60–64	553	466	143.3	138.8	–4.6	–5.2 to –3.9
65–69	433	419	146.1	142.0	–4.1	–4.7 to –3.5
70–74	370	410	148.8	144.8	–4.0	–4.6 to –3.5
75+	419	630	152.6	147.9	–4.6	–5.1 to –4.2

\* $P < 0.05$  for all the differences between means shown. CI, confidence interval; SBP, systolic blood pressure.

were constant across age groups and equivalent to the coefficients of the survey year 2002 estimated in the second-stage regression.

## Discussion

This paper presents the first attempt to measure the contributions of relevant factors to the decline of mean SBP in Japan. The study used the two-stage least squares method with the instrumental variable and pooled data of the nationally representative cross-sectional survey over a long period of time.

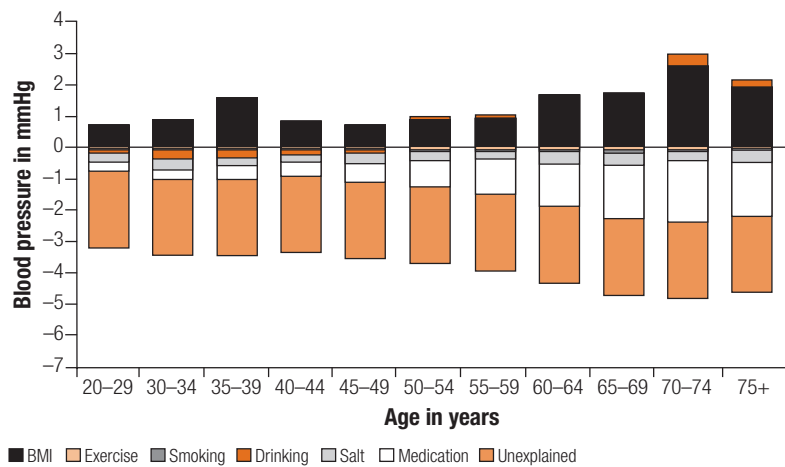
The study identified two major contributors to the change of mean SBP in Japan for the past 17 years. First, the effect of antihypertensive medications was substantial in older adults. It was a product of the association between SBP and antihypertensive medications and the change in the probability of taking medications. The considerable association of treatment with SBP that we ob-

served using this instrumental variable approach raises questions on whether this is an overestimation or whether patients that get treated in Japan have been managed well. Although the NNS did not ask which antihypertensive drug class the study participants used, thiazide diuretics and beta-blockers were the most frequently prescribed drugs during the 1980s,<sup>30,31</sup> and calcium channel blockers and angiotensin-converting enzyme inhibitors since the 1990s.<sup>32–34</sup> Previous meta-analyses assessed the average effects of antihypertensive medications on SBP to be 9–15 mmHg for single-drug standard-dose therapies and 20 mmHg for three-drug regimens in people having a cardiovascular event and usual pretreatment blood pressure at 150/90 mmHg.<sup>35,36</sup> Our estimates therefore approximate treatment effects well for this type of analysis using cross-sectional survey data. Moreover, the considerable increase in the probability

of being treated in older adults might be partly attributable to the better awareness of physicians about the importance of diagnosis and treatment of hypertension. Several recommendations and guidelines for the management of hypertension were published in Japan during this period.<sup>37-40</sup> In addition, this study suggested that there is still considerable room for further decrease in mean SBP through improving treatment coverage and control of hypertension. This is especially the case for men, having poorer coverage and control rates than women in 2002.

Another principal finding of this study is that the contribution of decreased mean BMI was substantial in women in their 30s and 40s, whereas increased mean BMI offset a large part of the decrease of mean SBP in men and elderly women. These different trends of BMI across sex and age groups in Japan have been reported elsewhere.<sup>41</sup> Although the decreasing trend of mean BMI brought favourable consequences in young women, it must be noted that the trend of excessive thinness would ultimately result in adverse health outcomes.<sup>42</sup> Moreover, our results confirmed for the first time in the Japanese context the adverse effect of overweight and obesity on mean SBP, which had been pointed out in previous studies.<sup>8,9,17</sup> Formulating effective policies to stop this trend is extremely urgent to further decrease mean SBP and the disease burden from CVD, particularly in Japanese men.

Fig. 2. Estimated contributions of explanatory variables to changes in mean predicted SBP in men between 1986 and 2002, based on data from the National Nutrition Survey, Japan, 1986-2002



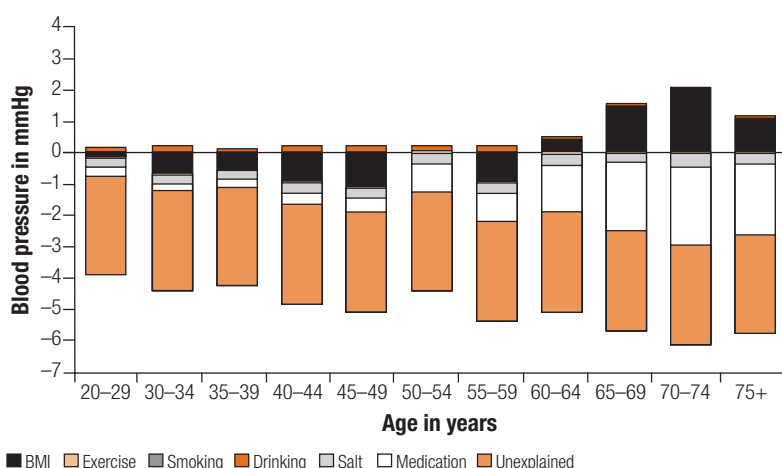
BMI, body mass index; SBP, systolic blood pressure.

Lifestyle-related factors such as physical activity, alcohol drinking and dietary salt intake made only limited contributions to the decline of mean SBP in this study. Nevertheless, improving lifestyle will undoubtedly have a beneficial effect on reducing mean SBP at the population level. The negligible contribution of regular exercise was largely attributable to its small association with SBP at the individual level, which was unexpected. However, it might be ascribed to potential confounding factors between physical activity and SBP that were not included in our model,<sup>43</sup> or to multiple physiological paths for its protective effects.<sup>44</sup>

Further investigation on the association between physical activity and blood pressure would be necessary in future research. Moreover, the contribution of alcohol drinking was very small because its prevalence did not change much during this period. Given that alcohol drinking showed a relatively large association with SBP, an adequate decrease in the prevalence of alcohol drinking would bring a considerable decline in mean SBP, especially in Japanese men. Furthermore, this study demonstrated that cigarette smoking had a negligible association with SBP, which was consistent with a finding of a study using Health Survey for England.<sup>45</sup> This might sound counterintuitive because it is well known that smoking cessation is important for total cardiovascular risk reduction. Smoking, however, raises blood pressure only acutely, and blood pressure returns to the baseline level a quarter of an hour after smoking ceases.<sup>25</sup> An SBP measured at surveys, therefore, does not reflect the effects of cigarette smoking, and it is safely said that the finding of this study is valid.

These findings and implications are relevant to health policies in countries where the prevalence of hypertension or mean SBP is expected to rise.<sup>7,9</sup> Continued efforts should be taken to encourage maintaining adequate body weight, keeping alcohol consumption and salt intake to a minimum, and improving the management of hypertension. Introduction of affordable medications such as multidrug regi-

Fig. 3. Estimated contributions of explanatory variables to changes in mean predicted SBP in women between 1986 and 2002, based on data from the National Nutrition Survey, Japan, 1986-2002



BMI, body mass index; SBP, systolic blood pressure.

mens would be particularly helpful in developing countries.<sup>46</sup>

The limitations of this study should be taken into consideration in the interpretation of its findings. First, the use of the instrumental variable cannot derive a causal relationship from these cross-sectional data. Longitudinal data obtained from a nationally representative sample are necessary to examine true causal relationships between blood pressure and relevant factors. Second, as with all data from interview and examination surveys, ours might contain measurement errors resulting from a white-coat effect on the first measurement of SBP, changes in questioning techniques over the study period of 17 years, and self-reports of antihypertensive medications and lifestyles.

Finally, a considerable part of the reduction in mean SBP remains unexplained, which may be partly attributable to the limited availability of explanatory variables from the survey. In our model we did not include the intake of key nutrients other than dietary salt, such as calcium, magnesium, po-

tassium and vegetable protein, in order to minimize estimation bias resulting from aggregation of data, as mentioned in Table 1. Other variables of interest that were not available from our data include educational background, marital status, occupation, income, urban/rural dwelling, psychosocial factors (e.g. family responsibilities and job strain), the amount of drinking, the quantity and intensity of physical activity, and birth weight. Data on these and other variables should be extensively collected and incorporated in the model in future research. Further enquiry into the statistical method to address treatment effects would also improve the model's capability to explain the decrease in mean SBP in some general populations.

In conclusion, the decline of mean SBP in Japan between 1986 and 2002 was partly attributable to increased use of antihypertensive medications, especially in older adults, and decreased mean BMI in young women. Mean SBP of Japanese adults would further decrease through improvements in

body weight management in men and elderly women, dietary salt intake, alcohol drinking, and treatment and control of high blood pressure. ■

### Acknowledgements

We thank Majid Ezzati, Dennis M Feehan, Dean T Jamison and Saeid Shahraz for their helpful comments and Stanislava Nikolova for her editorial assistance. This study was based on data prepared for research projects supported by Grants-in-Aid for Scientific Research from the Japan Ministry of Health, Labour and Welfare (PI: Dr Toshihiko Hasegawa; H12-iryō-002, H14-kenko-010 and H16-kenko-001).

**Funding:** Research support for this study was received from the Harvard Center for Population and Development Studies, Harvard Initiative for Global Health, the National Institute of Aging (PO1 AG 17625-01) and the Institute for Health Metrics and Evaluation at the University of Washington.

**Competing interests:** None declared.

## Résumé

### Comprendre la baisse de la pression systolique moyenne au Japon : analyse des données rassemblées à partir d'enquêtes nationales sur la nutrition, 1986-2002

**Objectif** Évaluer les relations entre la baisse de la pression systolique moyenne (PSM) observée au Japon sur la période 1986-2002, la prise d'un traitement antihypertenseur et des facteurs liés au mode de vie.

**Méthodes** Un échantillon représentatif à l'échelle nationale de 90 554 hommes et 101 903 femmes de 20 ans et plus a été constitué à partir des données regroupées d'enquêtes transversales annuelles, menées au Japon entre 1986 et 2002. En utilisant la méthode des moindres carrés en deux étapes à variable instrumentale, nous avons étudié l'association entre la PSM, la prise de médicaments antihypertenseurs et des facteurs liés au mode de vie, y compris l'indice de masse corporelle (IMC), l'activité physique, la consommation d'alcool, le tabagisme et l'ingestion de sel via l'alimentation. Aux fins des enquêtes, un exercice physique régulier été défini comme un exercice pratiqué pendant plus de 30 min et plus de deux fois par semaine sur un an. Le tabagisme actuel a été défini comme la consommation quotidienne ou occasionnelle de cigarettes et la consommation actuelle d'alcool comme l'ingestion de plus d'une coupe standard de saké japonais, d'une grande bouteille de bière ordinaire ou d'une double mesure de whisky plus de trois fois par semaine. Les évolutions de la PSM moyenne prédite pour chaque sexe et chaque tranche d'âges entre 1986 et 2002 ont été décomposées en différentes contributions des variables explicatives.

**Résultats** Les moyennes par âge de la PSM prédite ont baissé au cours de cette période de 1,8 (intervalle de confiance, IC à 95 % = 1,2-2,5) à 3,0 (IC à 95 % = 2,4-3,6) mm Hg chez l'homme et de 3,7 (IC à 95 % = 3,4-4,1) à 5,1 (IC à 95 % = 4,5-5,7) mm HG chez la femme. Ces baisses s'expliquent partiellement par l'usage accru des hypertenseurs chez les deux sexes et dans l'ensemble des tranches d'âges et par la diminution de l'IMC moyen des femmes au cours de la trentaine et de la quarantaine. Les contributions des effets du traitement antihypertenseur augmentent avec l'âge. L'élévation de l'IMC moyen chez l'homme et la femme plus âgés compense partiellement la baisse de leur PSM moyenne.

**Conclusion** La baisse de la PSM moyenne au Japon entre 1986 et 2002 est partiellement attribuable à l'usage accru des médicaments antihypertenseurs, notamment chez la population âgée, et à la diminution de l'IMC moyen chez les femmes jeunes. Cependant, une partie substantielle de cette baisse reste inexpliquée et doit faire l'objet d'une étude plus poussée. Une diminution encore plus importante de la PSM devrait pouvoir être obtenue par une meilleure gestion du poids corporel, une réduction de la consommation de sel et d'alcool et une amélioration du traitement et du contrôle de l'hypertension.

## Resumen

**Razones de la disminución de la presión arterial sistólica en el Japón: análisis de datos combinados de la Encuesta Nacional sobre Nutrición 1986–2002**

**Objetivo** Determinar la relación existente entre la caída de la presión arterial sistólica (PAS) media observada en el Japón en 1986-2002 y el uso de tratamiento antihipertensivo y diversos factores relacionados con el modo de vida.

**Métodos** A partir de datos combinados de encuestas transversales anuales realizadas en el Japón durante 1986-2002, se obtuvo una muestra representativa a nivel nacional de 90 554 hombres y 101 903 mujeres de 20 o más años de edad. Utilizando el método de mínimos cuadrados en dos etapas con una variable instrumental, analizamos la relación entre la PAS y el uso de medicación antihipertensiva y diversos factores relacionados con el modo de vida, incluidos el índice de masa corporal (IMC), la actividad física, el consumo de alcohol, el consumo de tabaco y la ingesta de sal en la dieta. En las encuestas, la realización regular de ejercicio se definió como la práctica de ejercicio durante más de 30 minutos más de dos veces a la semana a lo largo de más de un año. Se consideró que la persona fumaba cuando consumía tabaco de forma diaria u ocasional, y que bebía alcohol cuando la ingesta de éste superaba el equivalente a un vaso corriente de sake japonés, una botella grande de cerveza normal o un whisky doble más de tres veces a la semana. Las variaciones de las PAS medias predichas para cada sexo y grupo de edad entre 1986

y 2002 se descompusieron de acuerdo con las contribuciones respectivas de esas variables independientes.

**Resultados** Los valores predichos de la medias por edad de la PAS disminuyeron durante el periodo considerado entre 1,8 (intervalo de confianza del 95%, IC95%: 1,2–2,5) y 3,0 (IC95%: 2,4–3,6) mmHg en los hombres y entre 3,7 (IC95%: 3,4–4,1) y 5,1 (IC95%: 4,5–5,7) mmHg en las mujeres. Esas reducciones se explicaban en parte por el mayor uso de medicamentos en los dos sexos y en todos los grupos de edad y por la reducción del IMC medio en las mujeres de entre 30 y 50 años. La contribución del tratamiento a esos resultados aumentaba con la edad. La elevación del IMC medio en los hombres y entre las mujeres de edad contrarrestaba parte de la disminución de su PAS media.

**Conclusión** La disminución de la PAS media en el Japón entre 1986 y 2002 es atribuible en parte al mayor uso de medicamentos antihipertensivos, sobre todo en la población de edad avanzada, así como a una reducción del IMC medio entre las mujeres jóvenes. Sin embargo, queda por explicar una parte sustancial de la disminución observada, que habrá que investigar más a fondo. La PAS podría disminuir aún más introduciendo mejoras en el control del peso corporal, el consumo de sal y alcohol, y el tratamiento y control de la hipertensión.

## ملخص

**فهم الانخفاض في متوسط ضغط الدم الانقباضي في اليابان: تحليل للمعطيات المجمعة من المسح الوطني للتغذية، 1986 - 2002**

**الموجودات:** انخفاض القيم الوسطية الخاصة بعمر معين للمتوسط المتوقع لضغط الدم الانقباضي خلال هذه الفترة بمقدار يتراوح بين 8.1 (بفاصل ثقة 95% إذ تراوح الانخفاض بين 2.1 و5.2) وبين 0.3 (بفاصل ثقة 95% إذ تراوح الانخفاض بين 2.4 و3.6) مم زئبق لدى الرجال وبين 3.7 (بفاصل ثقة 95% إذ تراوح الانخفاض بين 4.3 و1.4) وبين 1.5 (بفاصل ثقة 95% إذ تراوح الانخفاض بين 5.4 و7.5) مليمتر زئبق لدى النساء. وقد فسرت هذه الانخفاضات جزئياً بزيادة تعاطي الأدوية في جميع فئات العمر والجنس وبنقص القيمة الوسطية لمنسب كتلة الجسم بين النساء في الثلاثينات والأربعينات من أعمارهن. وقد ازدادت مساهمة المعالجة في التأثير بتقدم العمر. وقد أدى ارتفاع القيمة الوسطية لمنسب كتلة الجسم لدى الرجال ولدى المُسنَّات إلى انحسار جزء من الانخفاض في متوسط ضغط الدم الانبساطي لديهم.

**الاستنتاجات:** يعزى الانخفاض في متوسط ضغط الدم الانبساطي في اليابان في المدة بين 1986 و2002 إلى زيادة تعاطي الأدوية الخافضة للضغط، ولاسيما لدى المُسنَّين، وإلى انخفاض متوسط منسب كتلة الجسم لدى الشباب؛ إلا أن جزءاً هاماً من الانخفاض لم يزل بحاجة لتفسير ويحتاج لمزيد من الاستقصاء في المستقبل. ويتوقع حدوث المزيد من الانخفاض في متوسط ضغط الدم الانقباضي من خلال تحسُّن المحافظة على وزن الجسم وتناول الملح والمسكرات ومعالجة فرط ضغط الدم وتضييبه.

**الهدف:** تقييم العلاقات بين الهبوط الملحوظ في متوسط الضغط الانقباضي في اليابان في المدة 1986–2002، واستخدام المعالجة بخافضات الضغط وبمعايير نمط الحياة.

**الطريقة:** أخذت عينة ممثلة على الصعيد الوطني تضم 90 554 رجلاً و101 903 امرأة ممن تتجاوز أعمارهم 20 عاماً، من المعطيات المجمعة لمسوحات سنوية مستعرضة في اليابان خلال المدة 1986-2002؛ ودرست العلاقة بين متوسط ضغط الدم الانقباضي والمداواة الخافضة للضغط وعوامل نمط الحياة والتي تتضمن منسب كتلة الجسم والنشاط البدني وتعاطي المسكرات وتدخين السجائر وتناول الملح في الغذاء باستخدام أقل المربعات على مرحلتين مع متغيرات أساسية. وفي المسوحات عرّف النشاط البدني بأنه التمرين الذي يستمر فترة أطول من ثلاثين دقيقة في المرة الواحدة، ويتكرّر أكثر من مرتين أسبوعياً لأكثر من عام، كما عرّف التدخين الحالي بتعاطي السجائر يومياً أو على فترات، فيما عرّف التعاطي الحالي للمسكرات بأنه تناول كأس معياري أو أكثر من المشروب البابابي (ساكي)، أو زجاجة كبيرة الحجم من البيرة العادية أو مكيايل مضاعف واحد من الويسكي في وقت واحد لأكثر من ثلاث مرات في الأسبوع. وحللت التغيرات في المتوسط المتوقع لضغط الدم الانقباضي في كل من مجموعات الجنس والعمر في المدة من 1986 إلى 2002 إلى المساهمات الخاصة بكل منها من هذه المتغيرات التي تفسرها.

## References

- He J, Whelton PK. Elevated systolic blood pressure as a risk factor for cardiovascular and renal disease. *J Hypertens Suppl* 1999;17:S7-13. PMID:10465061
- Lawes CM, Bennett DA, Lewington S, Rodgers A. Blood pressure and coronary heart disease: a review of the evidence. *Semin Vasc Med* 2002;2:355-68. PMID:16222626 doi:10.1055/s-2002-36765
- Lawes CMM, Bennett DA, Feigin VL, Rodgers A. Blood pressure and stroke: an overview of published reviews. *Stroke* 2004;35:1024-33. PMID:15053002 doi:10.1161/01.STR.0000116869.64771.5A
- Mathers CD, Lopez AD, Murray CJL. The global burden of disease and mortality by condition: data, methods, and results for 2001. In: Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJL, eds. *Global burden of disease and risk factors*. New York: Oxford University Press; 2006. pp. 45-240.
- Okayama A, Kadowaki T, Okamura T, Hayakawa T, Ueshima H. Age-specific effects of systolic and diastolic blood pressures on mortality due to cardiovascular diseases among Japanese men (NIPPON DATA80). *J Hypertens* 2006;24:459-62. PMID:16467648 doi:10.1097/01.hjh.0000209981.43983.cf
- Stamler J. The INTERSALT Study: background, methods, findings, and implications [published erratum appears in *Am J Clin Nutr* 1997;66:1297]. *Am J Clin Nutr* 1997;65:626S-642S. PMID:9022559
- Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet* 2005;365:217-23. PMID:15652604
- Burt VL, Cutler JA, Higgins M, Horan MJ, Labarthe D, Whelton P, et al. Trends in the prevalence, awareness, treatment, and control of hypertension in the adult US population: data from the Health Examination Surveys, 1960 to 1991. *Hypertension* 1995;26:60-9. PMID:7607734
- Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988-2000. *JAMA* 2003;290:199-206. PMID:12851274 doi:10.1001/jama.290.2.199
- Ong KL, Cheung BMY, Man YB, Lau CP, Lam KSL. Prevalence, awareness, treatment, and control of hypertension among United States adults 1999-2004. *Hypertension* 2007;49:69-75. PMID:17159087 doi:10.1161/01.HYP.0000252676.46043.18
- Kuulasmaa K, Tunstall-Pedoe H, Dobson A, Fortmann S, Sans S, Tolonen H, et al. Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations. *Lancet* 2000;355:675-87. PMID:10703799 doi:10.1016/S0140-6736(99)11180-2
- Okayama A, Ueshima H, Marmot MG, Nakamura M, Kita Y, Yamakawa M. Changes in total serum cholesterol and other risk factors for cardiovascular disease in Japan, 1980-1989. *Int J Epidemiol* 1993;22:1038-47. PMID:8144284 doi:10.1093/ije/22.6.1038
- Sakata K, Labarthe DR. Changes in cardiovascular disease risk factors in three Japanese national surveys 1971-1990. *J Epidemiol* 1996;6:93-107. PMID:8795949
- Sproston K, Primatesta P. *Health survey for England 2003: Volume 2. Risk factors for cardiovascular disease*. London: The Stationery Office; 2004.
- Ueshima H, Tataru K, Asakura S, Okamoto M. Declining trends in blood pressure level and the prevalence of hypertension, and changes in related factors in Japan, 1956-1980. *J Chronic Dis* 1987;40:137-47. PMID:3818867 doi:10.1016/0021-9681(87)90065-8
- Goff DC Jr, Howard G, Russell GB, Labarthe DR. Birth cohort evidence of population influences on blood pressure in the United States, 1887-1994. *Ann Epidemiol* 2001;11:271-9. PMID:11306346 doi:10.1016/S1047-2797(00)00224-6
- Tunstall-Pedoe H, Connaghan J, Woodward M, Tolonen H, Kuulasmaa K. Pattern of declining blood pressure across replicate population surveys of the WHO MONICA project, mid-1980s to mid-1990s, and the role of medication. *BMJ* 2006;332:629-35. PMID:16531419 doi:10.1136/bmj.38753.779005.BE
- Japanese Society of Hypertension guidelines for the management of hypertension (JSH 2004). *Hypertens Res* 2006;29:S1-105.
- Ministry of Health, Labor and Welfare. *Annual report of the National Nutrition Survey in Japan, 2000* [in Japanese]. Tokyo: Daiichi Shuppan Publishing Co.; 2002.
- Katanoda K, Matsumura Y. National nutrition survey in Japan - its methodological transition and current findings. *J Nutr Sci Vitaminol (Tokyo)* 2002;48:423-32. PMID:12656220
- Yoshiike N, Matsumura Y, Yamaguchi M, Seino F, Kawano M, Inoue K, et al. Trends of average intake of macronutrients in 47 prefectures of Japan from 1975 to 1994 - possible factors that may bias the trend data. *J Epidemiol* 1998;8:160-7. PMID:9782672
- Katanoda K, Nitta H, Hayashi K, Matsumura Y. Is the national nutrition survey in Japan representative of the entire Japanese population? *Nutrition* 2005;21:964-6. PMID:16039832
- Honaker J, King G, Blackwell M. Amelia II: A program for missing data, version: 1.1-23. Available from: <http://gking.harvard.edu/amelia/> [accessed on 2 September 2008].
- Angrist JD, Imbens GW, Rubin DB. Identification of causal effects using instrumental variables. *J Am Stat Assoc* 1996;91:444-55. doi:10.2307/2291629
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003;42:1206-52. PMID:14656957 doi:10.1161/01.HYP.0000107251.49515.c2
- King G, Honaker J, Joseph A, Scheve K. Analyzing incomplete political science data: an alternative algorithm for multiple imputation. *Am Polit Sci Rev* 2001;95:49-69.
- King G, Tomz M, Wittenberg J. Making the most of statistical analyses: improving interpretation and presentation. *Am J Pol Sci* 2000;44:347-61. doi:10.2307/2669316
- Tomz M, Wittenberg J, King G. *CLARIFY: software for interpreting and presenting statistical results, version 2.0*. 2001. Available from: <http://gking.harvard.edu> [accessed on 2 September 2008].
- 2000 Population of Japan. Ministry of Internal Affairs and Communication. Available from: <http://www.stat.go.jp/english/data/kokusei/2000/final/hyodai.htm> [accessed on 2 September 2008].
- Ebihara A. Antihypertensive drugs in the 21st century - history and perspective in the development of hypertensive drugs. *Clinic All-round* 1997;46:1718-21 [article in Japanese].
- Ishii T. Choice and use of antihypertensive drugs. *Japanese Journal of Clinical and Experimental Medicine* 1999;76:34-9 [article in Japanese].
- Saruta T. Current status of calcium antagonists in Japan. *Am J Cardiol* 1998;82:32R-4R. PMID:9822142 doi:10.1016/S0002-9149(98)00755-3
- Muratani H, Fukiyama K, Kamiyama T, Kimura Y, Abe K, Ishii M, et al. Current status of antihypertensive therapy for elderly patients in Japan. *Hypertens Res* 1996;19:281-90. PMID:8986459 doi:10.1291/hypres.19.281
- Mori H, Ukai H, Yamamoto H, Saitou S, Hirao K, Yamauchi M, et al. Current status of antihypertensive prescription and associated blood pressure control in Japan. *Hypertens Res* 2006;29:143-51. PMID:16755149 doi:10.1291/hypres.29.143
- Law MR, Wald NJ, Morris JK, Jordan RE. Value of low dose combination treatment with blood pressure lowering drugs: analysis of 354 randomised trials. *BMJ* 2003;326:1427-31. PMID:12829555 doi:10.1136/bmj.326.7404.1427
- Wu J, Kraja AT, Oberman A, Lewis CE, Ellison RC, Arnett DK, et al. A summary of the effects of antihypertensive medications on measured blood pressure. *Am J Hypertens* 2005;18:935-42. PMID:16053990 doi:10.1016/j.amjhyper.2005.01.011
- Hiwada K, Ogihara T, Matsumoto M, Matsuoka H, Takishita S, Shimamoto K, et al. Guidelines for hypertension in the elderly - 1999 revised version. Ministry of Health and Welfare of Japan. *Hypertens Res* 1999;22:231-59. PMID:10580391 doi:10.1291/hypres.22.231
- Japanese Society of Hypertension Guidelines Subcommittee for the Management of Hypertension. Guidelines for the management of hypertension for general practitioners. *Hypertens Res* 2001;24:613-34. PMID:11768720 doi:10.1291/hypres.24.613
- Handbook for the management of hypertension* [in Japanese]. Tokyo: Ministry of Health, Japan Medical Association. 1990.
- Ogihara T, Hiwada K, Matsuoka H, Matsumoto M, Shimamoto K, Ouchi Y, et al. [Guidelines on treatment of hypertension in the elderly, 1995 - a tentative plan for comprehensive research projects on aging and health - Members of the Research Group for "Guidelines on Treatment of Hypertension in the Elderly", Comprehensive Research Projects on Aging and Health, the Ministry of Health and Welfare of Japan]. *Nippon Ronen Igakkai Zasshi* 1996;33:945-75 [article in Japanese]. PMID:9059055

## Research

### Mean systolic blood pressure decline in Japan

Nayu Ikeda et al.

41. Yoshiike N, Seino F, Tajima S, Arai Y, Kawano M, Furuhashi T, et al. Twenty-year changes in the prevalence of overweight in Japanese adults: the National Nutrition Survey 1976-95. *Obes Rev* 2002;3:183-90. PMID:12164470 doi:10.1046/j.1467-789X.2002.00070.x
42. Takimoto H, Yoshiike N, Kaneda F, Yoshita K. Thinness among young Japanese women. *Am J Public Health* 2004;94:1592-5. PMID:15333320
43. Fagard RH. Physical activity in the prevention and treatment of hypertension in the obese. *Med Sci Sports Exerc* 1999;31 Suppl:S624-30. PMID:10593538 doi:10.1097/00005768-199911001-00022
44. *Physical activity and health: a report of the Surgeon General*. Atlanta, GA: United States Department of Health and Human Services; 1996.
45. Primates P, Falaschetti E, Gupta S, Marmot MG, Poulter NR. Association between smoking and blood pressure: evidence from the Health Survey for England. *Hypertension* 2001;37:187-93. PMID:11230269
46. Gaziano TA, Opie LH, Weinstein MC. Cardiovascular disease prevention with a multidrug regimen in the developing world: a cost-effectiveness analysis. *Lancet* 2006;368:679-86. PMID:16920473 doi:10.1016/S0140-6736(06)69252-0

## Letters

Please visit <http://www.who.int/bulletin/volumes/86/12/en/index.html> to read the following letters received in response to *Bulletin* papers:

**Caesarean birth as a component of surgical services in low- and middle-income countries**, by Cynthia Stanton & Carine Ronsmans

responding to: Ozgediz D, Jamison D, Cherian M, McQueen K. The burden of surgical conditions and access to surgical care in low- and middle-income countries. *Bull World Health Organ* 2008;86:646-7. PMID:18797625 doi:10.2471/BLT.07.050435

**Training for Lady Health Workers clarified**, by Zulfiqar A Bhutta, Sajid Soofi & Zahid Memon

responding to: Bin Nisar Y. Corrections needed to Pakistani programme details. *Bull World Health Organ* 2008;86:907. doi:10.2471/BLT.08.058131