多く、データベースでも欠損値を考慮した操作が必要であること、また統計ソフトに格納したデータをいったんデータベースに格納して再度統計ソフトに戻す際には変数の型が意図せず変更されてしまう可能性も考えられた。そこで広く使用されている統計ソフトであるSPSSのシンタックスを用いてSPSS内部で全ての操作を行うことを試みた。

SPSSはケース毎の変数間での操作を前提としており、一部のケースの変数情報を抽出して他のケースの係数を計算するなどの操作を行うことは一般的ではない。しかし条件に当てはまる最初のケースの値を保持して、他の全てのケースにも適用できるLEAVEコマンドを活用すれば、支援あり群の個々のケースの値と他のケースの値との差を計算することが出来た。更にSORTコマンドを用いるとケースの抽出と該当する対照候補の抽出および選択が可能なことが明らかとなった。最終的に自動的にSPSS内で複数ケースに対して条件に合致するペアを作成することが出来ることを明らかにした。また一旦設定した対照例を次のケースでは選択から除外するなどの処理も自動で行えることを確認した。

この仕組みに更にループ構造を持たせ一括処理する試みを行ったが、SPSSのループ内ではSORTコマンドが動作しないことが明らかになった。最終的には作成したプログラムを支援あり群のケース分羅列することで、対照を自動的に設定するシステムを構築することが出来た。

本研究を通じ、我々は回帰係数をそのまま記入すれば、対照となるケースを選択できるプログラムを開発した。これを用いれば統計ソフトSPSSだけで傾向性スコアを考慮した対照を選択することができるので、保健事業評価の際の有力なツールになると考えられる。

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ABSTRACT

Method for Evaluating Health Promotion Programs Using Propensity Score

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Evaluating the performance of a health promotion program to lower the risk of cardiovascular disease requires comparison with a suitably selected reference. Typically, the reference includes easily accessible participants who declined or were not enrolled in the intervention program. Unfortunately, the selected reference often fails to be comparable for many of the risk factor attributes that might determine the success or failure of the intervention. In response, we developed a propensity score that results in a reference sample with features that are similar to those enrolled in the health promotion program.

Participants who received repeat physical examinations in Japan from 2008 to 2009 were identified as candidates for enrollment in an intensive health promotion program to lower the risk of cardiovascular disease (N = 33,009). Those who attended at least one session of the health promotion program were selected as the intervention group (N = 1,114). The remainder were selected as reference group I (N = 31,895). Among the latter, those with a high propensity for enrollment into the intervention group based on a logistic regression model were selected as reference group II (N = 3,008). A group III reference was similarly defined based on a linear regression propensity score (N = 2,992). Characteristics of the intervention and reference groups were compared.

In the intervention group, subjects were younger and less likely to smoke cigarettes or eat breakfast than reference group I ($P<0.001$). Declines in body weight, waist circumference, and blood pressure between the repeated examinations from 2008 to 2009 were significantly greater in the intervention versus reference group I. Other than age, differences between the intervention and reference groups II and III failed to persist.

In conclusion, identifying a reference group based on a propensity score results in a group of individuals with characteristics similar to those enrolled in a health promotion program. Comparison of the reference and intervention groups could result in improved assessments of the performance of health promotion programs.

(HEP. 2014;41:418-427.)

KEY WORDS **health promotion program, propensity score, SPSS, evaluation**

Original Article

Treated and untreated hypertension, hospitalization, and medical expenditure: an epidemiological study in 314 622 beneficiaries of the medical insurance system in Japan

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See editorial comment on page 880

Objective: This study investigated the effect of hypertension on hospitalization risk and medical expenditure according to treatment status in a Japanese population.

Methods: A total of 314 622 beneficiaries of the medical insurance system in Japan, aged 40–69 years, without a history of cardiovascular, cerebrovascular, or end-stage renal disease were classified into seven blood pressure categories. These categories were used to compare the risk of undergoing hospitalization in the 1 year after the baseline survey and to examine the percentage of inpatient medical expenditure attributable to overall hypertension relative to total medical expenditure in the study population.

Results: During the follow-up period, 6.6% of men and 5.1% of women were hospitalized. In men and women aged 40–54 years, cases of hypertension, especially grade 3 untreated hypertension, led to more frequent hospitalization, compared with optimal blood pressure. Individuals who were hospitalized, especially long-term, incurred considerably higher medical expenditure compared with those who were not hospitalized, regardless of their hypertension status. In women aged 55–69 years, there was little variation in hospitalization risk across blood pressure categories. The inpatient medical expenditure attributable to overall hypertension represented 7.2 and 6.9% of the total medical expenditure for men aged 40–54 and 55–69 years, whereas it represented 2.8 and 3.8% for women, respectively.

Conclusion: Although cases of hypertension were an economic burden especially in men, grade 3 untreated hypertension was more likely to incur extremely high medical expenditure as a result of hospitalization, compared with other cases.

Keywords: epidemiology, hospitalization, hypertension, medical expenditure, treatment

INTRODUCTION

Hypertension is a major risk factor for cardiovascular, cerebrovascular, and renal disease [1–5]. The high prevalence of hypertension leads to a burden of premature disability and death because of serious vascular diseases [3,6–9]. This problem also needs to be considered from an economic perspective, as hypertension may incur medical expenditure through treatment of the condition itself, and also by treatment of cardiovascular, cerebrovascular, and renal diseases, which occur commonly in hypertensive individuals [10–17]. The treatment of hypertension itself incurs medical expenditure mainly in outpatient departments, and accounts for 7.3% of the total medical costs in the Japanese population aged 45–64 years [18]. However, it is necessary to focus on costs for treatment of serious, but preventable, vascular diseases attributable to hypertension under the assumption that use of antihypertensive medication is necessary to keep hypertensive individuals healthy [19]. The occurrence of these serious vascular diseases requires very expensive procedures such as percutaneous coronary intervention, coronary artery bypass graft, neurosurgical treatment, or hemodialysis mainly with hospitalization.

When evaluating the effect of hypertension on medical expenditure, well controlled hypertension on medication

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should be differentiated from other cases of hypertension. Well controlled hypertensive individuals on treatment have a lower risk of developing cardiovascular, cerebrovascular, and renal disease [20–22]. In other words, untreated hypertension, as well as poorly controlled hypertension on treatment, may incur extremely high medical expenditure, compared with well controlled hypertension on treatment. In Japan, hypertension is often identified at health checkups that are readily available in the community or at the workplace [12,23]. Nevertheless, some hypertensive individuals remain untreated despite being recommended to take antihypertensive medication [23]. To our knowledge, only a few epidemiological studies have provided detailed information on treated and untreated hypertension and medical expenditure [16,17]. Furthermore, little is known regarding the contribution of inpatient medical expenditure for hospitalized cases attributable to hypertension relative to total medical expenditure in Japan. These conditions include cardiovascular, cerebrovascular, and renal diseases, which are major medical expenses, mainly through hospitalization [18]. The present study examined this topic in a Japanese population, using a large dataset on blood pressure, history of antihypertensive medication, and medical expenditure in 314 622 beneficiaries of the medical insurance system in Japan.

METHODS

Medical expenditure

In Japan, many medical services are provided by the medical insurance system [18,24], which requires the enrollment of all Japanese residents ('health-insurance-for-all'). The medical insurance system consists of three insurance groups, with eligibility for each group depending on age and occupation. All residents age 75 years or older are enrolled in the Advanced Elderly Medical Service (coverage rate 11.0%), whereas those younger than 75 years are enrolled in either Employee's Health Insurance (58.3%) or National Health Insurance (30.7%) according to their occupation. Employee's Health Insurance is for employees and their dependants, whereas National Health Insurance is for those not covered by Employee's Health Insurance such as self-employed individuals (e.g. farmers and fishermen) and retirees and their dependants. Each insurance group consists of local insurance organizations based on company or region. Prices are controlled strictly by a fee schedule set by the National Government, and are determined on a 'fee-for-service' basis, with an exception of approximately 20% of acute care hospitals that use a flat-fee per day payment system applied to hospitalized patients according to diagnosis and procedure (Diagnosis Procedure Combination/Per-Diem Payment System [18,25]). The fee schedule is the same regardless of the insurance group, and applies to all the clinics and hospitals given approval to provide medical services to outpatients and hospitalization under the medical insurance system. However, some medical services including health checkups for asymptomatic individuals and inoculations are not covered by medical insurance. No taxes are imposed on medical expenditure. The fees for these services are recorded every month in an insurance claim history file. The medical expenditure recorded in this study was confined to the fee schedule range used in the medical insurance system in Japan.

Study design and participants

Participating local insurance organizations were recruited throughout Japan to investigate the relationship between lifestyles and cardiovascular risk factors and medical expenditure. Of the 2 270 694 beneficiaries aged 40–69 years in the Employee's Health Insurance ($n = 2\,077\,769$ in nine local organizations) and National Health Insurance ($n = 192\,925$ in 12 local organizations), 589 718 beneficiaries ($n = 549\,889$ and $n = 39\,829$, respectively) underwent an annual health checkup in 2008 (participation rate 26.0%), and were then followed up for 1 fiscal year (April 2009 to March 2010). In this report, we used a sub-dataset that comprised 382 382 beneficiaries ($n = 344\,047$ and $n = 38\,335$, respectively) with information recorded on history of cardiovascular, cerebrovascular, and end-stage renal disease, and fasting plasma glucose at the time of the baseline survey. The present study was approved by the Institutional Review Committee of the Japan Anti-Tuberculosis Association for Ethical Issues.

Of the 382 382 potential participants, 67 760 were excluded because of one or more of the following criteria: a history of cardiovascular, cerebrovascular, or end-stage renal disease at baseline ($n = 16\,919$); possibly inappropriate data on SBP, DBP, BMI, serum low-density lipoprotein cholesterol, or fasting plasma glucose at baseline as a result of extremely low or high values, defined as lower than 0.01th percentile values or higher than 99.99th percentile values of the normal distribution (SBP, <69 or >229 mmHg; DBP, <35 or >138 mmHg; BMI, <13.7 or >45.8 kg/m^2; serum low-density lipoprotein cholesterol, <0.52 or >8.02 mmol/l; and fasting plasma glucose, <3.11 or >23.43 mmol/l) ($n = 331$); missing information at the time of the baseline survey ($n = 49\,961$); and dropout before the follow-up survey ($n = 549$). The remaining 314 622 participants were considered eligible for the analyses.

Data collection

The baseline data were obtained at an annual health checkup carried out using standardized methods in accordance with the Basic Guidelines for Health Checkups and Healthcare Advice with a Particular Focus on the Metabolic Syndrome, issued by the Ministry of Health, Labour and Welfare of Japan in 2007 [26]. Blood pressure measurement in the sitting position was carried out by well trained nurses. Data collected in a self-administered questionnaire at study entry included age, medical history, and smoking habits. Height and body weight were measured, and BMI calculated as weight in kilograms divided by the square of height in meters. Fasting blood samples were obtained by cubital venipuncture. Fasting serum low-density lipoprotein cholesterol [27] and plasma glucose levels were measured enzymatically using separate automatic analyzers.

Monthly insurance claim history files in each insurance organization were used to obtain data on medical expenditure for the 1-year follow-up period. The insurance claim history files of the participants were linked with the baseline survey data files at each local organization. In order to

protect the participants' privacy, their names were deleted from the linked data at the organization. The data obtained from the local organizations were compiled for analysis at the study center. If a beneficiary withdrew from the insurance or died, follow-up was terminated at that point. Data on medical expenditure for each participant differed depending upon the period of subscription to the insurance scheme. The medical expenditure for each participant was therefore divided by the period of subscription and expressed in euros per month of follow-up (1 euro = 95.91 Japanese yen, 0.79 pounds sterling, and 1.22 US dollars, at foreign exchange rates on 1 August 2012).

Data analysis

Separate calculations were performed for sex and age (40–54 and 55–69 years at baseline). Participants who did not take any antihypertensive medication at baseline were classified into the following five blood pressure categories according to the criteria of the European Society of Hypertension and of the European Society of Cardiology in 2007 [19]: optimal blood pressure, SBP lower than 120 mmHg and DBP lower than 80 mmHg; normal-to-high normal blood pressure, SBP 120–139 mmHg and/or DBP 80–89 mmHg; grade 1 hypertension, SBP 140–159 mmHg and/or DBP 90–99 mmHg; grade 2 hypertension, SBP 160–179 mmHg and/or DBP 100–109 mmHg; and grade 3 hypertension, SBP at least 180 mmHg and/or DBP at least 110 mmHg. The remaining participants, who were taking antihypertensive medication, were defined as having hypertension on treatment and were classified as either well controlled on medication (SBP < 140 mmHg and a DBP < 90 mmHg) or poorly controlled on medication (SBP $\geq$ 140 mmHg and/or DBP $\geq$ 90 mmHg).

To assess whether hypertension is a risk factor for hospitalization resulting in considerably higher medical expenditure than normal blood pressure, we first compared the rate of undergoing hospitalization in the year after baseline in the seven blood pressure categories. The odds ratio for hospitalization in each category was calculated using a logistic regression model, with 'optimal blood pressure' acting as the reference. The logistic regression model incorporated the following variables as covariates: age (years), BMI (kg/m^2), smoking habits (nonsmoker or current smoker), serum low-density lipoprotein cholesterol (mmol/l), medication for hypercholesterolemia (yes or no), log-transformed fasting plasma glucose (mmol/l) (owing to skewed distribution), and medication for diabetes (yes or no). As the majority of patients with new-onset cardiovascular and cerebrovascular disease stayed in hospital for a few days or longer [28,29], we also compared the rate of hospitalization for 7 cumulative days or longer, and the rate of hospitalization for 14 cumulative days or longer in the year after baseline in the seven blood pressure categories. A similar logistic regression model was used to calculate the odds ratio for each hospitalization event (i.e. $\geq$7 days vs. 0–6 days; and $\geq$14 days vs. 0–13 days) in each blood pressure category relative to the 'optimal blood pressure' category. The odds ratio for each hospitalization event in each category was also calculated, with 'well controlled hypertension on treatment' acting as the reference. To link medical expenditure to the relationship between blood pressure and hospitalization risk, we calculated the median values and interquartile ranges of monthly medical and inpatient medical expenditure in the year after baseline in participants grouped according to hypertension status at baseline and hospitalization status in the year after baseline. It was not possible to calculate accurate mean values of medical expenditure in each blood pressure category, as the distribution of expenditure was positively skewed, with 20.6% of the participants incurring no costs.

Moturu *et al.* [30] suggested that a very small percentage of patients accounted for a substantial percentage of the total medical expenditure in the population. This underscored the importance of identifying and managing individuals who may fall into this group in the near future. To allow for this possibility, we defined extremely high medical expenditure as at least 99th percentile values of the sex-specific distribution of medical expenditure in the year after baseline. We then compared the rate of falling into this top 1% of medical expenditure in the seven blood pressure categories. The odds ratio for incurring such extremely high medical expenditure in the year after baseline in each blood pressure category was calculated using a similar logistic regression model to that described above, with either 'optimal blood pressure' or 'well controlled hypertension on treatment' acting as the reference.

In order to minimize the potential confounding effect of other medications, the analyses were repeated after excluding participants who took medication for hypercholesterolemia and/or diabetes.

Finally, we examined the percentage of inpatient medical expenditure attributable to overall hypertension relative to total medical expenditure in the study population using reference to a previous study [12]. Residual inpatient medical expenditure was calculated by subtracting the mean of inpatient medical expenditure in the 'optimal blood pressure' category from the corresponding mean in each blood pressure category. This represents inpatient medical expenditure per capita attributable to each blood pressure category. We calculated the inpatient medical expenditure attributable to each blood pressure category from a population perspective as follows: [(mean inpatient medical expenditure in each category) minus (mean inpatient medical expenditure in the 'optimal blood pressure' category)] multiplied by (number of subjects in the respective category). The inpatient medical expenditure percentage attributable to each blood pressure category was calculated as follows: (inpatient medical expenditure attributable to each blood pressure category) divided by (the total medical expenditure in the study population). The sum of the corresponding percentages of the six blood pressure categories other than the 'optimal blood pressure' category was then calculated.

The statistical analyses were performed using the Statistical Package for the Social Sciences Version 12.0J for Windows (SPSS Japan Inc., Tokyo, Japan). All probability values were two-tailed and the significance level was set at $P < 0.05$.

RESULTS

Characteristics of the study population

The baseline characteristics of the 183 862 male and 130 760 female study participants and the study population grouped

according to blood pressure levels and history of taking antihypertensive medication are summarized in Table 1 (data of the 40–54 and 55–69 years age groups combined). The mean age at study entry was 52.6 years in men and 53.2 years in women. The prevalence of untreated hypertension, including grade 1, grade 2, and grade 3 hypertension, was 18.5% in men and 12.2% in women, whereas the prevalence of hypertension on treatment, including well controlled and poorly controlled hypertension, was 14.6% in men and 11.3% in women. Blood pressure measured at the baseline survey showed that 51.5% of men and 55.9% of women on treatment were classified as having well controlled hypertension.

The profiles of most baseline risk characteristics worsened as the severity of untreated hypertension increased. Compared with the 'untreated hypertension' categories, the 'hypertension on treatment' categories had lower mean low-density lipoprotein cholesterol levels, but a higher prevalence of taking medication for hypercholesterolemia. The prevalence of taking diabetes medication was also higher in the 'hypertension on treatment' category than in the 'untreated hypertension' category.

Blood pressure, hospitalization, and medical expenditure

During the 1-year follow-up period, 6.6% ($n = 12\,120$) of male and 5.1% ($n = 6693$) of female participants underwent hospitalization, with the median period (interquartile range) of cumulative hospitalization being 8 (3–18) days and 9 (4–17) days, respectively. Men and women who underwent hospitalization in that year incurred 47.4 and 36.7% of this sex-specific total medical expenditure, respectively. The rate of being hospitalized for at least 14 cumulative days was 2.3% ($n = 4160$) in men and 1.7% ($n = 2177$) in women, with these groups incurring 32.2 and 23.7% of the total expenditure, respectively.

As shown in Table 2, in men aged 40–54 or 55–69 years, the risk of undergoing hospitalization, especially long-term hospitalization, in the year after baseline increased clearly with more severe untreated hypertension. The risk of being hospitalized for at least 14 cumulative days appeared to be higher in the 'grade 2-to-3 untreated hypertension' category than in the 'well controlled hypertension on treatment' category. In women aged 40–54 years, there appeared to be a further increase in the corresponding risk in the 'grade 3 untreated hypertension' category compared with the 'well controlled hypertension on treatment' category. However, in women aged 55–69 years, there was little variation in the risk of undergoing hospitalization across blood pressure categories. The corresponding risk did not show a marked difference between the 'well controlled' and 'poorly controlled hypertension on treatment' categories in any sex and age-group. Hospitalization, especially long-term hospitalization, resulted in considerably higher medical expenditure, compared with nonhospitalized individuals, with medical expenditure showing a broadly similar distribution across blood pressure levels at every given hospitalization period for every sex and age-group (Table 2).

Male and female participants who fell into the top 1% group of medical expenditure in the year after baseline each incurred at least 1571 euros/month ($n = 1838$) and at least 1249 euros/month ($n = 1307$), with the median (interquartile range) period of cumulative hospitalization being 38 (19–71) and 32 (16–59) days, respectively. The sum of medical expenditure in these top 1% male and female groups (5651 079 and 3234 324 euros/month) accounted for 25.6 and 21.2% of the sex-specific total medical expenditure (22 082 646 and 15 248 924 euros/month), respectively.

As shown in Table 3, the risk of incurring such extremely high medical expenditure in the year after baseline increased with more severe untreated hypertension in the age-stratified and sex-stratified groups, other than in women aged 55–69 years. In men aged 40–54 years, the corresponding risk was also higher in the 'grade 2-to-3 untreated hypertension' category than in the 'well controlled hypertension on treatment' category, whereas in women aged 40–54 years, the corresponding risk was also higher in the 'grade 3 untreated hypertension' category than in the 'well controlled hypertension on treatment' category.

A similar pattern was observed for the study groups when participants on medication for hypercholesterolemia and/or diabetes were excluded from the analyses (data not shown in the table).

In men aged 40–54 years, the inpatient medical expenditure attributable to normal-to-high normal blood pressure was estimated to be 164 252 euros, calculated as follows: (26 euros – 24 euros) × 41 063 participants with normal-to-high normal blood pressure (Table 4). Accordingly, the inpatient medical expenditure attributable to normal-to-high normal blood pressure represented 1.8% of the total medical expenditure for the respective male population (9191 780 euros), and was calculated as follows: 164 252 euros/9191 780 euros. The inpatient medical expenditure percentage attributable to the six blood pressure categories combined in the respective male population was 7.2%, with the percentage of each category being 1.8% for 'normal-to-high normal', 1.2% for 'grade 1', 1.1% for 'grade 2', 0.7% for 'grade 3', 1.2% for 'well controlled', and 1.2% for 'poorly controlled'. Similarly, the inpatient medical expenditure percentages attributable to the six blood pressure categories combined was estimated to be 6.9% for men aged 55–69 years, 2.8% for women aged 40–54 years, and 3.8% for women aged 55–69 years (see Table 4 for the percentage of each blood pressure category in these study populations).

DISCUSSION

We carried out an epidemiological study on the relationship between hypertension status at baseline and hospitalization risk and medical expenditure during the year after baseline in a Japanese population without any history of cardiovascular, cerebrovascular, or end-stage renal disease. Although cases of hypertension led to more frequent hospitalization, compared with optimal blood pressure, hospitalization risk was higher in grade 3 untreated hypertension than in well controlled hypertension on treatment, or grade 1-to-2 untreated hypertension. Participants who were hospitalized, especially long-term stays, incurred considerably higher medical expenditure, compared with nonhospitalized individuals,

TABLE 1. Baseline characteristics of the 183 862 male and 130 760 female beneficiaries of the medical insurance system in Japan, grouped according to hypertension status

	Optimal blood pressure	Normal-to-high normal blood pressure	Grade 1 untreated hypertension	Grade 2 untreated hypertension	Grade 3 untreated hypertension	Well controlled hypertension on treatment	Poorly controlled hypertension on treatment	*P* values for difference
Men	(*n* = 55 193)	(*n* = 67 789)	(*n* = 24 649)	(*n* = 7271)	(*n* = 2133)	(*n* = 13 829)	(*n* = 12 998)	
Age (years)	50.4 ± 7.4	52.0 ± 7.6	53.8 ± 7.4	54.0 ± 7.3	53.4 ± 7.2	57.0 ± 6.7	57.1 ± 6.7	<0.01
SBP (mmHg)	108.6 ± 7.3	126.7 ± 6.6	142.7 ± 8.6	158.1 ± 11.2	176.9 ± 16.2	125.7 ± 9.2	149.8 ± 13.3	<0.01
DBP (mmHg)	67.7 ± 6.6	78.8 ± 6.3	89.4 ± 6.3	99.0 ± 7.2	111.3 ± 9.2	78.0 ± 7.2	91.5 ± 9.3	<0.01
BMI (kg/m^2)	22.6 ± 2.9	23.7 ± 3.1	24.3 ± 3.3	24.5 ± 3.4	25.1 ± 3.7	24.8 ± 3.2	25.2 ± 3.5	<0.01
Current smoking (%)	58.4	50.2	46.5	46.7	50.1	41.1	37.1	<0.01
Serum low-density lipoprotein cholesterol (mmol/l)	3.26 ± 0.82	3.30 ± 0.84	3.29 ± 0.87	3.32 ± 0.88	3.33 ± 0.96	3.10 ± 0.75	3.14 ± 0.78	<0.01
Medication for hypercholesterolemia (%)	2.6	3.3	3.2	1.8	1.1	19.7	17.6	<0.01
Fasting plasma glucose (mmol/l)	5.27 (4.94–5.66)	5.38 (5.05–5.88)	5.55 (5.11–6.05)	5.61 (5.16–6.22)	5.66 (5.22–6.33)	5.66 (5.22–6.33)	5.77 (5.27–6.55)	<0.01
Medication for diabetes (%)	3.0	3.4	3.5	2.6	1.3	12.4	12.7	<0.01
Women	(*n* = 57 823)	(*n* = 42 116)	(*n* = 12 217)	(*n* = 2979)	(*n* = 821)	(*n* = 8279)	(*n* = 6525)	
Age (years)	50.7 ± 7.4	53.8 ± 7.6	55.7 ± 7.2	55.6 ± 7.2	55.1 ± 7.0	58.4 ± 6.3	58.8 ± 6.4	<0.01
SBP (mmHg)	106.2 ± 8.3	126.8 ± 6.3	144.5 ± 7.7	162.3 ± 9.5	184.2 ± 16.3	125.4 ± 9.6	150.8 ± 12.8	<0.01
DBP (mmHg)	64.9 ± 7.2	76.3 ± 7.0	86.3 ± 7.6	95.5 ± 8.6	106.9 ± 11.4	75.8 ± 7.6	87.9 ± 9.5	<0.01
BMI (kg/m^2)	21.2 ± 2.8	22.4 ± 3.3	23.4 ± 3.7	24.0 ± 4.1	24.8 ± 4.5	23.9 ± 3.7	24.6 ± 4.1	<0.01
Current smoking (%)	19.2	13.7	12.1	12.1	14.4	12.9	9.7	<0.01
Serum low-density lipoprotein cholesterol (mmol/l)	3.15 ± 0.80	3.36 ± 0.84	3.50 ± 0.86	3.56 ± 0.91	3.69 ± 0.94	3.28 ± 0.75	3.39 ± 0.77	<0.01
Medication for hypercholesterolemia (%)	4.0	6.3	6.8	5.8	2.9	27.2	26.6	<0.01
Fasting plasma glucose (mmol/l)	4.94 (4.66– 5.27)	5.11 (4.77–5.50)	5.22 (4.88–5.66)	5.33 (5.00–5.77)	5.38 (5.05–5.94)	5.27 (4.88–5.72)	5.38 (5.00–5.94)	<0.01
Medication for diabetes (%)	0.8	1.6	2.0	1.3	1.2	6.5	7.2	<0.01

Optimal blood pressure was defined as an SBP < 120 mmHg and a DBP < 80 mmHg; normal-to-high normal blood pressure as an SBP 120–139 mmHg and/or DBP 80–89 mmHg; grade 1 untreated hypertension as an SBP 140–159 mmHg and/or DBP 90–99 mmHg; grade 2 untreated hypertension as an SBP 160–179 mmHg and/or DBP 100–109 mmHg; grade 3 untreated hypertension as an SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg; well controlled hypertension on treatment as an SBP < 140 mmHg and DBP < 90 mmHg on antihypertensive medication; and poorly controlled hypertension on treatment as an SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg on medication. Values represent mean ± standard deviation, median (interquartile range), or the percentage of participants in that category. One-way analysis of variance, Kruskal–Wallis test, or a chi-squared test were used to compare each risk characteristic in the seven blood pressure categories.

TABLE 2. Odds ratios (95% confidence interval) for undergoing hospitalization and median values (interquartile range) of medical expenditure per month for respective hospitalization in the year after baseline in the 183 862 male and 130 760 female participants, grouped according to hypertension status at baseline, based on data from the medical insurance system in Japan

	Optimal blood pressure	Normal-to-high normal blood pressure	Grade 1 untreated hypertension	Grade 2 untreated hypertension	Grade 3 untreated hypertension	Well controlled hypertension on treatment	Poorly controlled hypertension on treatment
Men aged 40–54 years	(*n* = 38 320)	(*n* = 41 063)	(*n* = 12 599)	(*n* = 3594)	(*n* = 1136)	(*n* = 4473)	(*n* = 4112)
No hospitalization							
Cases (*n*)	36 685	39 148	11 929	3383	1049	4102	3757
Medical expenditure (euros)	13 (0–43)	14 (0–48)	15 (0–58)	18 (0–78)	27 (0–95)	144 (95–206)	132 (85–192)
Hospitalization							
Cases (*n*)	1635	1915	670	211	87	371	355
Rate (%)	4.27	4.66	5.32	5.87	7.66	8.29	8.63
Odds ratio (vs. optimal)	1.00 Reference	1.02 (0.96–1.10)	1.10 (1.00–1.21)	1.20 (1.03–1.40)	1.59 (1.27–2.00)	1.48 (1.31–1.68)	1.51 (1.33–1.71)
Odds ratio (vs. well controlled)	0.68 (0.60–0.77)	0.69 (0.61–0.78)	0.74 (0.65–0.85)	0.81 (0.68–0.97)	1.08 (0.84–1.38)	1.00 Reference	1.02 (0.88–1.19)
Medical expenditure (euros)	373 (176–730)	371 (196–765)	411 (203–854)	444 (251–1245)	623 (338–1460)	472 (275–895)	478 (248–913)
In hospitalization (euros)	229 (90–537)	239 (100–544)	274 (108–632)	302 (136–1028)	446 (179–1166)	214 (76–537)	195 (63–579)
Cases of ≥7 cumulative days/year (*n*)	869	1051	384	135	61	215	194
Rate (%)	2.27	2.56	3.05	3.76	5.37	4.81	4.72
Odds ratio (vs. optimal)	1.00 Reference	1.08 (0.98–1.18)	1.22 (1.07–1.38)	1.49 (1.23–1.80)	2.17 (1.66– 2.85)	1.61 (1.37–1.90)	1.56 (1.32–1.85)
Odds ratio (vs. well controlled)	0.62 (0.53–0.73)	0.67 (0.57–0.78)	0.75 (0.63–0.90)	0.92 (0.74–1.16)	1.35 (1.00–1.81)	1.00 Reference	0.97 (0.79–1.18)
Medical expenditure (euros)	661 (395–1233)	644 (393–1251)	698 (418–1199)	840 (435–1784)	1095 (545–2313)	726 (467–1292)	803 (470–1677)
In hospitalization (euros)	476 (275–976)	477 (283–1042)	527 (297–1020)	645 (299–1583)	971 (385–1679)	446 (254–991)	466 (246–1245)
Cases of ≥14 cumulative days/year (*n*)	490	584	213	87	41	113	114
Rate (%)	1.28	1.42	1.69	2.42	3.61	2.53	2.77
Odds ratio (vs. optimal)	1.00 Reference	1.08 (0.95–1.22)	1.22 (1.03–1.44)	1.73 (1.37–2.19)	2.64 (1.90–3.67)	1.55 (1.24–1.93)	1.68 (1.35–2.10)
Odds ratio (vs. well controlled)	0.65 (0.52–0.81)	0.70 (0.56–0.86)	0.79 (0.62–1.00)	1.12 (0.84–1.50)	1.71 (1.18–2.47)	1.00 Reference	1.09 (0.83–1.42)
Medical expenditure (euros)	1009 (612–1769)	1024 (624–1783)	1000 (627–1759)	1288 (732–2513)	1460 (992–2524)	1211 (729–2168)	1241 (659–2517)
In hospitalization (euros)	813 (453–1413)	813 (476–1513)	836 (472–1437)	1161 (581–2116)	1166 (830–2361)	866 (459–1812)	878 (424–1749)
Men aged 55–69 years	(*n* = 16 873)	(*n* = 26 726)	(*n* = 12 050)	(*n* = 3677)	(*n* = 997)	(*n* = 9356)	(*n* = 8886)
No hospitalization							
Cases (*n*)	15 594	24 534	11 024	3320	908	8338	7971
Medical expenditure (euros)	24 (0–84)	24 (0–85)	27 (0–93)	26 (0–100)	37 (0–118)	151 (92–225)	141 (85–210)
Hospitalization							
Cases (*n*)	1279	2192	1026	357	89	1018	915
Rate (%)	7.58	8.20	8.51	9.71	8.93	10.88	10.30
Odds ratio (vs. optimal)	1.00 Reference	1.05 (0.98–1.13)	1.06 (0.97–1.16)	1.24 (1.09–1.40)	1.12 (0.89–1.41)	1.27 (1.16–1.39)	1.18 (1.08–1.30)
Odds ratio (vs. well controlled)	0.79 (0.72–0.86)	0.83 (0.76–0.90)	0.83 (0.76–0.91)	0.97 (0.85–1.11)	0.88 (0.70–1.11)	1.00 Reference	0.93 (0.85–1.02)
Medical expenditure (euros)	472 (243–1071)	482 (246–1062)	512 (256–1179)	504 (277–1128)	596 (314–1102)	590 (356–1125)	589 (338–1202)
In hospitalization (euros)	292 (120–747)	302 (118–814)	335 (136–911)	324 (129–872)	385 (156–874)	280 (117–729)	297 (112–844)
Cases of ≥7 cumulative days/year (*n*)	783	1298	643	226	57	573	555
Rate (%)	4.64	4.86	5.34	6.15	5.72	6.12	6.25
Odds ratio (vs. optimal)	1.00 Reference	1.02 (0.93–1.12)	1.09 (0.98–1.22)	1.27 (1.09–1.49)	1.16 (0.88–1.54)	1.16 (1.04–1.31)	1.17 (1.04–1.32)
Odds ratio (vs. well controlled)	0.86 (0.77–0.97)	0.88 (0.79–0.97)	0.94 (0.83–1.06)	1.10 (0.93–1.29)	1.00 (0.75–1.33)	1.00 Reference	1.01 (0.89–1.14)
Medical expenditure (euros)	783 (448–1517)	833 (480–1589)	887 (489–1776)	822 (442–1507)	795 (583–1787)	934 (593–1780)	859 (562–1807)
In hospitalization (euros)	544 (309–1187)	595 (331–1283)	652 (333–1447)	610 (307–1277)	667 (365–1577)	586 (320–1356)	585 (311–1392)
Cases of ≥14 cumulative days/year (*n*)	449	796	401	141	39	350	342
Rate (%)	2.66	2.98	3.33	3.83	3.91	3.74	3.85
Odds ratio (vs. optimal)	1.00 Reference	1.10 (0.97–1.24)	1.19 (1.04–1.37)	1.38 (1.14–1.68)	1.38 (0.98–1.93)	1.24 (1.07–1.44)	1.26 (1.09––1.47)
Odds ratio (vs. well controlled)	0.81 (0.70–0.94)	0.89 (0.78–1.01)	0.96 (0.83–1.12)	1.12 (0.91–1.37)	1.11 (0.79–1.56)	1.00 Reference	1.02 (0.88–1.19)
Medical expenditure (euros)	1274 (754–2075)	1290 (744–2134)	1325 (761–2163)	1189 (716–1908)	1154 (687–2104)	1338 (859–2276)	1319 (817–2444)
In hospitalization (euros)	1017 (544–1679)	1009 (563–1747)	1058 (583–1841)	940 (571–1606)	908 (510–1884)	972 (533–1847)	1021 (562–1939)

(*Continued*)

TABLE 2 (*Continued*)

	Optimal blood pressure	Normal-to-high normal blood pressure	Grade 1 untreated hypertension	Grade 2 untreated hypertension	Grade 3 untreated hypertension	Well controlled hypertension on treatment	Poorly controlled hypertension on treatment
Women aged 40–54 years	(*n* = 39 090)	(*n* = 21 635)	(*n* = 5082)	(*n* = 1275)	(*n* = 371)	(*n* = 2089)	(*n* = 1530)
No hospitalization							
Cases (*n*)	37 410	20 776	4866	1215	353	1962	1428
Medical expenditure (euros)	26 (7–66)	25 (6–69)	28 (5–82)	32 (4–93)	50 (9–123)	144 (93–214)	136 (93–197)
Hospitalization							
Cases (*n*)	1680	859	216	60	18	127	102
Rate (%)	4.30	3.97	4.25	4.71	4.85	6.08	6.67
Odds ratio (vs. optimal)	1.00 Reference	0.91 (0.84–0.99)	0.96 (0.83–1.12)	1.07 (0.82–1.39)	1.09 (0.68––1.76)	1.33 (1.10–1.62)	1.45 (1.17–1.80)
Odds ratio (vs. well controlled)	0.75 (0.62–0.91)	0.69 (0.56–0.84)	0.72 (0.58–0.91)	0.80 (0.58–1.10)	0.82 (0.49–1.37)	1.00 Reference	1.09 (0.83–1.43)
Medical expenditure (euros)	453 (200–804)	476 (223–879)	461 (239–943)	591 (355–925)	583 (394–1584)	621 (380–1122)	642 (356–1106)
In hospitalization (euros)	293 (95–564)	322 (117–618)	315 (108–653)	351 (166–655)	422 (237–1489)	316 (132–764)	321 (138–661)
Cases of ≥7 cumulative days/year (*n*)	966	504	136	38	12	76	68
Rate (%)	2.47	2.33	2.68	2.98	3.23	3.64	4.44
Odds ratio (vs. optimal)	1.00 Reference	0.91 (0.82–1.02)	1.01 (0.84–1.22)	1.12 (0.80–1.56)	1.20 (0.67–2.14)	1.30 (1.01–1.66)	1.55 (1.19–2.03)
Odds ratio (vs. well controlled)	0.77 (0.60–0.99)	0.71 (0.55–0.91)	0.78 (0.59–1.04)	0.87 (0.58–1.29)	0.92 (0.50–1.72)	1.00 Reference	1.20 (0.86–1.68)
Medical expenditure (euros)	696 (485–1136)	726 (476–1268)	756 (419–1171)	720 (527–1226)	1210 (535–2210)	971 (610–1517)	863 (592–1581)
In hospitalization (euros)	515 (335–779)	542 (339–954)	559 (308–898)	501 (292–982)	857 (305–2000)	586 (342–980)	545 (289–1365)
Cases of ≥14 cumulative days/year (*n*)	455	247	68	19	9	48	37
Rate (%)	1.16	1.14	1.34	1.49	2.43	2.30	2.42
Odds ratio (vs. optimal)	1.00 Reference	0.91 (0.77–1.06)	0.98 (0.75–1.27)	1.07 (0.67–1.71)	1.70 (0.87–3.35)	1.50 (1.09–2.07)	1.49 (1.04–2.15)
Odds ratio (vs. well controlled)	0.67 (0.48–0.92)	0.60 (0.44–0.83)	0.65 (0.44–0.95)	0.71 (0.41–1.22)	1.13 (0.55–2.35)	1.00 Reference	1.00 (0.64–1.54)
Medical expenditure (euros)	1077 (688–1810)	1199 (714–2101)	1081 (716–2019)	1221 (645–1992)	1447 (581–2311)	1291 (777–2061)	1396 (922–3120)
In hospitalization (euros)	773 (518–1437)	926 (542–1723)	827 (560–1662)	949 (472–1740)	1402 (407–2162)	865 (493–1723)	1142 (601–2391)
Women aged 55–69 years	(*n* = 18 733)	(*n* = 20 481)	(*n* = 7135)	(*n* = 1704)	(*n* = 450)	(*n* = 6190)	(*n* = 4995)
No hospitalization							
Cases (*n*)	17 639	19 324	6702	1619	428	5707	4638
Medical expenditure (euros)	42 (10–107)	45 (10–113)	45 (9–118)	55 (10–132)	51 (5–130)	154 (100–232)	154 (99–226)
Hospitalization							
Cases (*n*)	1094	1157	433	85	22	483	357
Rate (%)	5.84	5.65	6.07	4.99	4.89	7.80	7.15
Odds ratio (vs. optimal)	1.00 Reference	0.90 (0.83–0.98)	0.93 (0.82–1.04)	0.74 (0.59–0.93)	0.71 (0.46–1.11)	1.11 (0.99–1.25)	0.97 (0.85–1.11)
Odds ratio (vs. well controlled)	0.90 (0.80–1.01)	0.81 (0.72–0.91)	0.83 (0.72–0.95)	0.67 (0.52–0.85)	0.64 (0.41–1.00)	1.00 Reference	0.88 (0.76–1.01)
Medical expenditure (euros)	489 (265–919)	508 (276–1021)	580 (287–1212)	674 (317–1327)	542 (282–908)	597 (345–1177)	663 (370–1399)
In hospitalization (euros)	287 (118–619)	323 (120–687)	389 (139–866)	488 (155–945)	444 (104–724)	293 (105–795)	328 (118–823)
Cases of ≥7 cumulative days/year (*n*)	623	719	278	60	14	319	225
Rate (%)	3.33	3.51	3.90	3.52	3.11	5.15	4.50
Odds ratio (vs. optimal)	1.00 Reference	0.99 (0.88–1.10)	1.04 (0.90–1.21)	0.92 (0.70–1.21)	0.79 (0.46–1.36)	1.27 (1.10–1.47)	1.06 (0.90–1.25)
Odds ratio (vs. well controlled)	0.79 (0.68–0.91)	0.78 (0.68–0.89)	0.82 (0.69–0.97)	0.73 (0.55–0.96)	0.62 (0.36–1.07)	1.00 Reference	0.83 (0.70–0.99)
Medical expenditure (euros)	785 (498–1379)	779 (476–1477)	873 (531–1654)	927 (559–1708)	777 (548–1070)	864 (520–1535)	933 (579–1838)
In hospitalization (euros)	542 (313–1029)	530 (316–1125)	599 (382–1323)	642 (408–1183)	637 (481–927)	572 (276–1105)	582 (314–1454)
Cases of ≥14 cumulative days/year (*n*)	358	405	178	43	11	170	129
Rate (%)	1.91	1.98	2.49	2.52	2.44	2.75	2.58
Odds ratio (vs. optimal)	1.00 Reference	0.95 (0.82–1.10)	1.12 (0.93–1.35)	1.10 (0.80–1.52)	1.00 (0.54–1.85)	1.11 (0.91–1.35)	0.98 (0.79–1.22)
Odds ratio (vs. well controlled)	0.90 (0.74–1.10)	0.85 (0.71–1.03)	1.01 (0.81–1.25)	0.99 (0.70–1.40)	0.90 (0.48–1.68)	1.00 Reference	0.89 (0.70–1.12)
Medical expenditure (euros)	1107 (727–1826)	1283 (750–1990)	1290 (740–1995)	1190 (750–2144)	883 (748–1232)	1336 (914–2112)	1595 (961–2368)
In hospitalization (euros)	827 (512–1496)	945 (529–1635)	997 (544–1672)	915 (581–1648)	678 (612–1025)	963 (635–1740)	1285 (552–91921)

Data are presented for the male and female population stratified according to age at baseline. Optimal blood pressure was defined as an SBP < 120 mmHg and a DBP <80 mmHg; normal-to-high normal blood pressure as an SBP 120–139 mmHg and/or DBP 80–89 mmHg; grade 1 untreated hypertension as an SBP 140–159 mmHg and/or DBP 90–99 mmHg; grade 2 untreated hypertension as an SBP 160–179 mmHg and/or DBP 100–109 mmHg; grade 3 untreated hypertension as an SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg; well controlled hypertension on treatment as an SBP < 140 mmHg and DBP < 90 mmHg on antihypertensive medication; and poorly controlled hypertension on treatment as an SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg on medication. Odds ratios were calculated using a logistic regression model with multivariate adjustment for age, BMI, smoking habits, serum low-density lipoprotein cholesterol, medication for hypercholesterolemia, log-transformed fasting plasma glucose, and medication for diabetes. One euro = 95.91 Japanese yen, 0.79 pounds sterling, and 1.22 US dollars at the foreign exchange rates on 1 August 2012.

TABLE 3. Odds ratios (95% confidence interval) for falling into the top 1% group of medical expenditure in the year after baseline in the 183 862 male and 130 760 female participants, grouped according to hypertension status at baseline

	Optimal blood pressure	Normal-to-high normal blood pressure	Grade 1 untreated hypertension	Grade 2 untreated hypertension	Grade 3 untreated hypertension	Well controlled hypertension on treatment	Poorly controlled hypertension on treatment
Men aged 40–54 years	(*n* = 38 320)	(*n* = 41 063)	(*n* = 12 599)	(*n* = 3594)	(*n* = 1136)	(*n* = 4473)	(*n* = 4112)
Cases (*n*)	191	220	80	41	19	52	56
Rate (%)	0.50	0.54	0.63	1.14	1.67	1.16	1.36
Odds ratio (vs. optimal)	1.00 Reference	1.03 (0.85–1.26)	1.15 (0.88–1.50)	2.07 (1.46–2.92)	3.12 (1.93–5.06)	1.63 (1.18–2.27)	1.92 (1.39–2.65)
Odds ratio (vs. well controlled)	0.61 (0.44–0.85)	0.63 (0.46–0.87)	0.70 (0.49–1.01)	1.27 (0.83–1.93)	1.91 (1.12–3.28)	1.00 Reference	1.17 (0.80–1.72)
Men aged 55–69 years	(*n* = 16 873)	(*n* = 26 726)	(*n* = 12 050)	(*n* = 3677)	(*n* = 997)	(*n* = 9356)	(*n* = 8886)
Cases (*n*)	203	351	187	56	18	183	181
Rate (%)	1.20	1.31	1.55	1.52	1.81	1.96	2.04
Odds ratio (vs. optimal)	1.00 Reference	1.09 (0.91–1.30)	1.25 (1.02–1.54)	1.24 (0.92–1.67)	1.44 (0.88–2.35)	1.46 (1.18–1.80)	1.53 (1.23–1.89)
Odds ratio (vs. well controlled)	0.69 (0.56–0.85)	0.74 (0.62–0.90)	0.86 (0.70–1.06)	0.85 (0.62–1.15)	0.99 (0.60–1.61)	1.00 Reference	1.04 (0.85–1.29)
Women aged 40–54 years	(*n* = 39 090)	(*n* = 21 635)	(*n* = 5082)	(*n* = 1275)	(*n* = 371)	(*n* = 2089)	(*n* = 1530)
Cases (*n*)	247	151	37	10	6	31	22
Rate (%)	0.63	0.70	0.73	0.78	1.62	1.48	1.44
Odds ratio (vs. optimal)	1.00 Reference	1.04 (0.84–1.28)	1.01 (0.71–1.45)	1.09 (0.57–2.08)	2.26 (0.99–5.18)	1.77 (1.19–2.65)	1.67 (1.05–2.67)
Odds ratio (vs. well controlled)	0.56 (0.38–0.84)	0.59 (0.39–0.88)	0.57 (0.35–0.93)	0.62 (0.30–1.27)	1.28 (0.53–3.11)	1.00 Reference	0.94 (0.54–1.64)
Women aged 55–69 years	(*n* = 18 733)	(*n* = 20 481)	(*n* = 7135)	(*n* = 1704)	(*n* = 450)	(*n* = 6190)	(*n* = 4995)
Cases (*n*)	198	250	108	23	2	117	105
Rate (%)	1.06	1.22	1.51	1.35	0.44	1.89	2.10
Odds ratio (vs. optimal)	1.00 Reference	1.08 (0.90–1.31)	1.28 (1.00–1.63)	1.11 (0.72–1.73)	0.35 (0.09–1.41)	1.46 (1.15–1.86)	1.57 (1.21–2.02)
Odds ratio (vs. well controlled)	0.69 (0.54–0.87)	0.74 (0.59–0.93)	0.88 (0.67–1.15)	0.76 (0.48–1.20)	0.24 (0.06–0.97)	1.00 Reference	1.07 (0.82–1.40)

Data are presented for the male and female population stratified according to age at baseline. Optimal blood pressure was defined as an SBP <120 mmHg and a DBP <80 mmHg; normal-to-high normal blood pressure as an SBP 120–139 mmHg and/or DBP 80–89 mmHg; grade 1 untreated hypertension as an SBP 140–159 mmHg and/or DBP 90–99 mmHg; grade 2 untreated hypertension as an SBP 160–179 mmHg and/or DBP 100–109 mmHg; grade 3 untreated hypertension as an SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg; well controlled hypertension on treatment as an SBP < 140 mmHg and DBP < 90 mmHg on antihypertensive medication; and poorly controlled hypertension on treatment as an SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg on medication. Male and female participants who fell into the sex-specific top 1% medical expenditure group each incurred ≥1571 euros/month and ≥1249 euros/month, respectively. Odds ratios were calculated using a logistic regression model with multivariate adjustment for age, BMI, smoking habits, serum low-density lipoprotein cholesterol, medication for hypercholesterolemia, log-transformed fasting plasma glucose, and medication for diabetes. One euro = 95.91 Japanese yen, 0.79 pounds sterling, and 1.22 US dollars, at the foreign exchange rates on 1 August 2012.

regardless of hypertension status. As a consequence, hospitalized cases attributable to overall hypertension, including normal-to-high normal blood pressure, untreated hypertension and treated hypertension incurred 6.9–7.2 and 2.8–3.8% of the total medical expenditure in the male and female study population solely as a consequence of hospitalization. Compared with well controlled hypertension on treatment or grade 1-to-2 untreated hypertension, grade 3 untreated hypertension also had a higher risk of incurring extremely high medical expenditure, such as falling into the top 1% group costing at least 1571 euros/month for men and at least 1249 euros/month for women.

A previous 10-year prospective cohort study in Japan reported that individuals with untreated hypertension had a higher risk of hospitalization and death, and incurred on average higher medical expenditure, compared with normotensive individuals [12]. In contrast to this long-term follow-up study, our 1-year follow-up period may have been suitable for comparing hospitalization risk and medical expenditure for normal blood pressure, untreated hypertension, and treated hypertension, but was unable to identify the reason for hospitalization. This suitability of our study is based on the fact that it is impossible to assume that baseline conditions (i.e., blood pressure levels and treatment status) remain unchanged throughout a long follow-up period. Our data also demonstrated that blood pressure was a predictor of short-term surges in medical expenditure. Although hypertension has an effect on medical expenditure in contrast to optimal blood pressure, good control of hypertension lowers the risk of surges in medical expenditure because of hospitalization of hypertensive individuals. A notable, relevant study carried out in Canada [17] suggested that better adherence to antihypertensive medication correlated with a lower risk of cardiovascular events, hospitalization, and lower total costs in newly treated hypertensive individuals. On the contrary, a study in the United States [16] suggested that hospitalization risk decreased with increased adherence to medication, although there was no significant difference in total costs across adherence levels. Our results on hospitalization risk are consistent with the findings of these previous studies, although our results do not indicate whether treatment of hypertension offsets long-term medical costs. However, our results indicate that hypertensive individuals on medication incur relatively low medical expenditure as long as they remain out of hospital for treatment of hypertension alone.

In Japan, cardiovascular, cerebrovascular, and renal disease incurs 17.8% of the total medical costs in the population aged 45–64 years through any medical cause, whereas the inpatient costs for treatment of these serious vascular diseases account for 9.2% of the total costs [18]. Our estimates suggest that overall hypertension contributes significantly to inpatient medical expenditure for treatment

TABLE 4. Mean values ± standard deviation of inpatient medical expenditure per month and percentages of inpatient medical expenditure attributable to hypertension relative to total medical expenditure in the year after baseline in the 183 862 male and 130 760 female participants, grouped according to hypertension status at baseline, based on the medical insurance system in Japan

	Optimal blood pressure	Normal-to-high normal blood pressure	Grade 1 untreated hypertension	Grade 2 untreated hypertension	Grade 3 untreated hypertension	Well controlled hypertension on treatment	Poorly controlled hypertension on treatment
Men aged 40–54 years	(*n* = 38 320)	(*n* = 41 063)	(*n* = 12 599)	(*n* = 3594)	(*n* = 1136)	(*n* = 4473)	(*n* = 4112)
Inpatient expenditure (euros)	22 ± 236	26 ± 278	31 ± 259	50 ± 377	80 ± 496	46 ± 315	49 ± 334
Percentage of inpatient expenditure attributable to that category relative to total expenditure (%)		1.8	1.2	1.1	0.7	1.2	1.2
Men aged 55–69 years	(*n* = 16 873)	(*n* = 26 726)	(*n* = 12 050)	(*n* = 3677)	(*n* = 997)	(*n* = 9356)	(*n* = 8886)
Inpatient expenditure (euros)	50 ± 332	57 ± 407	64 ± 370	69 ± 384	65 ± 329	72 ± 409	77 ± 447
Percentage of inpatient expenditure attributable to that category relative to total expenditure (%)		1.5	1.3	0.5	0.1	1.6	1.9
Women aged 40–54 years	(*n* = 39 090)	(*n* = 21 635)	(*n* = 5082)	(*n* = 1275)	(*n* = 371)	(*n* = 2089)	(*n* = 1530)
Inpatient expenditure (euros)	21 ± 195	23 ± 239	26 ± 251	38 ± 399	40 ± 247	36 ± 253	55 ± 427
Percentage of inpatient expenditure attributable to that category relative to total expenditure (%)		0.7	0.4	0.3	0.1	0.5	0.8
Women aged 55–69 years	(*n* = 18 733)	(*n* = 20 481)	(*n* = 7135)	(*n* = 1704)	(*n* = 450)	(*n* = 6190)	(*n* = 4995)
Inpatient expenditure (euros)	34 ± 286	35 ± 273	45 ± 335	42 ± 370	31 ± 244	53 ± 351	55 ± 402
Percentage of inpatient expenditure attributable to that category relative to total expenditure (%)		0.2	0.9	0.2	0	1.3	1.2

Data are presented for the male and female population stratified according to age at baseline. Optimal blood pressure was defined as an SBP <120 mmHg and a DBP <80 mmHg; normal-to-high normal blood pressure as an SBP 120–139 mmHg and/or DBP 80–89 mmHg; grade 1 untreated hypertension as an SBP 140–159 mmHg and/or DBP 90–99 mmHg; grade 2 untreated hypertension as an SBP 160–179 mmHg and/or DBP 100–109 mmHg; grade 3 untreated hypertension as an SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg; well controlled hypertension on treatment as an SBP <140 mmHg and/or DBP <90 mmHg on antihypertensive medication; and poorly controlled hypertension on treatment as an SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg on medication. Total medical expenditure was 9191 780 euros for men aged 40–54 years, 12 890 866 euros for men aged 55–69 years, 6441 909 euros for women aged 40–54 years, and 8807 015 euros for women aged 55–69 years. One euro = 95.91 Japanese yen, 0.79 pounds sterling, and 1.22 US dollars, at the foreign exchange rates on 1 August 2012.

of these serous vascular diseases, at least in men. Furthermore, as reported by a national survey in Japan, inpatient medical expenditure attributable to overall hypertension may be broadly comparable to medical expenditure for treatment of hypertension itself [18]. It should be noted that most inpatient medical expenditure attributable to overall hypertension may come from various cases of hypertension other than well controlled hypertension on treatment. In particular, from a population perspective based on the Rose's theory that 'a large number of people exposed to a small risk may generate many more cases than a small number exposed to high risk' [31], it is important not to ignore normal-to-high normal blood pressure and grade 1 untreated hypertension, which are usually nonurgent cases for antihypertensive medication [19]. This will ensure comprehensive prevention of serious clinical outcomes and increased medical expenditure.

Our results in all men and middle-aged women were in accordance with evidence of a positive, graded relationship between blood pressure and risk of cardiovascular, cerebrovascular, and renal disease in individuals not taking antihypertensive medication at baseline [1–5], and also that the efficacy of appropriate antihypertensive treatment lowers the risk of serious vascular diseases in a hypertensive population [20–22,32]. However, we observed a less apparent relationship of increased risk of hospitalization with the severity of untreated hypertension in presenile women, compared with the other sex and age-groups. Although it is difficult to explain these discrepant results, the following facts may account for these differences. In general, the positive relationship between blood pressure and morbidity and mortality risk is less apparent in older than in younger individuals [1,33]. In addition, it is possible the participants may have been misclassified because of a single random blood pressure measurement, especially in women who showed greater differences between screening and home blood pressure measurements (i.e. white-coat hypertension) than men [34,35]. Our results may therefore have been underestimated, especially in women. Furthermore, the small number of untreated severe hypertensive participants and the short-term follow-up period may have resulted in failure to identify the true relationship in women who have a lower morbidity and mortality rate than men [33,36].

The current study had several limitations. First, we could not identify particular diseases that directly increased the risk of undergoing long-term hospitalization or particular treatments that incurred inpatient medical expenditure in hypertensive participants. Second, information on the details of untreated hypertension (e.g. whether hypertension had been recently or previously identified) and the details of treated hypertension (e.g. hypertensive grade before starting medication, prescriptions, and usual control

status) was not available. Of the hypertensive participants on treatment, some may not have taken their antihypertensive medication the morning of the examination day, partially because of screening for gastric cancer at the same time, and may therefore have provided unreliable information on their usual blood pressure on medication. Consequently, they may have been misclassified as poorly controlled, despite their usual blood pressure being well controlled on treatment. Even though the majority of poorly controlled hypertensive participants on treatment were true cases at the baseline survey, medication added after the survey may have led to well controlled hypertension. This possible misclassification may have led to an underestimation of the true effect of poorly controlled hypertension on hospitalization risk. Our results regarding treated hypertension should also be interpreted with caution, as the Japan Arteriosclerosis Longitudinal Study [37] found no stepwise increase in stroke risk across blood pressure levels in hypertensive individuals on medication, and that the risk of stroke was significantly higher even at optimal levels of blood pressure in the medication group compared with optimal blood pressure in the group not taking medication. Third, we could not identify the reason why 0.48% ($n = 1522$) of the participants dropped out mid-study with a median (interquartile range) follow-up period of 7 (3–10) months. The rates of dropout in the five medication-off categories from optimal blood pressure to grade 3 untreated hypertension were 0.37, 0.48, 0.54, 0.46, and 0.24%, whereas the corresponding rates in the well controlled and poorly controlled hypertension on treatment categories were 0.77 and 0.76%, respectively. Further studies are therefore needed to refine the methodological study limitations mentioned above. Finally, this economic topic is dependent on the costs of medical services, which differ across countries. Therefore, our results cannot necessarily be extrapolated to other countries.

In conclusion, our study suggests that hospitalization status is an important determinant when considering medical expenditure associated with hypertension. From an individual viewpoint, severe untreated hypertension is more likely to incur extremely high medical expenditure as a result of hospitalization, compared with well controlled hypertension on treatment or mild untreated hypertension. Using antihypertensive medication to prevent serious clinical outcomes which incur extremely high medical costs may be a key strategy for reducing the disease and economic burden associated with hypertension.

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Conflicts of interest

There are no conflicts of interest.

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Reviewer's Summary Evaluation

Reviewer 1

Strengths: The study investigates the effect of hypertension on hospitalization risk and medical expenditures according to the treatment status in a Japanese population of 314 622 subjects classified into seven blood pressure categories. In both men and women grade 3 untreated hypertension led to a more frequent hospitalization and higher medical expenditures compared with treated hypertension and grade 1–2 untreated hypertension. These data confirm that in grade 3 hypertension medical expenditures of treated subjects are significantly lower than those of untreated subjects.

Weakness: The global cardiovascular risk of the subject has not been reported in detail. The causes directly increasing the risk of long term hospitalization in hypertensive subjects were not identified, and this is a consistent limitation.