Results

In this population, 1386 participants were classified as hypertensive (1141 screening hypertension and 245 screening normotensive with antihypertensive medication; Fig. 1). Approximately half (798/1386, 57.8%) of hypertensive individuals were taking antihypertensive medication.

Among 588 participants (aged 40–94 years) who had high screening BP measured in June–August 2003, who were not taking antihypertensive medication, and who then completed the questionnaire, 487 were reassessed at the screening office in June–August 2004 (follow-up rate 82.8%). No difference was observed in the follow-up rate between the intervention and control groups (Fig. 1). The percentage of participants who walked less than 1 h/day was lower in participants who did not complete follow-up (53.0%) than in those who completed (66.8%). Otherwise, no significant differences were observed between participants who completed follow-up and participants who did not (data not shown). Table 1 shows baseline characteristics, hypertension awareness and treatment status in 2003. The 2003 screening SBP was lower in the intervention group than in the control group. Percentages of current drinkers were higher in the intervention group than the control group. No other baseline differences were observed between the intervention and control groups. The 2003 screening SBP/DBP was not significantly different between the home HT group (146.9/85.3 mmHg) and the home NT group (145.3/84.8 mmHg). Table 2 shows the high BP awareness and treatment status in 2004 for the untreated screening HT in 2003. The intervention group had a higher rate of initiating antihypertensive medication (30.9%) compared with the control group (23.9%). Some 60.3% of the control group did not take any action against hypertension (9.0% were 'doing nothing about hypertension' and 51.3% claimed to be unaware). After stratification of the intervention group according to home BP status, compared with the control group home HT participants had a higher rate of starting to take antihypertensive medication (44.1%) and a lower percentage who took no action against hypertension (40.7%). Similarly, the home NT group had lower rates of action than the control group: 9.4% starting antihypertensive medication, and 84.4% taking no action against hypertension.

Table 3 shows the odds ratio for intervention versus the control group of not taking antihypertensive medication or of not taking action in 2004 among those who were untreated in 2003. Compared with the control group, the odds ratio for not starting antihypertensive medication was significantly lower in the home HT group [odds ratio (OR) 0.38, 95% confidence interval (CI) 0.21–0.68] and higher in the home NT group (OR 3.08, 95% CI 0.90–10.58). Similarly, the odds ratio for no action against hypertension was lower in the home HT group (OR 0.42, 95% CI 0.24–0.75) and higher in the home NT group (OR 3.30, 95% CI 1.23–8.86) compared with controls.

We also analysed the subgroup of participants whose screening BP was SBP 160 mmHg or greater and DBP 100 mmHg or greater at baseline, similar tendencies were observed, although their numbers were few. The

Table 1 Baseline characteristics of screening hypertensive individuals not taking antihypertensive medication, June–August 2003. Nishiaizu, Japan

	All participants			Participants who completed follow-up		
	Control	Intervention	*P* value	Control	Intervention	*P* value
n	468	120		390	97	
Age (years)	67.2	67.5	0.77	66.9	68.1	0.27
Women (%)	56.0	53.3	0.60	57.2	51.6	0.32
Body mass index (kg/m^2)	23.6	23.5	0.83	23.7	23.4	0.40
Screening SBP (mmHg)	149.8	146.7	< 0.01	149.7	146.6	< 0.01
Screening DBP (mmHg)	86.7	85.5	0.13	86.6	85.2	0.09
Smoking status (%)						
Current	19.0	14.6		17.4	13.2	
Former	22.9	28.1		23.9	32.9	
Never	58.1	57.3	0.42	58.7	54.0	0.24
Drinking status (%)						
Current	50.8	64.2		50.6	63.6	
Former	5.6	3.7		5.4	3.4	
Never	43.6	32.1	0.04	44.0	33.0	0.09
Time spent walking per day (%)						
Less than 0.5 h	64.0	66.1		66.4	68.4	
0.5–1 h	23.3	19.5		22.2	16.8	
1 h+	12.8	14.4	0.65	11.4	14.7	0.41
Awareness and action for hypertension in 2003						
Aware of hypertension[a]						
Modifying lifestyle	16.0	15.8		16.4	17.5	
Monitoring BP	12.2	11.7		11.8	13.4	
Doing nothing about hypertension	10.5	7.5		10.8	8.3	
Not aware of hypertension	61.3	65.0	0.78	61.0	60.8	0.87

BP, Blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure. [a]Actions taken in those aware of hypertension are in hierarchical order.

Table 2 Awareness and action concerning hypertension at follow-up in 2004, according to 2003 condition

Status in 2004	Control group All	Intervention group All	Home HT	Home NT	No home BP
No. of participants	390	97	59	32	6
Aware of hypertension[a]					
Treated hypertensives (%)	23.9	30.9	44.1	9.4	16.7
Modifying lifestyle (%)	10.8	9.3	11.9	6.3	0.0
Monitoring BP (%)	5.1	2.1	3.4	0.0	0.0
Doing nothing about hypertension (%)	9.0	16.5	15.3	15.6	33.3
Not aware of hypertension (%)	51.3	41.2	25.4	68.8	50.0

BP, Blood pressure; HT, hypertension; NT, normotension; Home HT, home systolic BP at least 135 mmHg or home diastolic BP at least 85 mmHg; Home NT, home systolic BP lower than 135 mmHg and home diastolic BP lower than 85 mmHg; No Home BP, participants who did not measure home BP. [a]Actions taken in those aware of hypertension are in hierarchical order.

percentage of participants who initiated taking antihypertensive medication was higher in the home HT group (4/9, 44.4%) and lower in the home NT group (1/3, 33.3%) compared with the control group (29/82, 35.4%). Similarly, the percentage taking no action against hypertension was lower in the home HT group (2/9, 22.2%) and higher in the home NT group (2/3, 66.7%) compared with the control group (37/82, 45.1%).

We assessed the follow-up screening BP level among the three groups, i.e. home HT group, home NT group, and control group. Follow-up screening BP was the highest in the control group (SBP/DBP 141.9/81.2 mmHg), followed by the home HT group (141.1/81.0 mmHg) and the home NT group (135.4/76.5 mmHg). The percentages of screening high BP in 2004 was higher in the control group (57.7%) compared with the intervention group (combined home HT, home NT, and no home BP group; 46.4%) ($P = 0.045$ by chi-squared test).

Discussion

In this clinical trial, we examined the effect on untreated hypertension management of incorporating home BP measurements followed by tailored advice into the primary care system for hypertension. Among untreated screening hypertensive individuals in 2003 in the present study, 76% of the control group were not taking antihypertensive medication 1 year later, and 60% of them had not taken any action against hypertension by 2004. However, in the corresponding untreated screening hypertensive individuals, the combination of home BP measurement for a month and tailored referral advice reduced the percentage not taking antihypertensive medication or not taking action in the home HT group. Therefore, as hypothesized, home BP monitoring identified those who did need treatment and improved the proportion of participants with antihypertensive treatment.

A recent report, based on the National Health and Nutrition Examination Survey (NHANES III) studies in the United States and the Canadian Heart Health Surveys (CHHS), showed that many north American adults were unaware of their hypertension (30% for NHANES III; 43% for CHHS) or aware of their hypertension but not treated (18% for NHANES III; 22% for CHHS) [4]. Therefore, 48 and 65% of hypertensive individuals were not treated for their BP in the USA and Canada, respectively. Furthermore, this rate was rather higher in European populations; only 26.8% for the pooled population were treated (range 24.8–32.0%)

Table 3 Risk of not taking antihypertensive medication or of no action for hypertension in 2004 among untreated screening hypertensives in 2003

Not taking antihypertensive medication in 2004

	n	Untreated in 2004	%	OR	95% CI
Control group	390	297	76%	1	
Intervention group					
HHT	59	33	56%	0.38	0.21–0.68
HNT	32	29	91%	3.08	0.90–10.58

No action for hypertension in 2004

	n	No action for hypertension through 2004	%	OR	95% CI
Control group	390	235	60%	1	
Intervention group					
HHT	59	24	41%	0.42	0.24–0.75
HNT	32	27	84%	3.30	1.23–8.86

CI, Confidence interval; OR, odds ratio; HHT, Home hypertensive, home systolic blood pressure of 135 mmHg or greater and home diastolic blood pressure of 85 mmHg or greater; HNT, home normotensive, home systolic blood pressure less than 135 mmHg and home diastolic blood pressure less than 85 mmHg. No action for hypertension, Doing nothing about hypertension (including untreated) plus not aware of hypertension.

[6]. Our study also showed that 43% (588 of 1386 hypertensive individuals) were untreated. The problem that many hypertensive individuals are not under medical management is thus a worldwide issue.

Twenty-four per cent of the control group initiated antihypertensive medication and 40% of them took some action against hypertension by 2004. Although we have no specific information about why so many of the screening participants took no action, it may be that they believed that high BP in screening is only a result of nervousness or related white-coat effects. Whatever the reason, this tendency towards inaction applied even to those participants whose untreated screening BP was SBP 160 mmHg or greater and DBP 100 mmHg or greater, even though they were immediately referred to see their physician. Only 35.4% of the 82 participants in this category in the control group initiated antihypertensive medication and 45.1% did not take any action against their hypertension. This finding might support the findings that the detection of high BP at screening solely is not a guarantee that it will be treated appropriately [4–6].

However, compared with the control group, the home HT group showed a lower proportion of participants who did not start medication or those who did not take any action against hypertension. As home HT participants had a higher cardiovascular disease risk than home NT participants [12–14], these participants did need antihypertensive medication. Therefore, incorporating home BP measurement followed by tailored advice into the primary care system reduced the risk of untreated hypertension and the risk of taking no action against hypertension in home HT participants.

On the other hand, the home NT group showed a rather lower proportion of participants who started medication. This might be because we defined their home BP as lower than the well-accepted home hypertension criteria by general guidelines. A recent study reported that the risk of cardiovascular events for white-coat hypertensive individuals, namely elevated BP in the office but not at home, did not differ from the risk in controlled hypertension, namely in those whose home and office BP were both controlled [13]. Therefore, individuals who do not have high home BP have less need for antihypertensive treatment than those who have high home BP. The overtreatment of BP can cause adverse effects, and may incur unnecessary costs [21]. Furthermore, the follow-up screening BP level was the lowest in the home NT group among the three groups, namely home NT, home HT, and the control group. Although the home NT group instruction led to less intense treatment, and they actually had less treatment, their follow-up BP level was relatively low, maybe because of their lower 'true BP level'. Therefore, this finding that the home NT group had lower rates of starting antihypertensive medication could be considered as an additional beneficial effect of home BP measurements after community screening. However, we draw this conclusion cautiously because the prognostic implications of white-coat hypertension are still debated [22]. A long-term study of BP and disease outcomes in a large group of home normotensive individuals would be desirable.

Among untreated hypertensives in the intervention area, 88% (106/120) measured home BP for at least 3 days. Therefore, using home BP measurement after mass BP screening is feasible. The feasibility may have been enhanced in the setting of this study, given the wide use of the home BP measurement device in Japan [9]. Further study would help to clarify the feasibility of home BP measurement in other primary care settings.

We have some methodological limitations in this paper. This study was not an individual randomized trial, with the result that some baseline characteristics were different between the control and intervention group. However, the treatment was realistic as we asked all residents aged 30 years or older in the intervention area to measure home BP and achieved a high response rate; the potential of self-selection bias is low. Another potential bias arises because home BP measurement devices are already in wide use in Japan [10], so a certain proportion of the control group might have measured their home BP. This would have caused an underestimate of the benefit of home BP measurement. Another possible bias is that we had only one measurement of screening BP, given Japanese rules for screening. Therefore, the initial BP status might be misclassified. A caveat is that participants in the home NT group were more likely to answer that they did not have hypertension in 2004. Although these participants might have altered their lifestyle (we did not ask about this in individuals who said they did not have hypertension), home monitoring could conceivably cause these individuals to underestimate their future risk of hypertension. We acknowledge that a periodic check-up on the participants to ensure they were using the correct home BP measurement technique should increase the reliability of participants' home BP report. However, as we asked all residents aged 30 years or over in the Onomoto district to measure home BP for 1 month (November 2003) [of 1714 residents aged $\geq$ 30 years who were asked, 1309 (76%) measured home BP], we had insufficient staff for this quality enhancement effort. Nevertheless, the procedure we used was a realistic model of how home BP measurement might be used in general practice. Finally, as we did not ask participants to measure follow-up home BP, we could not provide information on the degree of BP control assessed by home BP, which would not be biased by a white-coat effect. Nevertheless, the screening BP measurement that we carried out is highly relevant.

In conclusion, we found that incorporating home BP measurement followed by tailored advice into the primary care system reduced the risk of untreated hypertension and the risk of taking no action against hypertension in the home BP monitoring group with a high home BP value. Incorporating home BP monitoring with subsequent tailored advice into general practice could lead to a lower incidence of cardiovascular disease complications.

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The joint impact of cardiovascular risk factors upon medical costs

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Abstract

Objective. The joint impact of obesity, hypertension, and hyperglycemia upon medical costs is not well known. Our objective was to evaluate the joint impact of these cardiovascular risk factors upon medical costs in the rural Japanese population.

Methods. The data were derived from a 6-year prospective observation of National Health Insurance beneficiaries in rural Japan. Data on blood chemistry tests, blood pressure, weight, and height were obtained from an annual health check-up provided by the local municipalities in 1995. We prospectively collected data on medical costs over a 6-year period for 12,340 subjects (5306 men and 7034 women) without prior histories of cardiovascular disease or cancer.

Results. Mean medical costs for individuals being overweight/obese, hypertensive, and hyperglycemic were 91.0% higher than those for individuals without any of these three cardiovascular risk factors. In this cohort, 17.2% of total medical costs were attributable to these three risk factors.

Conclusion. Overweight/obesity, hypertension, and hyperglycemia could have a large impact on health care resources in rural Japan.

Keywords: Hypertension; Obesity; Hyperglycemia; Health care costs

Introduction

Medical costs are increasing much faster than Gross Domestic Product in most industrialized countries (Organisation for Economic Co-operation and Development, 2005), and this imbalance is now becoming a serious threat to the sustainability of national health insurance systems. Reducing the need and demand for medical services through health promotion and disease prevention is expected to stabilize medical costs and alleviate this imbalance (Fries et al., 1993). Several studies have estimated the economic impact of modifiable cardiovascular risk factors including hypertension, hyperglycemia, dyslipidemia, or obesity. Most of them were focused on the economic impact of a single risk factor (Nakamura et al., 2005; Brown et al., 1999; Nichols and Brown, 2005; Chenoweth, 2004; Selby et al., 1997; Thompson and Wolf, 2001; Quesenberry et al., 1998; Raebel et al., 2004; Kuriyama et al., 2002) or were based on hypothetical, cross-sectional, or retrospective study designs (Ray et al., 2000; Oliva et al., 2004; Hodgson and Cohen, 1999; Hogan et al., 2003). These cardiovascular risk factors often occurred together in the same individual (Ford et al., 2002; Greenland et al., 2003; Haffner and Taegtmeyer, 2003), and their combination synergistically increased the risk of morbidity and mortality (Stamler et al., 1993, 1999; Wilson et al., 1998; Greenland et al., 2003), consequently raising medical costs. However, the joint impact of these cardiovascular risk factors upon medical costs is still unclear.

A few previous cohort studies have tried to estimate the relationship between medical costs and combination of cardiovascular risk factors (Daviglus et al., 1998; Goetzel et al., 1998; Anderson et al., 2000; Jee et al., 2001; Lynch et al., 2005). Most of them were limited to working individuals, who were healthy enough to work at entry into the cohort and would later drop out when they ceased to work because of age or illness. Therefore, these studies would have underestimated the impact of cardiovascular risks upon medical costs. To fully examine the impact of cardiovascular risk factors upon medical

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costs, it is necessary to follow-up a large-scale population-based cohort that retains all individuals, regardless of age or health status.

Our objective was to evaluate the joint impact of cardiovascular risk factors upon medical costs in the rural Japanese population. The present data were derived from a 6-year follow-up observation of National Health Insurance (NHI) beneficiaries in rural Japan, known as the Ohsaki NHI Cohort Study (Tsuji et al., 1998, 2003; Izumi et al., 2001; Kuriyama et al., 2004; Anzai et al., 2005).

Methods

Study setting and design

The setting and design of the Ohsaki NHI Cohort Study have already been reported in detail (Tsuji et al., 1998). In brief, this prospective cohort study started in 1994, when we delivered a self-administered questionnaire on various health-related lifestyles to all NHI beneficiaries aged 40–79 years living in the catchments area of Ohsaki Public Health Center, Miyagi Prefecture, Japan. NHI in Japan is used by farmers, the self-employed, pensioners, and their dependents. Ohsaki Public Health Center, a local government agency, provides preventive health services for the residents of 14 municipalities. The questionnaires were delivered to and collected from the subjects' residences by public health officials in each municipality. This procedure yielded a high response rate of 94.6% (N=52,029). We excluded 774 subjects because they had withdrawn from the NHI before January 1, 1995, when we started the prospective collection of NHI claim files. Thus, 51,255 subjects formed the study cohort. This study was approved by the Ethics Committee of the Tohoku University Graduate School of Medicine. We considered the return of self-administered questionnaires signed by the subjects to imply their consent to participate in the study.

Exposure data

Data on cardiovascular risk factors were obtained from an annual health check-up conducted by physicians and provided by the local municipalities in 1995. This annual health check-up is provided free, or at low charge, to all people aged 40 years and over in Japan. The examinations include an interview, measurement of weight, height and blood pressure (BP), physical examination, and blood chemistry tests for serum total cholesterol, serum high-density lipoprotein (HDL), plasma glucose, and other parameters, without instructions to fast beforehand.

In this study, we defined hypertension as either a self-report of taking antihypertensive medication or systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg (Chobanian et al., 2003), and dyslipidemia as either a self-report of taking lipid-lowering medication or a serum total cholesterol level ≥220 mg/dl or serum HDL level <40 mg/dl (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001). Hyperglycemia was defined as either a self-reported history of diabetes or a plasma glucose level ≥150 mg/dl (Schauffler et al., 1993). Body Mass Index (BMI) was calculated as the weight (kg)/height (m)^2. We defined overweight/obesity as a BMI ≥25 (World Health Organization, 2000).

Follow-up

Among the participants of the Ohsaki NHI Cohort Study, 17,065 (33.3%) received the annual health check-up between June and November in 1995, and gave their consent for us to analyze their results for this study. We prospectively collected NHI claims files from the local NHI Association for all individuals in the cohort for the period from January 1, 1996, to the date of withdrawal from the NHI because of death or emigration, or until December 31, 2001. When a beneficiary withdraws from the NHI, the date and reason are entered in the NHI withdrawal files. Both NHI claims and withdrawal files were linked to our baseline survey data and annual health check-up data files, using each beneficiary's identification number as the key code.

Out of 17,065 examines, we excluded 439 because they had withdrawn from the NHI before January 1, 1996. We also excluded 1522 subjects who reported having had cancer, stroke, or myocardial infarction and 2764 subjects who had missing data for BP, body measurements, and blood tests. Consequently, 12,340 subjects (5306 men and 7034 women) were included in this analysis.

Assessment of medical costs

NHI covers almost all medical care, including diagnostic tests, medication, and surgery. When medical providers treat a patient, they receive co-payment from the patient and then file a claim to the local NHI Association for reimbursement. Payment to medical providers is made on a fee-for-service basis, where the price of each service is determined by a uniform national fee schedule. The local NHI Association has provided us with subjects' NHI claim files every month.

Monthly medical costs for each subject were calculated by dividing the total medical costs throughout the observation period by the number of months observed. We used monthly values rather than cumulative values to avoid underestimating medical costs for subjects who died or emigrated during the follow-up (Kuriyama et al., 2004; Anzai et al., 2005).

Statistical analysis

Like previous studies (Daviglus et al., 1998; Kuriyama et al., 2004; Anzai et al., 2005), we chose an ordinary least-squares model based on non-log-transformed data in a general linear model because the results in the original dollar units are more easily interpretable and because total medical costs for groups can be estimated from adjusted mean-per-individual costs.

We estimated the relative contribution of each of four cardiovascular risk factors (hypertension, dyslipidemia, hyperglycemia, and overweight/obesity) to medical costs. We estimated medical costs within three categories-inpatient, outpatient, and total cost-for subjects with and without these index risk factors using analysis of covariance (ANCOVA) adjusted by age at the baseline (continuous variable), sex, smoking (current smoker, past smoker, or never smoker), alcohol drinking (current drinker, past drinker, or never drinker), and comorbidity of the other three cardiovascular risk factors.

To assess the joint impact of cardiovascular risk factors upon medical costs, we classified the subjects into categories according to the combination of risk factors that were significantly associated with medical costs, and calculated the adjusted mean monthly medical costs of each category by ANCOVA.

We estimated the proportion of risk-attributable medical costs (RAC%) related to the cardiovascular risk factors. First, we calculated the adjusted excess costs per individual for each risk category by subtracting the mean medical costs among those without any of overweight/obesity, hypertension, and hyperglycemia from the mean medical costs for each risk category. Second, to estimate risk-attributable medical costs for each risk category, the adjusted excess costs per individual for each risk category were multiplied by the person-months for each risk category observed. Risk-attributable medical costs were divided by total medical costs for the entire cohort. The results provided the estimates of RAC%.

All analyses were conducted with SAS software version 9.1 (SAS Institute Inc., 2004). We estimated the P-value using the F-value of the general linear model and estimated the 95% confidence interval (CI) from the least squares standard error. For multiple comparisons, we used the Tukey test. All of the statistical tests reported here were two-sided, and differences at $P<0.05$ were accepted as statistically significant. In this paper, monetary values are converted to U.S. dollars ($) using an exchange rate of $1.00=115 Japanese yen.

Results

Among 51,255 participants in the Ohsaki NHI Cohort Study, 24.1% (N=12,340) were available for the present study. They were more likely to be female, current nonsmoker, normotensive, and normoglycemic as compared with non-participants (N=38,915) (Table 1).

Table 1
Baseline characteristics of the Ohsaki Study subjects in 1995, Japan

	Non-participants	Study participants	P-value [a]	Overweight/Obesity [b]		Hypertension [c]		Hyperglycemia [d]		Dyslipidemia [e]	
				(−)	(+)	(−)	(+)	(−)	(+)	(−)	(+)
N	38,915	12,340		8152	4188	7158	5182	11,292	1048	6790	5550
Age (year) (SD)	61.0 (10.6)	61.1 (9.4)	0.25	61.2 (9.6)	61.0 (8.9)	59.1 (9.7)	63.9 (8.2)	60.8 (8.3)	64.0 (8.3)	60.5 (9.8)	61.8 (8.9)
Male (%)	49.4	43.0	<0.0001	45.5	38.2	41.7	44.8	41.6	58.2	47.1	38.0
Current smoker (%)	30.0	22.3	<0.0001	24.7	17.7	23.0	21.3	21.6	30.3	23.9	20.4
Current drinker (%)	42.1	42.6	<0.0001	43.6	40.8	41.3	44.4	42.0	49.6	47.9	36.2
Overweight/Obesity (%)	28.7 [f]	28.8 [f]	0.75	0.0 [b]	100.0 [b]	27.8 [b]	42.5 [b]	33.7 [b]	36.1 [b]	27.9 [b]	41.4 [b]
Hypertension (%)	27.5 [g]	23.8 [g]	<0.0001	36.6 [c]	52.5 [c]	0.0 [c]	100.0 [c]	41.0 [c]	52.5 [c]	39.5 [c]	45.1 [c]
Hyperglycemia (%)	7.2 [h]	4.7 [h]	<0.0001	8.2 [d]	9.0 [d]	7.0 [d]	10.6 [d]	0.0 [d]	100.0 [d]	7.9 [d]	9.2 [d]
Dyslipidemia (%)	–	–		39.9 [e]	54.9 [e]	42.6 [e]	48.3 [e]	44.6 [e]	48.9 [e]	0.0 [e]	100.0 [e]

SD denotes standard deviation.
[a] Variables were compared between study participants and non-participants by the *t*-test or the χ^2 test, as appropriate.
[b] Measured Body Mass Index ≥25.0.
[c] Blood pressure ≥140/90 mm Hg or self-report of taking antihypertensive medication.
[d] Casual blood glucose ≥150 mg/dl or self-reported history of diabetes.
[e] Casual serum cholesterol ≥220 mg/dl, or HDL <40 mg/dl, or self-report of taking lipid-lowering medication.
[f] Body Mass Index calculated by self-reported weight/(height*height) ≥25.0.
[g] Self-reported history of hypertension.
[h] Self-reported history of diabetes.

Of the 12,340 study participants, 12,054 (97.7%), 4215 (34.2%), and 12,047 (97.6%) used total, inpatient, and outpatient medical care and had more than zero costs for the 6-year period. During the follow-up, 584 subjects (4.7%) died and 921 (7.5%) were lost to follow-up. Table 1 shows the baseline characteristics of the subjects in terms of presence/absence of overweight/obesity, hypertension, hyperglycemia, and dyslipidemia. Cardiovascular risk factors were often present together in the same individual. Among the study participants, 39.1% had no risk factor, 39.3% had a single risk factor, and 21.6% had two or more risk factors. In comparison with those without overweight/obesity, those with overweight/obesity had a higher prevalence of the other three cardiovascular risk factors and were less likely to be current smokers or current drinkers. Also, hypertension, hyperglycemia, and dyslipidemia were associated with a higher prevalence of the other three cardiovascular risk factors.

Table 2 shows the adjusted monthly medical costs of the subjects in terms of presence/absence of these cardiovascular risk factors. The adjusted mean total and outpatient medical costs among overweight/obese subjects were significantly higher than those among subjects who were not overweight/obese ($P=0.013$, 0.030, respectively). The mean inpatient cost among overweight/obese subjects was higher than that among subjects who were not overweight/obese, but the difference was not significant ($P=0.068$). The adjusted mean total, inpatient, and outpatient medical costs among subjects with hypertension were significantly higher than among subjects without hypertension ($P<0.0001$, 0.0008, <0.0001). The adjusted mean total, inpatient, and outpatient medical costs among subjects with hyperglycemia were significantly higher than among subjects without hyperglycemia ($P<0.0001$, 0.0004, <0.0001). There was no difference in total, inpatient, and outpatient medical costs between subjects with and without dyslipidemia ($P=0.74$, 0.50, 0.55).

Table 2
Adjusted monthly medical costs by the presence/absence of the cardiovascular risk factors in the Ohsaki Study, Japan, 1996–2001

		N	Adjusted inpatient cost [a], $		Adjusted outpatient cost [a], $		Adjusted total cost [a], $		Increasing rate (%)
			(95%CI)	P-value	(95%CI)	P-value	(95%CI)	P-value	
Overweight/Obesity [b]	(−)	8152	87.1 (78.8–95.5)	(Referent)	139.5 (135.4–143.6)	(Referent)	226.6 (216.9–236.3)	(Referent)	(Referent)
	(+)	4188	100.6 (88.9–112.3)	0.068	147.4 (141.6–153.2)	0.030	248.0 (234.4–261.6)	0.013	9.4
Hypertension [c]	(−)	7158	81.5 (72.5–90.5)	(Referent)	122.0 (117.6–126.4)	(Referent)	203.5 (193.0–213.9)	(Referent)	(Referent)
	(+)	5182	105.8 (95.1–116.4)	0.0008	170.1 (164.8–175.3)	<0.0001	275.9 (263.5–288.2)	<0.0001	35.6
Hyperglycemia [d]	(−)	11,292	88.0 (80.9–95.0)	(Referent)	137.8 (134.3–141.3)	(Referent)	225.8 (217.6–234.0)	(Referent)	(Referent)
	(+)	1048	131.8 (108.4–155.1)	0.0004	189.4 (177.9–200.9)	<0.0001	321.1 (294.0–348.2)	<0.0001	42.2
Dyslipidemia [e]	(−)	6790	93.8 (84.7–103.0)	(Referent)	141.3 (136.7–145.8)	(Referent)	235.1 (224.5–245.7)	(Referent)	(Referent)
	(+)	5550	89.1 (79.0–99.2)	0.50	143.3 (138.3–148.3)	0.55	232.4 (220.6–244.2)	0.74	−1.1

CI denotes confidence interval. The plus (+) denotes the presence of each of the index risk factors. The minus (−) denotes the absence of each of the index risk factors.
[a] Tested by analysis of covariance (ANCOVA) using non-log-transformed data on charges adjusted by age at baseline (continuous variable), sex, smoking (current smoker, past smoker, or never smoker), alcohol drinking (current drinker, past drinker, or never drinker), and comorbid condition of other three cardiovascular risk factors.
[b] Body Mass Index ≥25.0.
[c] Blood pressure ≥140/90 mm Hg or self-report of taking antihypertensive medication.
[d] Casual blood glucose ≥150 mg/dl or self-reported history of diabetes.
[e] Casual serum cholesterol ≥220 mg/dl, or HDL <40 mg/dl, or self-report of taking lipid-lowering medication.

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Table 3
The joint impact of cardiovascular risk factors upon medical costs in the Ohsaki Study, Japan, 1996–2001

No. of risks	N	Person-months	Inpatient costs						Outpatient costs	
			Adjusted cost[a], $				Risk-attributable costs[b], $	RAC%[c] (%)	Adjusted cost[a], $	
				(95%CI)	P-value	Increasing rate (%)				(95%CI)
0	4821	323,036	76.2	(65.3–87.1)	(Referent)	(Referent)			117.2	(111.9–122.6)
1										
Overweight/Obesity[d]	1839	123,039	82.8	(65.2–100.4)	0.99	8.7	812,054	1.1	120.4	(111.8–129.0)
Hypretension[e]	2661	177,066	95.3	(80.6–110.0)	0.47	25.1	3,381,967	4.5	161.9	(154.7–169.1)
Hyperglycemia[f]	349	23,080	126.7	(86.6–166.8)	0.25	66.3	1,165,524	1.5	160.2	(140.5–179.9)
2										
Overweight/Obesity[d]+ Hypretension[e]	1971	131,829	111.1	(94.2–128.1)	0.017	45.8	4,600,825	6.1	170.1	(161.8–178.4)
Overweight/Obesity[d]+ Hyperglycemia[f]	149	10,117	105.4	(44.2–166.7)	0.98	38.3	295,418	0.4	173.4	(143.4–203.5)
Hypretension[e]+ Hyperglycemia[f]	321	20,718	134.7	(92.7–176.7)	0.13	75.8	1,211,976	1.6	223.5	(202.9–244.1)
3										
Overweight/Obesity[d]+ Hypretension[e]+ Hyperglycemia[f]	229	15,173	158.2	(108.7–207.7)	0.034	107.6	1,244,169	1.6	211.2	(186.9–235.5)
Total	12,340	824,056					12,711,934	16.8		

CI denotes confidence interval. RAC% denotes percentage of risk-attributable medical costs.

[a] Tested by analysis of covariance (ANCOVA) adjusted by age at baseline (continuous variable), sex, smoking (current smoker, past smoker, or never smoker), and alcohol drinking (current drinker, past drinker, or never drinker).

[b] The increment in medical costs attribute to cardiovascular risk factors were calculated by multiplying the adjusted excess costs by the number of person-months observed.

[c] The proportion of medical costs in the entire cohort that would not occur if no one had cardiovascular risk factors, which were calculated by dividing the risk-attributable medical costs by the total medical costs for entire cohort during the 6-years of observation period.

[d] Body Mass Index ≥25.

[e] Blood pressure ≥140/90 mm Hg or self-report of taking antihypertensive medication.

[f] Casual blood glucose ≥150 mg/dl or self-reported history of diabetes.

Table 3 lists the monthly mean medical costs according to the combination of cardiovascular risk factors. Medical costs increased significantly as the number of risk factors increased. Subjects without any of overweight/obesity, hypertension, and hyperglycemia (the 'no-risk-factor' group) had an adjusted mean total medical cost of $193.4 per month. Relative to this group, among subjects who had one risk factor, the presence of overweight/obesity alone was associated with a 5.1% increase in total medical costs, but this was not statistically significant; the presence of hypertension alone was associated with a 33.0% significant increase in total medical costs, and the presence of hyperglycemia alone was associated with a 48.3% significant increase. The combinations of overweight/obesity+hypertension, overweight/obesity+hyperglycemia, and hypertension+hyperglycemia were associated with 45.4%, 44.2%, and 85.2% increases in total medical costs, respectively. Subjects who had all three risk factors had total medical costs that were 91.0% higher than those of the no-risk-factor group.

During the 6-year observation period, the whole study population consumed medical costs totaling $192.6 million (824,056 person-months). Risk-attributable medical costs for each risk category were estimated by multiplying the excess cost and the person-months for each risk category observed. For example, the risk-attributable total medical cost for overweight/obesity alone was estimated by multiplying the adjusted total excess cost per individual who had the single risk factor of overweight/obesity ($9.8) by the associated person-months (123,039 person-months). By multiplying these values, it was estimated that a medical cost of $1.2 million (0.6%) was attributable to this risk factor. Although the degree of increase in medical cost per individual was greater among subjects with hyperglycemia alone than among subjects with hypertension alone, the RAC% for hyperglycemia alone was smaller than that for hypertension because of its lower prevalence. Total RAC% was 17.2%. RAC% for inpatient medical care was 16.8%, and that for outpatient care was 17.5%. There was no notable interaction between risk categories and age or sex in adjusted mean total cost.

For sensitivity analysis, we redefined overweight/obesity, hypertension, hyperglycemia, and dyslipidemia and re-estimated the economic impact of these factors (Table 4). Among subjects who had BP ≥140/90 mm Hg, 42.2% reported taking antihypertensive medication. Among subjects who had a casual blood glucose level of ≥150 mg/dl, 32.0% reported a history of diabetes. Among subjects who had a casual serum cholesterol level of ≥220 mg/dl or HDL <40 mg/dl, 4.0% reported taking lipid-lowering medication. Self-reporting of antihypertensive medication and a self-reported history of diabetes, and a BMI of ≥30 were associated with significantly

Outpatient costs				Total costs					
Adjusted cost[a], $		Risk-attributable costs[b], $	RAC%[c] (%)	Adjusted cost[a], $				Risk-attributable total costs[b], $	RAC%[c] (%)
P-value	Increasing rate (%)				(95%CI)	*P*-value	Increasing rate (%)		
(Referent)	(Referent)			193.4	(180.8–206.0)	(Referent)	(Referent)		
0.99	2.7	393,723	1.3	203.2	(182.8–223.6)	0.99	5.1	1,204,956	0.6
0.0010	38.1	7,914,864	6.8	257.2	(240.1–274.3)	<0.0001	33.0	11,298,260	5.9
<0.0001	36.7	992,427	0.8	286.9	(240.3–333.5)	0.038	48.3	2,157,869	1.1
0.0074	45.1	6,973,743	6.0	281.2	(261.5–300.9)	<0.0001	45.4	11,575,527	6.0
0.0003	48.0	568,579	0.5	278.9	(207.7–350.0)	0.28	44.2	864,735	0.4
<0.0001	90.7	2,202,274	1.9	358.3	(309.5–407.0)	<0.0001	85.2	3,415,376	1.8
<0.0001	80.2	1,426,243	1.2	369.4	(311.9–426.9)	<0.0001	91.0	2,670,227	1.4
		20,471,853	17.5					33,186,950	17.2

increased total medical cost (P <0.0001, <0.0001, 0.0030, respectively). Subjects who self-reported taking lipid-lowering medication had a higher mean cost than those with a serum cholesterol level of <220 mg/dl and HDL ≥40 mg/dl and who did not self-report taking lipid-lowering medication, but the difference was not significant (P=0.76). Among subjects who did not self-report a history of diabetes, those who had a blood glucose level of ≥150 mg/dl and <200 mg/dl had a significantly higher mean total cost than those who had a blood glucose level of <150 mg/dl (P=0.017).

Discussion

Mean medical cost among subjects who were overweight/obese, hypertensive, and hyperglycemic was 91.0% higher than that among subjects without any of these three risk factors, after adjustment for a variety of potential confounders. In this cohort, 17.2% of the total medical cost was attributable to these three cardiovascular risk factors.

One cohort study in Korea (Jee et al., 2001) and one cohort study in the U.S. (Anderson et al., 2000) have estimated RAC%

Table 4
Adjusted monthly medical costs by the cardiovascular risk status in the Ohsaki Study, Japan, 1996–2001

		N	Adjusted cost[a], $ (95%CI)	*P*-value	Increasing rate (%)
Overweight/Obesity	Body Mass Index <25	8152	226.6 (216.8–236.3)	(Referent)	(Referent)
	Body Mass Index ≥25 and <30	3747	242.3 (228.0–256.7)	0.17	7.0
	Body Mass Index ≥30	421	299.9 (257.2–342.5)	0.0030	32.4
Hypertension	Without self-report of taking antihypertensive medication				
	Systolic BP <140 mm Hg and diastolic BP <90 mm Hg	7158	202.9 (192.5–213.3)	(Referent)	(Referent)
	Systolic BP ≥140 mm Hg or diastolic BP ≥91 mm Hg	2247	223.0 (204.6–241.4)	0.15	9.9
	Self-report of taking antihypertensive medication	2935	317.7 (301.3–334.1)	<0.0001	56.6
Hyperglycemia	Without self-reported history of diabetes				
	Casual blood glucose <150 mg/dl	11,292	225.8 (217.6–234.0)	(Referent)	(Referent)
	Casual blood glucose ≥150 mg/dl and <200 mg/dl	354	296.6 (250.2–343.0)	0.017	31.4
	Casual blood glucose ≥200 mg/dl	111	255.9 (173.2–338.6)	0.89	13.3
	Self-reported history of diabetes	583	348.5 (312.2–384.8)	<0.0001	54.4
Dyslipidemia	Without self-report of taking lipid-lowering medication				
	Casual serum cholesterol <220 mg/dl and HDL ≥40 mg/dl	6790	235.1 (224.5–245.7)	(Referent)	(Referent)
	Casual serum cholesterol ≥220 mg/dl or HDL <40 mg/dl	5328	231.4 (219.4–243.4)	0.9	−1.6
	Self-report of taking lipid-lowering medication	222	256.5 (198.0–315.1)	0.76	9.1

CI denotes confidence interval. BP denotes blood pressure. HDL denotes high-density lipoprotein.

[a] Tested by analysis of covariance (ANCOVA) using non-log-transformed data on charges adjusted by age at baseline (continuous variable), sex, smoking (current smoker, past smoker, or never smoker), alcohol drinking (current drinker, past drinker, or never drinker), and comorbid condition of other three cardiovascular risk factors.

for combination of cardiovascular risk factors in terms of total medical costs. Anderson et al., based on a prospective observation of a large employee cohort in the U.S., reported the RAC% for obesity, hyperglycemia, and hypertension of 6.3% (Anderson et al., 2000). In their study, dyslipidemia was not associated with any increase in medical cost. Jee et al. (2001) found that the RAC% for obesity, hyperglycemia, and hypertension was 10.4% for men and 5.5% for women, using a large employee cohort in Korea. In the present study, the RAC% for overweight/obesity, hyperglycemia, and hypertension was 17.2%, and was thus higher than in the previous studies. This may have been partly due to the fact that the previous studies were based on observations of healthy young workers; the impact of cardiovascular risk factors upon medical costs would become larger with age. In addition, as these previous studies excluded subjects who became too ill to work during the follow-up, they would have underestimated the impact of cardiovascular risks upon medical costs.

The result of sensitivity analysis (Table 4) showed that being on treatment at the baseline rather than having a raised level of risk factors without treatment was associated with higher cost. Especially in hyperglycemia, most of the costs associated with hyperglycemia were attributable to diabetes rather than pre-diabetic hyperglycemia.

Study limitations and strengths

The present study had a number of strengths. First, we followed up a large population-based cohort retaining the elderly and those who became ill during follow-up. In our cohort, only 921 subjects (7.5%) withdrew from the NHI and were thus lost to follow-up because of emigration. Second, because NHI claim files were obtained directly from the local NHI Association and included almost all available medical treatment, our charge calculation was accurate. Third, in this study, the joint impact of cardiovascular risk factors was analyzed after adjustment for a variety of potential confounders.

Our study also had some limitations. Among all this study population, participation rate in the annual health check-up was as low as 33.3%. However, the participation rate in the annual health check-up was similar to that for Japan as a whole. According to the Ministry of Health, Labour and Welfare, the participation rate in the annual health check-up in Japan was 36.5% in 1995. Second, only 24.1% of the study population participated in the annual health check-up and had no prior history of cancer, stroke, or myocardial infarction and were available for the present study. The present study subjects were less likely to be hypertensive and hyperglycemic and might have been healthier than the rest of the study population. Therefore, we might have underestimated the RAC% because of the lower prevalence of cardiovascular risk factors in these individuals. Third, the present study does not prove whether prevention of these cardiovascular risk factors can reduce medical costs. Further interventional strategies could reduce these cardiovascular risk factors and potentially lower medical costs. Fourth, we did not identify individual reasons for medical treatment, and thereby we were unable to distinguish treatment costs from comorbid costs. However, each of the cardiovascular risk factors was associated with an increase not only in outpatient medical costs but also inpatient medical cost. In Japan, because hypertension and obesity rarely become main reasons for hospitalization, inpatient costs mainly reflect the costs of comorbidity. Moreover, the fact that RAC% for inpatient care was comparable to RAC% for outpatient care (16.8% vs. 17.5%) implies that overweight/obesity, hypertension, and hyperglycemia are related to not only high prescription costs for treatment of the primary disease but also severe medical events requiring inpatient treatment.

Conclusion

We have demonstrated that 17.2% of medical costs are attributable to overweight/obesity, hypertension, and hyperglycemia. These cardiovascular risk factors could have a large impact on health care resources in rural Japan.

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