Table 2 Association of daily alcohol intake (1 drink=11.5 g of ethanol) with SBP and DBP in each company (whole participants; *N*=4335)

		Dependent variables for regression model					
		Systolic blood pressure			*Diastolic blood pressure*		
Companies	N	*Regression coefficient*[a]	*Standard error*	P-*values*	*Regression coefficient*[a]	*Standard error*	P-*values*
A	300	0.01	0.36	0.974	0.18	0.27	0.509
B	446	1.39	0.35	<0.001	0.97	0.23	<0.001
C	395	0.99	0.26	<0.001	0.83	0.17	<0.001
D	420	0.54	0.28	0.049	0.44	0.19	0.021
E	179	1.63	0.53	0.002	1.27	0.33	<0.001
F	236	1.05	0.55	0.056	0.67	0.32	0.035
G	736	0.71	0.21	0.001	0.70	0.14	<0.001
H	411	1.12	0.33	0.001	0.93	0.22	<0.001
I	288	0.99	0.35	0.005	1.09	0.23	<0.001
J	289	0.60	0.36	0.098	0.42	0.24	0.087
K	635	1.20	0.28	<0.001	1.06	0.19	<0.001
Total	4335	0.87[b]	0.09	<0.001	0.77[b]	0.06	<0.001

[a]Partial regression coefficient was adjusted for age, BMI, urinary *sodium* excretion and potassium excretion.
[b]Weighted each partial regression coefficient by the square reciprocal of the standard error in each company.

Table 3 Means or adjusted means of SBP and DBP according to the type of alcoholic beverage that was mainly consumed in drinkers (*N*=2553)

Type of alcoholic beverage	N	*Crude*		*Age-adjusted*[a]		*Age and amount of alcohol consumption adjusted*[a]		*Age, amount of alcohol consumption, BMI, sodium and potassium excretion adjusted*[a]	
		Means	*s.e.*	*Means*	*s.e.*	*Means*	*s.e.*	*Means*	*s.e.*
Systolic blood pressure (mmHg)									
Beer	1293	118.2	0.4	118.4	0.4	119.3	0.5		0.4
Sake	125	119.7	1.6	118.9	1.4	118.2	1.4		1.3
Shochu	343	123.3	0.8	123.0	0.8	121.2	0.9		0.8
Whisky	68	121.3	1.9	120.9	1.9	120.7	1.9		1.7
Wine	50	116.4	1.9	116.6	2.2	117.1	2.2		2.0
Other	674	119.3	0.6	119.1	0.6	118.5	0.6		0.6
P-values		*P*<0.001		*P*<0.001		*P*=0.120			
Diastolic blood pressure (mmHg)									
Beer	1293	71.7	0.3	72.4	0.3	73.1	0.3		0.3
Sake	125	76.1	1.1	73.8	0.9	73.3	0.9		0.9
Shochu	343	76.7	0.6	76.0	0.6	74.5	0.6		0.6
Whisky	68	75.3	1.3	74.2	1.3	74.0	1.2		1.2
Wine	50	72.0	1.6	72.6	1.5	73.0	1.5		1.4
Other	674	73.9	0.4	73.5	0.4	72.9	0.4		0.4
		P<0.001		*P*<0.001		*P*=0.359			

[a]Adjusted by the analysis of covariance.

These relations did not change after adjusting for age. However, analysis of covariance involving as adjustment for alcohol consumption resulted in the disappearance of the significant difference in SBP and DBP. After further adjustment for BMI, sodium and potassium excretion, the *P*-values of the analysis of covariance for both SBP and DBP were increased more. Finally, the difference between the highest SBP group (whiskey) and the lowest SBP group (wine) was 2.8 mmHg, and the difference between the highest DBP group (sake) and the lowest DBP group (other) was 1.3 mmHg.

The prevalence of 'high-normal blood pressure or greater' and hypertension among drinkers was 25.2% ($n=643$) and 13.0% ($n=331$), respectively. Table 4 shows the results of a logistic regression analysis. In model 1, in which we adjusted for age, the *Shochu* group showed a significant positive association with 'high-normal blood pressure or greater', with an odds ratio (OR) of 1.85 (95% confidence interval (95% CI); 1.43–2.41), compared with the beer group. There was no significant relation between any type of alcoholic beverage and hypertension, although the OR of the shochu

Table 4 Multivariate adjusted relative prevalence odds ratios and 95% CIs of the type of alcoholic beverage for 'high-normal blood pressure or greater' and hypertension[a] in drinkers (*N*=2553)

Type of alcoholic beverage	*High-normal blood pressure or greater (N=643)*		*Hypertension (N=331)*	
	Odd ratio (95% CI)	*P-values*	*Odd ratio (95% CI)*	*P-values*
Model 1 (age-adjusted[b])				
Beer	1.00 (reference)		1.00 (reference)	
Sake	0.93 (0.60, 1.43)	0.727	0.99 (0.58, 1.69)	0.982
Shochu	1.85 (1.43, 2.41)	0.000	1.34 (0.96, 1.88)	0.086
Whisky	1.31 (0.76, 2.26)	0.328	0.86 (0.40, 1.84)	0.696
Wine	1.15 (0.59, 2.23)	0.684	0.50 (0.16, 1.63)	0.249
Other	1.17 (0.94, 1.46)	0.168	1.13 (0.86, 1.51)	0.371
Model 2 (age and amount of alcohol consumption adjusted[b])				
Beer	1.00 (reference)		1.00 (reference)	
Sake	0.80 (0.51, 1.25)	0.33	0.88 (0.51, 1.51)	0.64
Shochu	1.43 (1.06, 1.95)	0.02	1.08 (0.73, 1.60)	0.71
Whisky	1.18 (0.68, 2.04)	0.56	0.78 (0.36, 1.69)	0.53
Wine	1.11 (0.57, 2.16)	0.76	0.49 (0.15, 1.59)	0.23
Other	1.01 (0.79, 1.28)	0.95	1.00 (0.74, 1.36)	1.00
Model3 (age, amount of alcohol consumption, BMI, sodium a potassium excretion adjusted[b])				
Beer	1.00 (reference)		1.00 (reference)	
Sake	0.88 (0.55, 1.41)	0.60	0.97 (0.55, 1.70)	0.91
Shochu	1.27 (0.92, 1.76)	0.14	0.95 (0.63, 1.43)	0.82
Whisky	1.17 (0.66, 2.07)	0.57	0.77 (0.35, 1.69)	0.52
Wine	1.16 (0.57, 2.36)	0.68	0.47 (0.14, 1.56)	0.22
Other	0.98 (0.77, 1.27)	0.90	0.98 (0.71, 1.34)	0.88

[a]Hypertension was defined as ⩾140 mmHg in SBP and/or ⩾90 mmHg in DBP, and 'high-normal blood pressure or greater' was defined as ⩾130 mmHg in SBP and/or ⩾85 mmHg in DBP.
[b]Adjusted by the logistic regression analysis (including hypertension).

group was of borderline significance (OR 1.34, 95% CI 0.96–1.88, $P=0.086$). In model 2, in which we adjusted for alcohol consumption, the shochu group still exhibited a significant positive association with 'high-normal blood pressure or greater' (OR 1.43, 95% CI 1.06–1.95). However, in model 3, a logistic regression analysis adding adjustments for BMI, and sodium and potassium excretion resulted in a loss of the significant difference of the shochu group. These results did not substantially differ once we excluded three companies (A, F and J) that did not have a significant association of alcohol consumption with SBP and/or DBP in a linear regression analysis.

Discussion

The present study of middle-aged Japanese workers demonstrated that both SBP and DBP were different according to the type of alcoholic beverage that was mainly consumed. The *Shochu* drinker group presented the highest SBP and DBP, and the highest prevalence of 'high-normal blood pressure or greater'. However, adjustments for confounding factors including total alcohol consumption, BMI, urinary sodium and potassium excretion resulted in the disappearance of any significance.

Potential mechanisms by which moderate ethanol intake might reduce the incidence of cardiovascular disease have previously been reported.[14,26–29] Alcohol intake has been associated with elevated serum high-density lipoprotein (HDL) cholesterol,[14,28] as well as reductions in blood clotting factors,[27] platelet aggregation,[28] and insulin resistance.[29] Some studies have demonstrated a more beneficial effect for wine than for other alcoholic beverages.[17,18] For example, Ruidavets *et al*[18] suggested that wine drinkers had better blood lipid profiles than nonwine drinkers . However, most researchers have suggested that the benefit of wine intake was due to the advantageous lifestyle characteristics related to wine drinking.[15–17] There is not sufficient evidence to support the contention that the type of alcoholic beverage *per se* has any effect on cardiovascular risk factors or the development of cardiovascular disease.[30,31]

Japanese lifestyle, particularly dietary habits, has changed dramatically in the past four decades. Traditional Japanese food is low in fat and high in salt. However, the Japanese diet increasingly resembles the Western diet.[32] Although the incidence of stroke has remarkably decreased following advances in the control of hypertension,[33–35] hypertension is still the most important cardiovascular risk factor in Japan.[36] However, there have been few studies in Japan focusing on the difference in blood pressure with respect to the type of alcoholic beverage consumed. Kitamura *et al*[5] reported that drinkers who consume mainly sake have a higher prevalence of hypertension than those consuming other

beverages. Takashima *et al*[8] reported that 'exclusively sake' drinkers exhibited higher SBP and DBP than those of 'exclusively beer' drinkers.

However, neither of these studies included information on urinary sodium or potassium excretion. In the present study, shochu drinkers had the highest total alcohol consumption, body mass index and urinary sodium excretion. These factors may explain the highest blood pressure and the highest prevalence of 'high-normal blood pressure or greater' in the shochu group in the crude analysis.

We observed the lowest SBP and DBP in the wine group; however, the differences did not reach statistical significance after adjusting for confounding factors. Furthermore, because the prevalence of wine drinkers was very small in this population ($n=50$, 2% of drinkers), wine consumption is not thought to play an important role concerning the development of cardiovascular disease in the Japanese population, which has a markedly lower coronary mortality rate than Western populations.[37]

There are some limitations in the present study. The first is the issue of residual confounding factors affecting blood pressure. We do not adjust for the possible confounding effects of physical activity,[38] mental stress,[39] protein intake[40] or genetic factors.[22,41] The second is the use of a simple formula to estimate the urinary sodium and potassium excretion. However, this formula was validated based on the Intersalt study, a large, international study with 24-h urinary collection,[25,42] and is considered useful for estimating population mean levels of 24-h sodium and potassium excretion.[24] Finally, because most of the participants consumed many kinds of alcoholic beverages, we had to classify them according to the type of alcoholic beverage consumed, which provided two-thirds of their ethanol intake. Therefore, our results do not indicate a pure effect for each type of alcoholic beverage.

In conclusion, there may be no discernible differences in the effects of popular types of Japanese alcoholic beverages on blood pressure. This result is consistent with the results of other epidemiologic or metabolic studies concerning the effects of different types of alcoholic beverages on blood pressure[43] or lipids.[14,30] To decrease blood pressures nationwide, it is important to reduce, or at least not to increase, alcohol consumption in the Japanese population, irrespective of the type of beverage consumed.

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Appendix

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ORIGINAL ARTICLE

The High-risk and Population Strategy for Occupational Health Promotion (HIPOP-OHP) study: study design and cardiovascular risk factors at the baseline survey

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In order to establish the methodology of a population strategy for improving cardiovascular risk factors, we have planned the High-risk and Population Strategy for Occupational Health Promotion Study (HIPOP-OHP study). This study is a nonrandomized control trial in approximately 6500 participants in six intervention and six control companies. Our population strategy is based on three factors, nutrition, physical activity, and smoking. For each factor, a researcher's working team was organized and has been supporting the intervention. A standardized method to obtain comparable data has also been established. In the baseline survey, urinary sodium excretion in male subjects was higher, and urinary potassium excretion was lower in both genders in the intervention group compared to the control group. The prevalence of hypertension for both genders was also higher in the intervention group. Male subjects in the intervention group had higher serum total cholesterol than controls, while high-density lipoprotein cholesterol was lower in both genders in the intervention group compared to the control group. These differences were reflected by our finding that the predicted relative risk of coronary heart disease for male subjects was significantly higher in the intervention group (relative risk, RR: 1.17; 95% confidence interval, 95% CI.: 1.09, 1.25) and significantly lower in the control group (RR: 0.93; 95% CI.: 0.89, 0.98) compared to a model Japanese population. Similar results were observed in the female subjects. Taken together, these findings indicate that it is possible to compare trends of predicted relative risk for coronary heart disease between two groups.
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Keywords: population strategy; high-risk strategy; blood pressure; cholesterol; smoking; intervention

Introduction

Lifestyle modification is an important method for controlling cardiovascular disease risk factors. Many studies have shown that intervention programs combined with health education result in clear improvement in these risk factors.[1–10] However, the majority of these studies incorporated high-risk strategies such as comprehensive intervention following risk factor screening of the study population. While high-risk strategy can be readily understood and strongly motivates subjects to change their behavior, it may not have a marked influence on subjects with low latent risk. As a result, these strategies may not significantly reduce overall

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cardiovascular risk in the population. In order to effectively reduce a specific disease in a population, it is useful to shift the distribution of its risk factors towards the low-risk side, even if this shift is minimal.[11,12] For example, Stamler *et al*[13] found that a mean reduction in systolic blood pressure (SBP) of 2.2 mmHg in middle-aged subjects was associated with a 4% reduction in the risk of coronary death and a 6% lower risk of stroke death. These findings demonstrate that population-based strategy, involving intervention in a large number of low-risk subjects, is effective for reducing risk in the whole population.[14–16]

The majority of trials that have attempted to improve cardiovascular risk factors by population strategy in communities[17–23] or in worksites[24] have been carried out in Western populations. Accordingly, in 1998 we initiated the High-risk and Population Strategy for Occupational Health Promotion study (HIPOP-OHP study[25]) that incorporated a program for improving cardiovascular risk factors at workplaces. In this report, the study design of this intervention study is described, and the baseline data of the intervention and control groups are compared using predicted risk assessment analyses.

Materials and methods

Study population

Companies participating in our study were recruited from throughout Japan. The companies were divided into an intervention group, in which the environment was improved based on a population strategy in addition to individual intervention, and a control group that was provided with only the individual intervention teaching material. Initially we planned to allocate the companies randomly to the intervention or control groups. However, as some companies were forced to withdraw from the study either because of bankruptcy, or opposition from board members regarding participation in the study, we eventually modified the first allocation based on the hope that each company would comply with the aims and conditions of the study.

There were six companies in each group. The intervention group consisted of Companies A–F with Company A, the headquarters office of a life insurance company in Tokyo; Company D, factory of chemical products and other companies, electrical appliance manufacturers. Company C was located in the Kanto area in east Japan, while the other four companies were located in west Japan either in the Kinki (Companies D, E, and F) or Hokuriku areas (Company B). The control group consisted of Companies H–L. Company H was a chemical company factory in Tokyo, while four companies were factories of electrical appliance manufacturers, with Companies G and K being located in the Kanto area and Companies I and J in the Hokuriku area. Company L was a research laboratory of an electrical appliance manufacturer in the Kinki area in West Japan. Initially we had planned to recruit for the study from invited companies with less than 1000 workers. However, since Companies A, C, G, and H had more than 1000 workers, the number of workers selected for evaluation in these companies was reduced to about 500–1000, either by random sampling (Companies A and H) or by limiting the sections involved (Companies C and G). Of the 7226 workers who underwent a baseline survey in 1999 or 2000, those aged 56 years or older were excluded as they would have reached the retirement age of 60 years old before the end of the intervention study. The final number of participants included in this study was 6589 with all participants scheduled to have annual blood pressure measurements and approximately half of the study group, mainly aged 40 years or older, scheduled to have a blood sample collected each year.

The original sample size estimate of 1500 in each group provided the study with 80% power to detect a 1.5 mmHg decrease in SBP or a 1.0 mmHg decrease in diastolic blood pressure (DBP) in the intervention group compared with the control group. This power analysis was calculated using a two-sided test with the probability level (α) being set at 0.05 and s.d. of 15.0 and 10.0 for SBP and DBP, respectively. This magnitude of blood pressure reduction was comparable to about half of that observed in an earlier 6-month intervention trial in Japanese subjects with mild to moderate hypertension.[26] This number of participants in our study was considered to be sufficient to also detect differences between the two groups for both total cholesterol reduction and the prevalence of smoking.

Intervention methods

The intervention plan for this study is shown in Table 1. For the high-risk strategy, individual guidance is given for 6 months to subjects with either high-normal or greater blood pressure levels, hypercholesterolemia, or impaired glucose tolerance. This guidance is given by nurses or public health nurses hired by each enterprise, with the research group supporting the nurses by providing expert knowledge. The population strategy for health promotion consisted of three factors, nutrition, physical activity, and smoking. For each of these factors, a working team of researchers was organized with the researchers in charge of each company making contact with the three specialist groups in order to plan the necessary interventions. After health assessment of each population, information on the diseases and skills for lifestyle modification were provided. Posters and stand-type Point of Purchase advertising menus (POP menus) were placed on the tables of the workplace dining rooms. In addition, intraworkplace web-sites were utilized, with events with health-related themes

being organized. With regard to nutrition, the contents of dishes in the workplace dining rooms and box lunches delivered by caterers were evaluated, followed by recommendations for improving the amount of sodium and potassium intake, nutritional balance, and caloric intake from fat. For physical activity, walking paths were constructed or walking maps prepared. An 'Active Point Campaign' using pedometers is to be carried out twice a year in order to promote individual and departmental competition and increase physical activity in the workers. In order to promote smoking cessation, designated smoking areas have been established based on the advice of the specialist team. These interventions are to be performed in 6 monthly cycles.

Informed consent was obtained from the participants regarding individual guidance for the high-risk strategy. The Safety Hygiene Committee in each company examined the plan and ethical problems in the population strategy every month. Approval for this study was obtained from the Institutional Review Board of Shiga University of Medical Science for Ethical Issues (Nos. 10–16).

Data collection and standardization

Biological data are collected at the time of annual health check-ups in accordance with the 'Law for workers' safety and health'. The parameters include blood pressure, and the serum levels of total and HDL cholesterol and plasma level of glucose, all of which are measured at the regular health check-ups. A spot urine sample for every participant was also collected for the determination of daily sodium and potassium excretion.[27] Evaluation of drinking, smoking, diet, stress, and physical activity was carried out by a standardised questionnaire produced by the researchers. Self-reported lost work days due to disease within the last year were also recorded for each participant.

In addition, 2% of the workers were selected randomly for a nutritional survey performed using the 24-h recall method, as described in the INTERMAP, an international collaborative study.[28] In total, 10% of the workers were also selected to carry pedometers (J-MANPO EM-700, Yamasa), in order to count the number of steps during a 1-week period.

Blood pressure was measured in duplicate after the subjects had rested for 5-min using the same newly calibrated automatic sphygmomanometer at each company (Nippon Colin, BP-103iII) with the mean value being used in the analyses. Company L did not use this type of sphygmomanometer. For the measurement of lipids, general laboratories to which blood examination was entrusted by each company were standardized through the US Cholesterol Reference Method Laboratory Network (CRMLN).[29]

Risk assessment and statistical analysis

For comparison of risk factors between the two groups, age was compared by the *t*-test, while the mean values of the other factors, adjusted for age, were compared using analysis of covariance.

The risk of coronary heart disease based on baseline data was used as the risk assessment parameter. Although the Framingham scale is used often for assessing coronary heart disease risk, there are controversies as to whether it is applicable for use in non-Western populations.[30] The study by Kitamura *et al*[31] remains the only prospective study on the development of coronary heart disease in a Japanese worksite population. This study followed 6408 workers in Osaka for a period of 7.7 years.

The relative risk for each cardiovascular risk factor was determined using a Cox proportional hazard model, and the value of β (beta) for each risk factor was calculated. The value of β for the development of coronary heart disease was then applied to each individual in the study. This calculation incorporated SBP, total and HDL cholesterol, and the number of cigarettes smoked per day, as these factors have been shown by Kitamura *et al*[31] to be associated significantly with the development of coronary heart disease.[32] The National Survey on Circulatory Disorders 2000, Summary June 2001.[33] was used to obtain the following mean values for each gender in the age group 30–59 years that were used to construct a model for calculating individual relative risk. Male subjects: SBP 127 mmHg, total cholesterol 199 mg/dl, HDL cholesterol 53 mg/dl; Female subjects: SBP 119 mmHg, total cholesterol 188 mg/dl, HDL cholesterol 63 mg/dl. The number of cigarettes in the model group was assumed to be zero. The relative risk of coronary heart disease in individuals (Rm for male and Rf for female subjects) was calculated from the SBP (SBPi), total cholesterol (TCi), HDL cholesterol (HDLi), and the number of cigarettes smoked (SMi) using the following equations.

$$\text{Male subjects}: Rm = \exp(0.017(SBPi - 127) + 0.019(TCi - 199) - 0.058(HDLi - 53) + 0.02 \times Smi)$$

$$\text{Female subjects}: Rf = \exp(0.017(SBPi - 119) + 0.019(TCi - 188) - 0.058(HDLi - 63) + 0.02 \times Smi)$$

Rm and Rf were then transformed logarithmically and the mean values calculated. A *t*-test was used to compare one sample with the case with the constant assumed to be 0, that is, the relative risk is the same as that in the model group (=1.00). The log-transformed mean values of Rm and Rf in the two

Table 1 Initial plans for intervention in the High Risk and Population Strategy for Occupational Health Promotion study (HIPOP-OHP study)

Contents			
High-risk strategy Individual counselling	*Population strategy*		
	Nutrition	*Physical activity*	*Smoking*
Standardized face to face health guidance, five times during 6 months *Recruiting criteria* (1) High-normal or greater blood pressure level SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg and/or taking antihypertensive agents (2) Hypercholesterolemia Total Cholesterol ≥ 5.69 mmol/l (220 mg/dl) and/or taking lipid-lowering agents (3) Impaired glucose tolerance Fasting blood glucose ≥ 6.11 mmol/l (110 mg/dl) or nonfasting blood glucose ≥ 6.66 mmol/l (120 mg/dl) and/or taking antidiabetic agents	*Assessment* (1) Knowledge (2) Dietary habits (3) Nutritional intake (4) Urinary electrolyte excretion (5) Alcohol intake (6) Dining room in or near the workplace (7) Grocery store in or near the workplace (7) Vending machine for beverages in the workplace (8) History of health promotion	*Assessment* (1) Knowledge (2) Physical activity (3) Number of steps per week (4) Past and present history of sports (5) Gymnasium in or near the workplaces (6) Athletic field in or near the workplaces (7) Sports circle in or near the workplaces (8) History of health promotion	*Assessment* (1) Knowledge (2) Number of smokers (3) Number of cigarettes per day of smokers (4) Past and present history of smoking (5) Awareness for smoking cessation (6) Designation of smoking areas (7) Tobacco store in or near the workplaces (8) Vending machine for tobacco in or near the workplaces
	Interventional method 1. Presenting information for a healthy diet (1) Stand-type mini-poster presentation the table weekly: Pop menu 'Point Purchase advertising menu' Poster on the wall Web-site Intraworkplace newspaper	*Interventional method* Presenting information for physical activity (1) Stand-type mini-poster presentation on the table weekly: Pop Menu 'Point Of Purchase advertising menu' Poster on the wall Web-site Intraworkplace newspaper	*Interventional method* 1. Presenting information for smoking cessation (1) Poster on the wall (seasonal) (2) Web-site (3) Intraworkplace newspaper
	Intervention for the dining room in the workplace (1) Assesment of salt concentration of miso soup Change for soy sauce serving Use of low-calorie salad dressing Serving of healthy menu Disclosure of nutrition balance of the menu	Campaign for increasing physical activity (1) Self-recorded diary for physical activity 'active point campaign' Lecture of 'active walking' Lecture of 'stretching' Sport event in the workplaces	2. Antismoking campaign (1) Recruiting for smoking cessation program, smoking cessation program done by clerical staff 'without nicotine replacement' 'with nicotine gum' smoking cessation program done by medical staff 'with nicotine patch' (2) Lecture of 'stop smoking' (3) Lecture of 'promotion of smoking area designation' for managerial workers
	Inspection of total sales for beverages (1) Grocery store in the workplace (2) Vending machine in the workplace	Installment of places or tools for walking (1) Path construction for walking in the workplaces (2) Making maps for walking in or near the workplaces (3) Distribution of pedometer to all workers	3. Advise for the reconstruction for promotion of smoking area designation
	4. Intervention for the household (1) Health education for the person who cooks (2) Presentation of health menu for the household		4. Inspection of the designation of smoking areas

groups were also compared. The blood glucose level was not included in this model as it had not been included in the study in which the values of β had been calculated. In addition, the extra number of coronary events predicted to occur in the next 20 years compared to the model group was calculated, as this was approximately equal to the mean period before retirement in the study population. We assumed that the coronary event rate in the model group was 0.94 per 1000 person-years.[31]

In this study, as 10 of the 12 workplaces were factories, we calculated the predicted relative risks by using the data of all 12 companies and also the data of 10 companies with companies A (intervention group) and L (control group) being excluded from this latter analysis.

All probability values were two-tailed and all confidence intervals were estimated at the 95% level. The statistical Package for Social Sciences (SPSS Japan Inc. version 10.0J, Tokyo, Japan) was used for the analyses.

Results

Analysis of the data of all the participants ($N=6589$) showed no significant difference in age-adjusted SBP between the intervention and control groups in both genders (118. 8 *vs* 118.4 mmHg for male and 109.0 mmHg *vs* 107.9 mmHg for female subjects, respectively). There was also no difference in age-adjusted DBP between the two groups (72.4 *vs* 72.5 mmHg for male and 65.0 *vs* 65.3 mmHg for female subjects, respectively).

Table 2 compares the risk characteristics between the two groups in 3810 male and 794 female subjects from whom blood samples were obtained. No difference was observed between the two groups for both genders for BMI, SBP, DBP, or the prevalence of subjects taking antihypertensive agents. In the male subjects, the intervention group had higher total cholesterol and urinary sodium excretion, lower HDL cholesterol level and potassium excretion, and a higher prevalence of subjects with either hypertension, hypercholesterolemia, low serum HDL cholesterol, or impaired glucose tolerance, compared with the control group. In the female subjects, the intervention group had lower HDL cholesterol levels and potassium excretion and a higher prevalence of subjects with either hypertension, low serum HDL cholesterol, or impaired glucose tolerance than the control group.

Table 3 summarizes the status of drinking, smoking, and lost workdays due to disease within the last year in subjects without missing values in the questionnaire. This table also shows the mean number of steps per day and results of the nutritional survey in the randomly selected subjects. The prevalence of subjects who drank daily was lower in the intervention group in both genders, while no difference was observed in the other risk characteristics between the two groups.

A comparison of risk factors at the baseline survey, predicted relative risks, and extra numbers of coronary events are listed in Table 4. Subjects

Table 2 Age and age-adjusted means and prevalences of risk characteristics [a]at the baseline survey in subjects [b]with blood examination up to 55 years

	Male subjects			*Female subjects*		
Risk characteristics	*Intervention*	*Control*	*Significance*	*Intervention*	*Control*	*Significance*
Number	1341	2469		362	432	
Age (years)	41.7 (8.65)	39.8 (8.95)	**	42.6 (8.74)	40.9 (8.68)	NS
Body mass index (kg/m^2)	23.2 (0.08)	23.1 (0.06)	NS	22.2 (0.19)	21.9 (0.18)	NS
Systolic blood pressure (mmHg)	118.3 (0.44)	119.2 (0.32)	NS	112.2 (0.87)	111.0 (0.80)	NS
Diastolic blood pressure (mmHg)	73.1 (0.30)	73.6 (0.22)	NS	67.6 (0.57)	67.2 (0.52)	NS
Urinary sodium excretion (mmol/day)	157.3 (1.01)	152.2 (0.75)	***	151.8 (0.18)	148.8 (1.64)	NS
Urinary potassium (K) excretion (mmol/day)	42.7 (0.24)	43.4 (0.18)	*	39.5 (0.44)	43.7 (0.41)	***
Total cholesterol (mmol/l)	5.13 (0.02)	5.05 (0.02)	**	5.06 (0.04)	5.00 (0.04)	NS
HDL cholesterol (mmol/l)	1.40 (0.01)	1.45 (0.01)	***	1.68 (0.02)	1.74 (0.02)	**
Subjects taking antihypertensive agents (%)	4.0	3.3	NS	3.0	2.8	NS
Subjects taking antihypertensive agents (%)	2.6	2.1	NS	2.5	4.2	NS
Subjects taking antidiabetic agents (%)	1.1	1.2	NS	1.2	0.3	NS
High-normal or greater blood pressure level[c] (%)	26.8	25.3	NS	17.7	13.4	NS
Hypertension[c] (%)	16.5	14.2	*	12.4	7.4	*
Hypercholesterolemia[c] (%)	27.7	24.4	*	26.8	22.5	NS
Low serum HDL cholesterol[c] (%)	13.4	7.4	***	3.6	0.5	**
Imparied glucose tolerance[c] (%)	13.1	6.5	***	9.1	2.5	***

NS, not significant; *$P<0.05$, **$P<0.01$, ***$P<0.001$.
[a]The numbers in parentheses are standard deviation (s.d.) for age and standard error (s.e.) for other variables.
[b]No subject had a past history of coronary heart disease and/or stroke.
[c]Hypertension was defined as SBP$\geq$140 mmHg, DBP$\geq$90 mmHg, use of antihypertensive agents, or any combination of these.
Low serum high-density lipoprotein (HDL) cholesterol was defined as an HDL cholesterol level $<$1.03 mmol/l (40 mg/dl).
High-normal or greater blood pressure level, hypercholesteroleamia and impaired glucose tolerance are defined as in Table 1.

Table 3 Age and age-adjusted means and prevalences of lifestyle-related factors and lost workdays within the last year at the baseline survey

Risk characteristics	*Male subjects*			*Female subjects*		
	Intervention	*Control*	*Significance*	*Intervention*	*Control*	*Significance*
Number	1908	2666		612	586	
Age (years)	37.1 (9.00)	38.4 (8.70)	***	35.9 (9.90)	38.5 (8.40)	***
Drinking						
Daily drinker (%)	56.7	60.8	**	19.0	24.7	**
Daily intake of alcohol (g/day)[a]	23.2 (0.72)	22.0 (0.61)	NS	3.5 (0.45)	4.2 (0.46)	NS
Heavy drinker (%)[a], >46g/day	18.3	17.8	NS	1.6	1.4	NS
Smoking						
Current smoker (%)	54.4	53.2		10.6	7.0	
Exsmoker (%)	16.7	17.6	NS	4.9	4.1	NS
Never-smoker (%)	28.9	29.3		84.5	88.9	
Heavy smoker (%)[a], >20 cigarettes/day	14.5	13.2	NS	0.7	0.3	NS
Lost workdays due to disease within last year (days)	1.57 (0.01)	1.55 (0.01)	NS	1.57 (0.02)	1.63 (0.02)	NS
Subjects from random sampling						
Walking measured by pedometer for 1 week						
Number of subjects (10% from whole subjects)	252	339		90	70	
Steps per day	9702 (197)	9352 (170)	NS	8875 (292)	8607 (332)	NS
24-h recall nutrition survey						
Number of subjects (2% from whole subjects)	35	46		7	11	
% Fat energy	25.1	26.2	NS	28.2	28.0	
Saturated fat (g/day)[b]	(8.4)	16.4 (7.4)	NS	14.8 (7.1)	15.7 (6.4)	
Polyunsaturated fat (g/day)[b]	(8.4)	18.0 (7.7)	NS	15.0 (7.5)	12.2 (3.6)	

NS; not significant, $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$.
[a]Intake of alcohol, heavy drinkers, and heavy smokers are means or prevalence for all subjects combined.
[b]Crude mean, the age-adjusted mean could not be calculated because of the small number of the subjects.

were included in these analyses only if they had complete data for SBP, total and HDL cholesterol, and number of cigarettes per day. No difference was observed in SBP or the number of cigarettes smoked per day between the two groups. However, the total cholesterol level was higher, and the HDL cholesterol level lower in the intervention group compared to the control group for both genders. In the male subjects, the predicted relative risk for coronary heart disease was significantly higher in the intervention group (relative risk 1.17, 95% confidence interval 1.09–1.25) and significantly lower in the control group (relative risk 0.93, 95% confidence interval 0.89–0.98) than in the model Japanese population. This finding suggested that the intervention group was a high-risk group compared with the control group. The predicted extra number of coronary events in the next 20 years compared to the model population was 3.6 in the intervention group and −2.9 in the control group.

In the female subjects, the relative risk for coronary heart disease was significantly lower in the control group (relative risk 0.77, 95% confidence interval 0.70–0.85) than in the model group. The predicted extra number of coronary events in the next 20 years compared to the model population was 0.2 in the intervention group and −1.7 in the control group.

In the male subjects, a small decrease equivalent to one tenth of the s.d. in SBP and total cholesterol, a reduction in the number of cigarettes smoked per day, and a small increase in HDL cholesterol were predicted to effectively reduce the relative risk for coronary heart disease. For example, when all four risk factors were assumed to have improved by one tenth of a s.d. in the intervention group, the predicted relative risk decreased to 0.94, a value similar to that found in the control group (0.93). In the female subjects, when all four risk factors were assumed to be improved by one tenth of a s.d., the predicted relative risk decreased to 0.86, although it was still higher than that in the control group (0.77).

These results did not change substantially when company L was excluded from the analyses, for the reason that it had used a different automatic sphygmomanometer for blood pressure measurements. There was also no change when the two nonfactory populations, companies A and L, were excluded from the analyses.

Discussion

There is no doubt regarding the importance of population strategy for controlling lifestyle-related diseases.[11,12] In Japan, preventive strategies for

Table 4 Predicted relative risk for coronary heart disease according to increase or decrease of each mean value of coronary risk factors in the intervention and control groups compared to Japanese model population

	Male subjects				*Female subjects*			
	Intervention		*Control*	*Significance*	*Intervention*		*Control*	*Significance*
Number	1129		2184		318		398	
Risk characteristics	Means	s.d.	s.d.		Means	s.d.	s.d.	
Age (years)	41.3	8.7	9.0	***	42.2	8.8	8.7	*
Systolic blood pressure (SBP) (mmHg)	118.4	17.1	15.3	NS	112.8	18.4	16.3	NS
Total cholesterol (TC) (mmol/l)	5.16	0.89	0.87	***	5.08	0.85	0.87	NS
HDL cholesterol (HDLC) (mmol/l)	1.40	0.36	0.34	***	1.65	0.37	0.36	***
Number of cigarettes per day (Smoking)[a]	11.9	12.9	11.7	NS	1.0	3.8	3.6	NS

	Relative risk	*Predicted extra number of coronary events*[c]	*Relative risk*	*Predicted extra number of coronary events*[c]	*Relative risk*	*Predicted extra number of coronary events*[c]	*Relative risk*	*Predicted extra number of coronary events*[c]
Risk for coronary incidence predicted by means of β for each subject[b] (95% confidence inerval of estimated relative risk)	1.17 (1.09, 1.25)	3.6	0.93 (0.89, 0.98)	−2.9	1.04 (0.93, 1.17)	0.2	0.77 (0.70, 0.85)	−1.7
Recalculated risks for 0.1 s.d. increase or decrease of each variables								
SBP, 0.1 s.d. decrease, 1.7 mmHg for males and 1.8 mmHg for female subjects, recalculated risks	1.14	3.0			1.01	0.1		
TC, 0.1 s.d. decrease, 0.089 mmol/l for males and 0.085 mmol/l for female subjects, recalculated risks	1.09	1.9			0.98	−0.1		
HDLC, 0.1 s.d. increase, 0.036 mmol/l/dl for males and 0.037 mmol/l for female subject, recalculated risks[d]	1.08	1.7			0.95	−0.3		
Smoking[b], 0.1 s.d. decrease, 1.3 cigarette/day for males and 0.4 cigarette/day for female subjects, recalculated risks[d]	1.13	2.8			1.03	0.2		
Every four risk factors above combined, recalculated risks[d]	0.94	−1.3			0.86	−0.8		

NS not significant, $*P<0.05$, $**P<0.01$, $*P<0.001$.
The numbers in parentheses are standard deviation (s.d.).
The mean values of cardiovascular risk factor in the Japanese model population were as follows. Male subjects: systolic blood pressure, 127 mmHg; total cholesterol, 199 mg/dl; and HDL cholesterol, 53 mg/dl. Female subjects: systolic blood pressure, 119 mmHg; total cholesterol, 188 mg/dl; and HDL cholesterol, 63 mg/dl. The number of cigarettes per day in the model group was assumed to be zero.
[a]Number of cigarettes smoked per day are means for all subjects combined.
[b]Relative risk compared with that of the Japanese model population (=1.00).
[c]Predicted extra number of coronary events in the next 20 years.
[d]The relative risk for coronary morbidity was calculated after assuming 0.1 s.d. decrease or increase (for HDLC) of each risk factor.

lifestyle-related diseases started with the early detection of patients with gastric cancer[34] or severe hypertension,[35] with the detection of high-risk individuals playing a major role in these strategies. Some areas have attempted to control hypertension by cooperation between researchers, local municipalities, and residents and have achieved excellent results.[23,36] However, several have not been as successful with promotions of population strategy remaining unpopular in Japan.

There have been a number of community trials in Western populations. Several of these studies have shown the difficulty of inducing individuals to change their behavior by providing only information about health promotion.[19,20,24] For example, in the British population of European collaborative trial of multifactorial prevention of coronary heart disease, which included both high-risk and population strategies, Rose *et al*[37] reported a disappointing low response to mass advice using posters, evening meetings, film shows, and question-and-answer sessions. The specific features of population strategy that are optimal but difficult to put into practice[38] have been described in earlier studies. To solve these problems, the North Karelia Project attempted to change the form of the agriculture and livestock industry by improving the marketing system of the food supply in addition to presenting information on these changes.[21,22] In the present study, the main method of intervention was to attempt to induce individuals to change their behavior by wide circulation of information. We also attempted to make specific environmental changes such as decreasing sodium content in food and constructing pathways for walking. The effect of our intervention study will be influenced strongly by the personal response to the information presented. Therefore, it remains important in the present study that effective methods are developed for presenting information to induce individuals to change their behavior.

In intervention studies using individuals, differences are homogenized by randomization and an adequate sample size. However, if workers in the same population are divided randomly, although homogenous groups are obtained, the effects of the population strategy are not limited to the participants in whom intervention is attempted. For this reason, we planned to construct paired intervention and control groups and then allocate them randomly. However, we were not able to implement the plan for nonscientific reasons and therefore the predicted risk for coronary heart disease differed between the two groups due to the nonrandomized design of the study.

Not withstanding this limitation, we are planning to use the trend of predicted coronary risk observed in this study as a marker for assessing the effect of the interventions. This is a useful method for assessing the effect of short interventions that target multiple cardiovascular risk factors and do not use cardiovascular incidence and/or mortality as end points. In male subjects, the difference in predicted coronary risk between the two groups was negated by the combined effects of small changes (0.1 s.d.) in each risk factor. This feature will enable us to compare real changes in predicted coronary risk, even when there are differences in baseline risk between the two groups.

The intervention group in our study had higher mean urinary sodium excretion in male subjects and lower mean potassium excretion, and a higher prevalence of hypertension and a higher prevalence of impaired glucose tolerance compared with controls despite the mean levels of SBP and DBP being similar in the two groups. Consequently, we suspect that the difference in predicted risk between the two groups may be greater than that shown in Table 4, as the formula we used included only a limited number of risk factors. Our results do not reflect the difference in prevalence of hypertension and impaired glucose tolerance. Furthermore, the differences in urinary electrolytes excretion may be expected to be associated with increased blood pressure in the future.[39] Therefore, health promotion is required in the intervention group to reduce sodium intake and increase potassium intake despite these already being part of the population strategy.

In the present study, the risk of coronary heart disease was used as a parameter of risk assessment. Another major category of cardiovascular disease is stroke. The East Again Population study that included Japan showed that development of stroke was affected more by hypertension than by other risk factors.[40] Since the present study aimed to reduce cardiovascular risk by multiple risk factor intervention, the assessment of risk factors other than hypertension is also required. In addition, there have been no prospective studies on the incidence of stroke in the Japanese worksite population that have determined the relative risk of each risk factor. Furthermore, a cohort study of workers in Osaka[31] with a similar age range to that in our study showed the incidence of coronary heart disease was higher than stroke. Therefore, we consider it appropriate to use coronary artery disease risk as a parameter for assessing risk of cardiovascular disease.

There are some limitations in the present study. The first of these was establishing the required sample size. Unfortunately, as we did not have any data regarding the effect of population strategies in Japan, we had to set sample size based on the results of a 6-month intervention trial in Japanese subjects with mild to moderate hypertension.[26] Although we assumed that the decrease in blood pressure decrease would be about half that seen in this earlier study in high-risk participants, the effect of the intervention may be smaller than expected. We were, however, successful in collecting about twice the sample size (>6000) of that estimated during planning of the study (3000). This has provided the

study with stronger statistical power to detect small but important changes in risk factors.

Another limitation of this study was that Cox's regression equation for the development of coronary artery disease in male subjects was also applied to the data obtained from female subjects. This equation was used as there have been no prospective studies in female workers in Japan that have used the development of coronary heart disease as an end point.

Finally, there may be a kind of Hawthorne effect,[41] which results in 'groups that are willing to participate tending to have better results'. However, participation in this study was decided mainly by board members or the Safety Hygiene Committee in each company at the time of first recruitment irrespective of each employee's will or hope. Informed consent was obtained after the decision to participate in the study had been made and therefore we consider that the Hawthorne effect in the present study will be relatively minor.

This study involved many researchers cooperating with the staff in each company with the aim of improving cardiovascular risk factors based on high-risk and population strategy. Furthermore, because we can distinguish participants who are receiving individual counselling base on a high-risk strategy, we are able to clarify the benefits of a combined high-risk and population approach in individuals receiving both interventions, compared to those receiving the population strategy only. It will be interesting to learn whether or not the combined strategy was more effective than the population strategy alone.

Owing to the recent long recession in the Japanese economy, there has been a very tight budget for health promotion in workers. Lay-off of workers has involved even health medical workers who have hindered the intervention trial. However, these problems have been solved in this study, and at present the population strategy is being carried out in all the intervention companies. It is anticipated that the protocol developed in this study will contribute greatly to health promotion in Japan.

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Appendix

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Special Issue

Original Article

Methodological Issues for a Large-Scale Intervention Trial of Lifestyle Modification: Interim Assessment of the High-Risk and Population Strategy for Occupational Health Promotion (HIPOP-OHP) Study

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Abstract

Objective: To clarify the methodological issues for the High-risk and Population Strategy for Occupational Health Promotion Study (HIPOP-OHP study), which is a 4-year non-randomized control trial, an interim assessment of male participants was performed 3 years after the baseline survey.

Methods: We had approximately 2,500 and 4,000 participants in the intervention and control groups, respectively. The population measures and prevalence of risk factors at each year, and between the baseline and 4th examinations were compared between the two groups. The personal trends of returning participants who were in the study at the 1st and 4th examinations were also evaluated.

Results: During the 3 years, an increase in serum HDL cholesterol (2.7 mg/dl), and a reduction in the prevalence of hypertriglycemia detected with fasting blood samples (3.6%) and current smokers (5.4%) were observed in the intervention group. The mean HDL cholesterol level was significantly higher in the intervention group than in the control group at the 4th examination, reversed from the baseline survey. The serum non-HDL cholesterol level was significantly increased only in the control group. There was also a significant increase in the prevalence of hypertriglycemia and high plasma glucose detected with fasting blood samples in the control group. The return participation rate after 3 years was 72.2% for the intervention group and 74.9% for the control group. The above-mentioned changes for risk factors were mainly due to returning participants at each examination.

Conclusion: These interventional methods may be effective in improving overall cardiovascular risk factors in the population. However, the low return participation rate will dilute the effect of the intervention.

Key words: population strategy, intervention, interim assessment, return participation, cardiovascular risk factor

Introduction

Many intervention studies have shown successful results by clear improvements in cardiovascular risk factors (1–6). However, the majority of these studies targeted high-risk subjects who had at least moderate levels of cardiovascular risk factors. Because a high-risk strategy does not have a sufficient influence on subjects with low latent risk, it may not significantly reduce overall cardiovascular risk in the population. To effectively reduce a specific disease in a population, it is beneficial to shift the distribution of its risk factors towards the low-risk side (7). For example, a mean reduction in systolic blood pressure (SBP) of 2.2 mmHg in middle-aged subjects was

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associated with a 4% reduction in the risk of coronary death and a 6% lower risk of stroke death (8). These findings demonstrate that such population-based strategies involving intervention in a large number of low-risk subjects are effective in reducing risk in the whole population.

There have been a number of trials using a population strategy in Western populations (9–14). However, there have been few studies promoting a population strategy in Japan, except in some local municipalities (15,16). Accordingly, in 1998 we initiated the High-risk and Population Strategy for Occupational Health Promotion Study (HIPOP-OHP study), which incorporated a program with combined population and high-risk strategies for improving cardiovascular risk factors in workplaces (17–19). In this report, the results of an interim assessment of this intervention trial for male participants are described, and the methodological issues related to a large-scale intervention trial in worksite populations are discussed.

Methods

Study population

The details of this non-randomized control trial have been described elsewhere (17–19). Briefly, employee groups from 12 companies were divided into an intervention group (6 companies: A-F), in which the environment was improved based on a population strategy in addition to individual intervention (high-risk strategy), and a control group (6 companies: H-L) that was provided with only the individual intervention teaching material. We had 2,515 and 3,289 participants in the intervention and control groups, respectively, at the baseline survey conducted in 1999-2000. After the baseline survey, approximately 6,500 (2,500 for the intervention group and 4,000 for the control group) employees participated in this study every year.

Company A was the head office of a life insurance company, Companies D and H were factories of chemical companies, Company L was a research laboratory of an electrical appliance manufacturer, and the other eight companies were factories of electrical appliance manufacturers. The details of the intervention methods have been previously reported elsewhere (18,19). The population strategy for health promotion consists of 3 fields, i.e., nutrition, physical activity, and smoking. In each field, a researcher's working team was organized and has been handling intervention for its field. These interventions are planned to be performed in 6 monthly cycles over 4 years. As a high-risk strategy, individual health education programs of 6 months were provided for any participants with high-normal or greater blood pressure levels, hypercholesterolemia, or high plasma glucose.

Informed consent was obtained from the participants regarding individual guidance for the high-risk strategy. The safety hygiene committee in each company examined the plan and ethical problems in the population strategy every month. Approval for this study was obtained from the Institutional Review Board of Shiga University of Medical Science for Ethical Issues (No. 10–16).

Data collection and standardization

Biological data were collected at the time of annual health check-ups. A spot urine sample for every participant was also collected for determination of daily sodium and potassium excretion (20). Blood pressure was measured in duplicate after the participants had rested for 5 minutes using the same newly calibrated automatic sphygmomanometer at each company (Nippon Colin, BP-103iII), with the mean value being used in the analyses. For the measurement of lipids, general laboratories to which blood examination was entrusted by each company were standardized through the US Cholesterol Reference Method Laboratory Network (CRMLN) controlled by the CDC (Centers for Disease Control and Prevention, Atlanta) (21).

We did not use mean values of LDL (low-density lipoprotein) cholesterol, serum triglyceride or plasma glucose because about one-third of the participants did not have their fasting blood samples collected. Accordingly, we used the mean level of non-HDL (high-density lipoprotein) cholesterol (serum total cholesterol–serum HDL cholesterol), or the prevalence of hypertriglycemia and high plasma glucose as assessment variables. Hypertriglycemia was defined as a fasting serum triglyceride of 150 mg/dl (1.69 mmol/L) or higher, or a non-fasting serum triglyceride of 200 mg/dl (2.26 mmol/L) or higher, and high plasma glucose was defined as a fasting plasma glucose of 110 mg/dl (6.11 mmol/L) or higher, or a non-fasting plasma glucose of 120 mg/dl (6.66 mmol/L) or higher. "Fasting" was defined as at least 8 hours passing since the subject's previous meal. Evaluation of smoking habits was carried out using a standardized questionnaire produced by the researchers.

Statistical analysis

In this study, we performed an interim assessment of this intervention trial. The trends for main cardiovascular risk factors during the 3 years after the baseline survey were analyzed. For comparison of risk factors between the intervention and the control group at each year, and for population differences between baseline characteristics and findings after 3 years, unpaired t-tests or chi-square tests were used. We defined a person who participated in both the 1st and 4th examinations as a returning participant. The changes in returning participants between the 1st and 4th examinations were analyzed by paired t-tests or McNemar tests. Concerning the comparison of returning participant change for the prevalence of each risk factor between the two groups, Mann-Whitney U tests were used after we defined the change into three categories: getting worse=1, no change=2, improving=3.

The Statistical Package for Social Sciences (SPSS Japan Inc. version 11.0J, Tokyo, Japan) was used for the analyses. All probability values were two-tailed and all statistical tests were considered to be significant with a probability value of less than 0.05.

Results

Table 1 shows the risk characteristics between the intervention group and the control group during the 3 years. No difference was observed between the two groups in age, SBP, diastolic blood pressure (DBP), body mass index (BMI) or the prevalence of current smokers in the 1st examination (baseline survey). However, the intervention group had higher non-HDL

Table 1 Trend for major risk characteristics in the surveyed population during 3 years, males

Risk characteristics	Group	1st examination (baseline) N	Mean or Prevalence	SD	P-value between two groups	2nd examination (after 1 year) N	Mean or Prevalence	SD	P-value between two groups	3rd examination (after 2 years) N	Mean or Prevalence	SD	P-value between two groups	4th examination (after 3 years) N	Mean or Prevalence	SD	P-value between two groups	
Age, years	Intervention	2,515	39.4	10.1	0.439	2,493	40.1	10.0	0.137	2,465	39.8	9.9	0.644	2,413	40.4	9.4	0.747	0.001
	Control	3,289	39.6	9.4		4,218	39.7	9.9		4,024	39.7	9.7		3,960	40.3	9.5		0.002
Systolic blood pressure, mmHg	Intervention	2,512	119.0	16.5	0.601	2,436	119.0	16.4	0.829	2,400	120.1	16.1	0.019	2,292	119.5	16.2	0.166	0.290
	Control	3,193	118.8	15.2		4,163	118.9	15.6		3,985	119.1	15.4		3,890	119.0	15.6		0.693
Diastolic blood pressure, mmHg	Intervention	2,512	72.5	11.4	0.180	2,436	72.7	11.6	0.729	2,400	73.8	11.5	0.034	2,292	73.5	11.7	0.002	0.002
	Control	3,193	72.9	11.1		4,163	72.8	11.5		3,985	73.2	11.4		3,890	72.6	11.6		0.215
Non-HDL cholesterol †, mg/dl	Intervention	1,589	145.7	35.2	<0.001	1,830	145.3	36.2	<0.001	1,629	147.7	36.8	<0.001	1,633	145.4	36.6	0.030	0.814
	Control	2,642	139.2	35.9		3,396	139.6	36.4		3,247	142.4	35.7		3,184	143.0	35.7		<0.001
HDL cholesterol, mg/dl	Intervention	1,589	54.1	14.4	<0.001	1,830	54.6	14.3	<0.001	1,629	55.1	14.2	0.579	1,633	56.8	14.5	0.009	<0.001
	Control	2,642	56.1	13.1		3,396	56.8	13.4		3,247	54.9	13.3		3,184	55.7	13.6		0.251
Hypertriglycemia (fasting) ‡, %	Intervention	1,150	24.4		<0.001	1,340	24.4		0.909	1,034	24.6		0.212	1,089	20.8		0.542	0.044
	Control	2,420	18.6			3,053	24.6			2,827	22.6			2,763	21.7			0.002
Hypertriglycemia (non-fasting) ‡, %	Intervention	435	29.2		0.017	452	29.6		<0.001	569	27.1		0.021	502	29.3		<0.001	0.948
	Control	66	15.2			320	17.8			377	20.4			250	13.6			1.000
High plasma glucose (fasting) ¶, %	Intervention	1,150	13.7		<0.001	1,355	13.3		<0.001	1,034	16.0		<0.001	1,089	13.8		0.017	0.953
	Control	2,420	7.4			3,050	7.8			2,823	11.0			2,763	11.0			<0.001
High plasma glucose (non-fasting) ¶, %	Intervention	435	20.2		<0.001	450	19.3		<0.001	570	15.3		0.001	502	16.5		<0.001	0.234
	Control	66	3.0			185	2.7			273	7.0			250	4.0			1.000
Body mass index, kg/m²	Intervention	2,514	23.0	3.1	0.106	2,478	23.0	3.1	0.022	2,463	23.2	3.2	0.87	2,347	23.3	3.2		0.001
	Control	3,292	23.1	3.0		4,217	23.2	3.1		4,023	23.2	3.1		3,955	23.3	3.1		0.026
Urinary salt excretion, g/day	Intervention	2,376	9.4	2.2	<0.001					2,410	9.3	2.2	0.00	2,250	9.3	2.2		0.046
	Control	3,256	9.0	2.2						3,087	9.1	2.2		2,991	9.0	2.2		0.709
Current smokers, %	Intervention	2,362	55.0		0.173	2,339	52.7		0.979	2,374	51.8			2,280				<0.001
	Control	3,171	53.1			3,957	52.7			3,926	50.7			3,642				<0.001

P values were calculated by unpaired t tests or chi square tests. SD means standard deviation.
† Non-HDL cholesterol was calculated as follows: total cholesterol - HDL cholesterol. HDL means "High-density lipoprotein".
‡ Hypertriglycemia was defined as fasting serum triglyceride>=150 mg/dl (1.69 mmol/L) or non-fasting serum triglyceride>=200 mg/dl (2.26 mmol/L).
¶ High plasma glucose was defined as fasting plasma glucose>=110 mg/dl (6.11 mmol/L) or non-fasting plasma glucose>=120 mg/dl (6.66 mmol/L).
§ Urinary salt excretion was not measured in this year.

Table 2 Number of participants at the 4th examination who had participated in the baseline survey, males

Companies	Number of participants at the 1st examination, baseline survey (A)	Number of participants at the 4th examination who had participated in the 1st examination (B)	B*100/A (%)
A †	402	206	51.2
B	622	521	83.8
C	481	336	69.9
D	494	317	64.2
E	233	186	79.8
F	283	250	88.3
Intervention Group	2,515	1,816	72.2
G	964	809	83.9
H	509	419	82.3
I	337	297	88.1
J	336	287	85.4
K	674	444	65.9
L †	462	203	43.9
Control Group	3,282		74.9
Total	5.797		73.7

† Non-factory population.

cholesterol levels and urinary sodium excretion, lower HDL cholesterol levels, and a higher prevalence of participants with hypertriglycemia or high plasma glucose, compared with the control group. These differences between the two groups were not substantially changed in the 2nd examination. In the 3rd examination, the difference in HDL cholesterol between the two groups was not significantly different, whilst the intervention group had higher SBP and DBP. In the 4th examination, the

Table 3 Trends for blood pressure, cholesterol, BMI and urinary salt excretion in the returning participants during 3 years, males

Risk characteristics	Group	N	1st examination (baseline)	SD	4th examination (after 3 years)	SD	change	SD	P-value † between 1st and 4th examinations	P-value ‡ between two groups
Age, years	Intervention	1,816	37.5	9.2	41.0	9.2	3.5	0.34	<0.001	0.994
	Control	2,470	38.1	8.8	41.6	8.8	3.5	0.28	<0.001	
Systolic blood pressure, mmHg	Intervention	1,728	118.7	16.4	120.2	16.5	1.5	11.4	<0.001	<0.001
	Control	2,367	118.9	15.1	118.9	15.8	0	11.4	0.957	
Diastolic blood pressure, mmHg	Intervention	1,728	71.8	11.1	74.2	11.8	2.4	7.68	<0.001	<0.001
	Control	2,367	72.7	11.0	73.1	11.6	0.4	7.89	0.012	
Non-HDL cholesterol, mg/dl	Intervention	957	145.5	35.7	147.2	36.4	1.7	24.3	0.031	
	Control	1,857	138.4	35.9	143.6	36.1	5.2	23.2	<0.001	
HDL cholesterol, mg/dl	Intervention	957	54.3	14.6	56.5	15.0	2.2	8.70	<0.001	
	Control	1,857	56.0	12.9	56.1	13.6	0.1	7.71	0.406	
Body mass index, kg/m2	Intervention	1,750	22.8	3.1	23.2	3.2	0.4	1.13	<0.001	
	Control	2,470	23.1	2.9	23.3	3.0	0.2	1.08	<0.001	
Urinary salt excretion, g/day	Intervention	1,619	9.3	2.2	9.3	2.2	0	2.58	0.894	0.638
	Control	2,420	9.1	2.2	9.1	2.2	0	2.50	0.559	

Non-HDL cholesterol was defined as in Table 1.
† P values were calculated by paired t tests.
‡ P values were calculated by unpaired t tests.

Table 4 Trends in the prevalence (%) of hypertriglycemia, high plasma glucose and current smokers in the returning participants during 3 years, males

Risk characteristics	Group	N	1st examination (baseline)	4th examination (after 3 years)	change	P-value between 1st and 4th examinations †	P-value ‡ between two groups
Hypertriglycemia (fasting), %	Intervention	601	24.1	22.5	−1.6	0.337	0.139
	Control	1,579	19.6	20.9	1.3	0.247	
	P-values ¶		0.021	0.447			
Hypertriglycemia (non-fasting), %	Intervention	199	35.7	41.2	5.5	0.178	0.353
	Control	8	25.0	12.5	−12.5	1.000	
	P-values ¶		0.715	0.148			
High plasma glucose (fasting), %	Intervention	601	11.5	16.0	4.5	0.001	0.909
	Control	1,579	6.8	11.6	4.8	<0.001	
	P-values ¶		0.001	0.008			
High plasma glucose (non-fasting), %	Intervention	199	27.6	27.6	0.0	1.000	1.000
	Control	8	12.5	12.5	0.0	1.000	
	P-values ¶		0.686	0.686			
Current smokers, %	Intervention	1,683	56.5	51.3	−5.2	<0.001	0.035
	Control	2,317	54.1	50.7	−3.4	<0.001	
	P-values ¶		0.130	0.701			

Hypertriglycemia and high plasma glucose were defined as in Table 1.
† P values were calculated by McNemar tests.
‡ P values were calculated by Mann-Whitney U tests.
¶ P values between two groups were calculated by chi square tests.

intervention group had higher DBP and HDL cholesterol levels than those of the control group, and the difference in the prevalence of hypertriglycemia detected with fasting blood samples between the two groups was not significant.

Comparing results between the 1st and 4th examinations in the intervention group, there was a significant increase in age, DBP, HDL cholesterol and BMI, and a significant decrease in urinary salt excretion level and the prevalence of hypertriglycemia detected with fasting blood samples and current smokers. In the control group, there was a significant increase in age, DBP, non-HDL cholesterol and BMI level and the prevalence of hypertriglycemia and high plasma glucose detected with fasting serum samples, and a significant decrease in the prevalence of current smokers. The prevalence of participants who were taking anti-hypertensive, lipid-lowering and anti-diabetic medicines was relatively low in this population, at 3.6%, 2.1% and