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An Analysis of Blood Pressure Situations in Japan Using the Large-Scale Medical Checkup Dataset

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Abstract

Background: The high blood pressure (BP) or hypertension is a widely prevalent disease and its costs are very high, and many studies about the relationships between BP and health conditions have been done. We need to know the precise distributions of BP and factors affecting BP. **Data and Methods:** The distributions of BP are analyzed using 12,877,653 observations obtained from the JMDC Claims Database. The factors that may affect the BP are analyzed by the regression models using 4,615,346 observations. **Results:** The averages of systolic BP (SBP) and diastolic BP (DBP) are 120.4 and 74.2 mmHg with standard deviations of 15.9 and 11.3 mmHg, respectively. Among the nonmodifiable factors, age and gender are important factors. Among the modifiable factors, variables related to obesity are important risk factors. Taking antihypertensive drugs makes SBP and DBP 13.4 mmHg and 7.8 mmHg lower. **Conclusion:** The criteria of BP should be carefully determined considering age and gender. The effects of age may be a little different for SBP and DBP. It is necessary to use the proper model to evaluate the effect of antihypertensive drugs correctly. **Limitations:** The dataset is observatory. Although there are various types of treatment methods and antihypertension drugs, their effects are not evaluated.

Keywords

Blood Pressure, Hypertension, SBP and DBP, Medical Checkups, Antihypertensive Drugs

1. Introduction

The high blood pressure (BP) or hypertension is considered as a major risk fac-

tor of noncommunicable diseases (NCDs). The World Health Organization (WHO) ([1], p. 14) states "Raised blood pressure (hypertension) is considered a major risk factor for the development of several NCDs, including heart and brain diseases." WHO [2] estimated that 1.13 billion people worldwide have hypertension, two-thirds living in low- and middle-income countries, 1 in 4 men and 1 in 5 women had hypertension in 2015, and fewer than 1 in 5 people with hypertension have the problem under control. WHO [3] also provided the percentages of people with hypertension in various countries in 2015. They declared that "one of the global targets for noncommunicable diseases is to reduce the prevalence of hypertension by 25% by 2025 (baseline 2010)." Benjamin *et al.* [4] reported that 874 million adults worldwide had systolic BP (SBP) ≥ 140 mm Hg. According to Blood Pressure UK [5], a general guide of SBP and diastolic BP (DBP) is given by 140/90 mmHg (SBP/DBP) or over (that means at least one of them are equal to or higher than the given figures): high blood pressure or hypertension; 120/80 mmHg up to 140/90 mmHg: pre-high blood pressure; 90/60 mmHg up to 120/80 mmHg: ideal blood pressure; and 90/60 mmHg or lower: low blood pressure.

Although the 140/90 mmHg criterion had been used in the United States, the American College of Cardiology (ACC), American Heart Association (AHA) and nine other organizations presented the new guideline in 2017 (2017 ACC/AHA Guideline). In the 2017 ACC/AHA Guideline, the criterion for hypertension is 130/80 mmHg [6] [7] [8]. Based on the 2017 ACC/AHA Guideline, the Center for Disease Control and Prevention (CDC) [9] classifies the BP category as normal: SBP < 120 mmHg and DBP < 80 mmHg; elevated: SBP is 120 - 129 mmHg and DBP < 80 mmHg; Hypertension Stage 1: SBP is 130 - 139 mmHg or DBP is 80 - 89 mmHg; and Hypertension Stage 2: SBP ≥ 140 mmHg or DBP ≥ 90 mmHg. Ostchega *et al.* [10] reported that the prevalence of age-adjusted hypertension in the United States was 45.4% in the survey period 2017-2018 under the 2027 ACC/AHA Guideline. They also reported that hypertension increased with age.

However, other organizations such as the American Diabetes Association (ADA) [11], the American Academy of Family Physicians (AAFP) [12], an organization that initially adopted the 2017 ACC/AHA Guideline, the European Society of Cardiology and the European Society of Hypertension (ESC/ESH) [13], Hypertension Canada [14] [15], and the Japanese Society of Hypertension [16] maintained the diagnostic guideline of 140/90 mmHg for hypertension.

In Japan, the number of hypertension patients who visited hospitals and clinics on the survey day was 9937 thousand in 2017 [17]. The hypertension cost 1.748 trillion yen or 4.0% of the total medical expenditures, 43.395 trillion yen in fiscal year 2018 [18].

Since hypertension is a widely prevalent disease and its costs are very high, enormous studies about the relationships between BP and health conditions, especially heart diseases (HD), have been done. Framingham Heart Study (FHS) [19] has been continuously conducted 1948 in Framingham, Massachusetts in

the United States. The study has found that gender (being male), age, cholesterol, SBP and diabetes are risk factors of cardiovascular disease (CVD). Joffres *et al.* [20] analyzed BP using the Canadian Heart Health Survey and the US National Health and Nutrition Examination Survey (NHANES) III data. They reported about half of diabetes patients had hypertension and were poorly managed. The Prospective Studies Collaboration [21] performed a meta-analysis using individual data for one million adults obtained from the results of 61 prospective studies. They reported that deaths due to ischemic HD increased as SBP and DBP increased in all age cohorts. Rapsomaniki *et al.* [22] conducted an analysis of 1.25 million people using the CALIBAR (CArdiovascular research using LInked Bespoke studies and Electronic health Records). They concluded that the lifetime risks of CVD with hypertensive individuals were higher than those with normotensive individuals.

The Systolic Blood Pressure Intervention Trial (SPRINT) [23] was a trial in which individuals with SBP of 130 mmHg or higher and an increased CVD risk, but without diabetes, were randomly assigned into two groups. One group was the intensive treatment group with an SBP target less than 120 mmHg and the other was the standard treatment group. Lower rates of fatal and nonfatal major cardiovascular events and of death from any cause in the intensive treatment group were reported in this study. This study was heavily weighted in the 2017ACC/AHA Guideline. The Action to Cardiovascular Risk in Diabetes (ACCORD) study [24] was done to individuals with type 2 diabetes. SPRINT used the style of this study. Unlike SPRINT, the ACCORD study did not find that lowering the SBP below 120 mmHg reduced the major CVD or death rates. Ettehad *et al.* [25] *et al.* performed a meta-analysis based on selected 123 studies that focused on lowering BP from 1966 to 2015. They reported that treatments for lowering BP significantly reduced the major CVD risk. Muntner *et al.* [26] used data from the 2011-2012 and 2013-2014 cycles of NHANES. They mentioned that the 2017 ACC/AHA Guideline would increase the use of hypertension drugs and lower the prevalence of CVD events.

In Japan, the Ministry of Health, Labour and Welfare conducted a survey of SBP and DBP for individuals age 20 or over in 2019 [27]. The averages and standard deviations (SD) of SBP were 132 mmHg and 17.7 mmHg for male, and 126.5 mmHg and 11.4 mmHg for female. Those of DBP were 76.2 mmHg and 11.4 mmHg for male, and 73.1 mmHg and 10.7 mmHg for female. The problem of the survey is that the data contains only 2601 individuals, 1089 males and 1512 females. The Hisayama Study [28] has been done since 1961 to residents of Hisayama in Fukuoka Prefecture. Honda *et al.* [29] analyzed the data of residents aged 40 - 84 for 24 years. They found that age, gender, SBP, hemoglobin A1c (HbA1c), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), smoking and daily exercise as significant factors of CVD. Fujiyoshi *et al.* [30] analyzed the relation between BP and reported a positive relation between CVD and BP. Asayama *et al.* [31] analyzed the mortality risk caused by CVD using the dataset of selected 6 cohorts and reported that the

higher of CVD mortality risk for individuals without treatment even if the effects of various characteristics of individuals were removed.

Nawata *et al.* [32] evaluated BP using a dataset of 113,979 medical checkup observations obtained from 48,022 individuals belonging to one health insurance society in Japan from April, 2013 to March, 2016. They performed regression analysis and reported that factors affecting BP were age, gender, some eating habits, daily activities, smoking, drinking alcohol, sleeping and wages. Especially, age was a very important factor. Nawata and Kimura [33] discussed about the accuracy of the BP measurements. They found that the "white coat effect" was significant and suggested that the careful payments for upward errors of BP measurements were necessary. Nawata, Sekizawa and Kimura [34] pointed out the problems of the previous BP studies. They are: since the participants and doctors (or researchers) can easily know that the groups (treated or controlled) that they are belonging, the double blinded randomized clinical trials are impossible for the BP studies; trials with positive results are more likely to be published than those with negative or questionable results; researchers themselves might not have strong incentives to publish when the expected results are not obtained; in many studies sponsored by the pharmaceutical companies, biases toward the sponsor's products and conflicts of interest (CI) might occur; and practices are often terminated in the early stages for various reasons especially when expected results are not obtained (termination or endpoint biases). Moreover, in the meta-analyses or systematic reviews, that make the numbers of observations larger by combining various studies, the selection criteria of studies should be determined in advance. However, the criteria were often determined after studies finished. Therefore, we need reliable protocols such as proposed by Yu *et al.* [35] for the meta-analyses or systematic reviews.

Nawata and Kimura [36] [37] evaluated the medical expenditures using a dataset containing 175,123 medical checkup observations and 6,312,125 receipts from 88,211 individuals obtained from April 2013 to March 2016. They could not find evidence that higher SBP made the medical costs and probability of having HD higher. They concluded the results did not support the new 2017 ACC/AHA guideline for SBP and suggested that a wide and careful range of reviews not only for HD but also for other disease types would be absolutely necessary. Nawata, Sugano and Kimura [38] analyzed the effects of BP, antihypertensive drugs and other factors on the probability of undergoing HD treatments using a dataset containing 83,287 medical check-up and treatment records obtained from 35,504 individuals in 5 fiscal years. They could not find evidence that a higher SBP increased the probability of undergoing HD treatment. However, DBP increased the probability of HD in most of the models. Taking antihypertensive drugs also increased the probability of undergoing HD treatment. Nawata [39] evaluated the risk factors for ischemic stroke using with 59,341 and 50,542 observations. The factors were divided into nonmodifiable and modifiable factors. He reported that age, gender and cerebrovascular disease history were important risk factors among the nonmodifiable factors. For modifiable

factors, he found that taking antihypertensive drugs and recent large weight change were risk factors but sleeping well significantly reduced the risk of ischemic stroke.

More recently, Kaneko *et al.* [40] evaluated the heart failure (HF) and atrial fibrillation (AF). They used the JMDC Claims Database from 2005 and 2018 containing 2,196,437 observations. Individuals that were neither taking antihypertensive medication nor had a known history of cardiovascular disease were selected. The Cox-Proportional hazard model was used. 28,056 HF incidents and 7774 AF incidents occurred over a mean follow-up of 1112 ± 854 days. They reported that both Stage 1 (SBP 130 - 139 mm Hg or DBP 80 - 89 mm Hg) and Stage 2 (SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg) hypertension were associated with a greater incidence probability of HF and AF. They concluded that the ACC/AHA BP classification system might help identify adults at higher risk for HF and AF incidents. However, the individuals taking antihypertensive drugs were not included and some factors that might affect BP were not considered in their study. Akbay *et al.* [41] reported that a disruption of the circadian rhythm damaged target organs more seriously than the BP level in masked hypertension.

In addition to traditional NCDs, the relation of the coronavirus disease 2019 (COVID-19), caused by syndrome coronavirus 2 (SARS-CoV-2), and hypertension has become a very important issue that the world has been facing now. WHO ([1], p. viii) states "In the event of a health emergency such as COVID-19, patients with pre-existing NCD conditions such as hypertension and diabetes, become more vulnerable and at higher risk of dying, ...". The major antihypertensive drugs include angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists (ARB) [42]. It was suggested that ACE2 might be related to the infection of SARS [43] [44] and SARS-CoV-2 [45] [46]. ACE inhibitors and ARB might affect the rennin-angiotensin-aldosterone system (RAAS) and the ACE2 generating process. European Medicines Agency (EMA) [47] states "EMA therefore reiterates its previous advice that patients should continue to use ACE inhibitors or ARBs as advised by their doctors." WHO [48] mentions "There is low-certainty evidence that patients on long-term therapy with ACE inhibitors or ARBs are not at higher risk of poor outcomes from COVID-19." ACC, AHA and Heart Failure Society of America (HFSA) [49] admits "but there are no experimental or clinical data demonstrating beneficial or adverse outcomes among COVID-19 patients using ACE-I or ARB medications." Quite a few studies have been doing for these subjects [50]-[69].

Since BP is an important health factor, we need to know the precise distributions of SBP and DBP including healthy individuals. It is also important to find out factors that may affect SBP and DBP. In the study of Nawata [32] *et al.*, the number of observations was limited. Moreover, since the data were obtained from only one health insurance society, the sample selection bias might occur. The sample period was 3 years and it was not possible to evaluate the long term trend of BP. In this paper, I use the JMDC Claims Database and reevaluate BP in Japan. The database contains information of medical payments, treatments and

13,157,681 medical checkup observations obtained from 3,233,271 individuals in Japan. Studies using this size of observations were never done before and it would help us to get fundamental knowledge of the BP situation. First, the distributions of SBP and DBP are evaluated, and then factors affecting the SBP and DBP are analyzed.

2. Data and Distribution of BP

2.1. Medical Checkup Observations

In Japan, the Industrial Safety and Health Act requires for most employees age 40 or older to take mandatory medical checkups once a year independent of their health conditions. Their family members may also take medical checkups on a voluntary basis. In this paper, I use the JMDC Claims Database that is a nationwide health claims database collecting medical information from various health insurance societies throughout Japan. The results of health and medical checkups, including BP measurements, of all employees (including normal healthy ones) and their family members (voluntary) of companies joining the health insurance societies are available. It contains 13,157,681 medical checkup observations obtained from 3,233,271 individuals, and the sample period is the January 2005 and to September 2019; that is, for 15 years and 9 months.

2.2. Distributions of SBP and DBP

Figure 1 and Figure 2 are the distributions of SBP and DBP obtained from 12,877,653 medical checkup observations and the summary of SBP and DBP distribution is given in Table 1. The averages and SD of all observations are 120.4 mmHg and 15.9 mmHg for SBP and 74.2 mmHg and 11.3 mmHg for DBP, respectively. Among all observations, 10.6% and 25.4% are classified as SP hypertension for 140 mmHg and 130 mmHg criteria, respectively. On the other hand, 9.6% and 32.3% are classified as DP hypertension for 90 mmHg and 80 mmHg criteria. For 140/90 and 130/90 mmHg criteria, 14.0% and 38.0% are classified as hypertension.

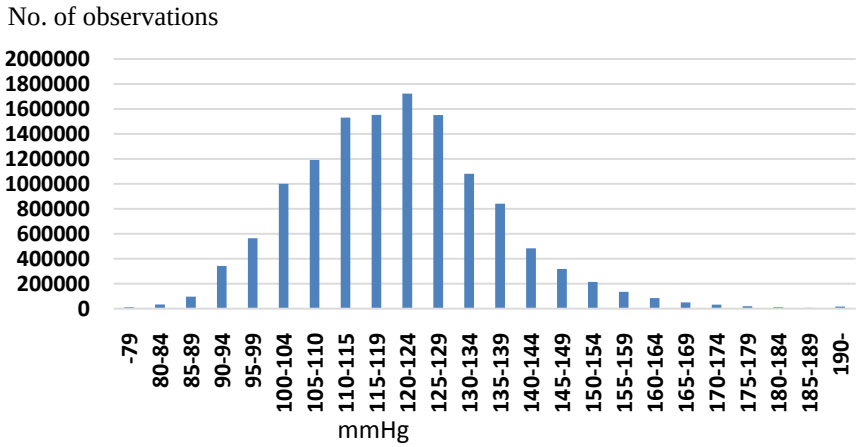

Figure 1. Distribution of systolic blood pressure (SBP).

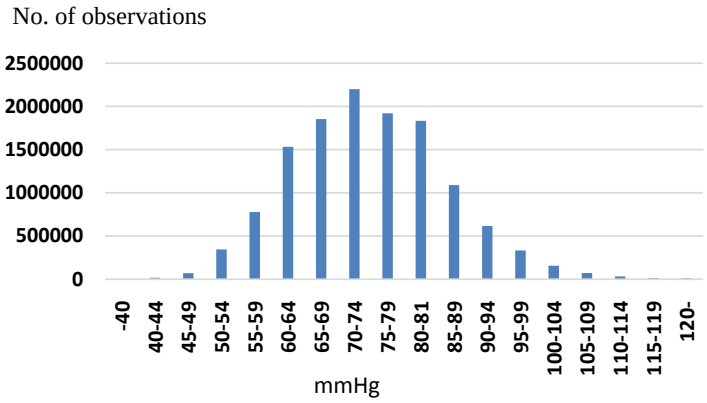

Figure 2. Distribution of systolic blood pressure (DBP).

Table 1. Summary of BP distributions.

	All		Male		Female	
	SBP	DBP	SBP	DBP	SBP	DBP
Average	120.4	74.2	123.1	76.3	115.0	70.0
Median	120	74	122	76	113	69
Maximum	297	150	297	150	270	150
Minimum	60	30	62	30	60	30
SD	15.9	11.7	14.9	11.3	16.5	11.3
No. of observations	12,877,653		8,704,744		4,172,909	

SD: Standard deviation.

3. Analyses of Factors Affecting BP by Regression Models

In this section, I analyze the factors that may affect the BP. Age, gender, a type of a membership and time trend are used as nonmodifiable factors. Body mass index (BMI), results of blood and urine tests, eating habits, physical conditions, alcohol consumptions and smoking are used as nonmodifiable factors.

3.1. SBP

First, I consider a simple model to evaluate the gross effects of nonmodifiable factors given by (Model 1A):

$$SBP_i = \beta_1 + \beta_2 Age1 + \beta_3 Age1^2 + \beta_4 Family + \beta_5 Female + \beta_6 t1 + u_i \quad (1)$$

where $Age1$ = age-17 because the youngest age in the data set is 18 and $t1$ represents the time trend, $t1$ = year-2004. Excluding observations with missing values, a total of 12,877,653 observations are used in the estimation. The annual numbers of observations are given in **Figure 3**. The average and SD of age are 45.4 and 11.3 years, respectively. The effect of age may not be a linear function, so the quadric term of $Age1$ is included. *Female* represents gender (1: female, 32.4%; 0: otherwise, 67.6%), and *Family* represents a type of memberships (1: family member, 15.6%; 0: employee, 84.4%). The results of the estimation are given under "Model 1A" in **Table 2**. Since the number of observations is quite

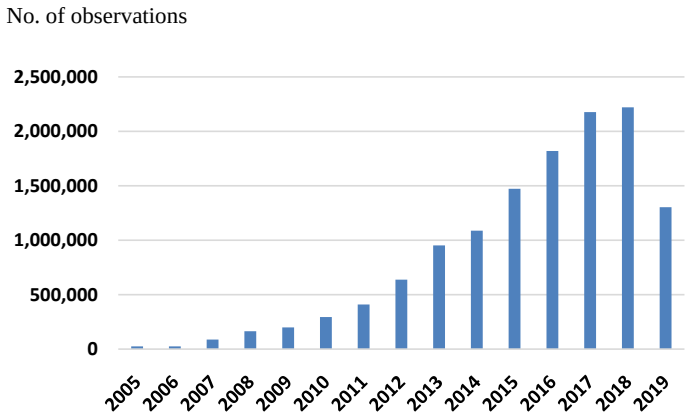

Figure 3. Annual numbers of observations.

Table 2. Results of estimation: SBP equations.

	Model 1A		Model 1B		Model 1C	
Variable	Estimates	SE	Estimates	SE	Estimates	SE
Constant	106.1904	0.0445	76.4662	0.1007	70.4536	0.1206
*Age*1	0.0103	0.0015	−0.1176	0.0032	−0.2974	0.0050
$Age1^2$	0.0064	0.0000	0.0076	0.0001	0.0063	0.0001
Female	−7.8498	0.0113	−4.1308	0.0207	−4.2669	0.0209
Family	−0.6589	0.0148	0.3901	0.0221	0.3117	0.0225
*t*1	−0.2322	0.0015	−0.2395	0.0033	−0.2607	0.0033
BMI			1.3260	0.0025	1.5357	0.0032
HDL			0.0739	0.0005	0.0703	0.0005
LDL			0.0133	0.0002	−0.0032	0.0003
Triglyceride			0.0129	0.0001	0.0133	0.0001
ALT			−0.0126	0.0007	−0.0133	0.0008
AST			0.0428	0.0011	0.0483	0.0015
GGP			0.0174	0.0002	0.0220	0.0002
B_Sugar			0.1199	0.0006	0.1337	0.0007
HbA1c			−2.0173	0.0175	−1.8342	0.0197
U_Sugar			−0.5545	0.0186	−0.4784	0.0209
U_Protein			0.7996	0.0142	1.3231	0.0168
*Weight_*1			−0.6715	0.0158	−0.7016	0.0155
*Weight_*20			0.2249	0.0174	0.4025	0.0177
Eat_fast			−0.2824	0.0147	−0.1661	0.0146
Late_supper			−0.1235	0.0153	−0.2055	0.0151
No_breakfast			0.7229	0.0183	0.5541	0.0182
Exercise			−0.2817	0.0172	−0.3971	0.0174
Activity			0.0632	0.0147	0.0273	0.0147
Speed			−0.0963	0.0138	−0.2862	0.0139
Sleep			0.3104	0.0138	0.3071	0.0137

Continued

Alcohol_freq		0.9488	0.0131	1.0050	0.0131
Alcohol_amount		−0.0366	0.0089	0.0557	0.0088
Smoke		−0.6200	0.0166	−0.9886	0.0169
E(*Antihypertensive*)				−13.3434	0.1264
R^2	0.1254	0.2432		0.2451	
No. of Observations	12,877,653	4,620,677		4,615,346	

SE: Standard error.

larger, all variables are highly significant. SBP increases by 3.4 mmHg from age 40 to 50 and 5.0 mmHg from age 50 to 60, respectively. The estimate of Female is −7.8 mmHg and there is a big difference between males and females. Being a family member slightly reduces SBP. The estimate of $t1$ is negative and we admit ted that there is a declining time trend in BP.

Next, I consider the model containing both nonmodifiable and modifiable factors. First, I consider the model (Model 1B):

$$\begin{aligned} SBP_i = {} & \beta_1 + \beta_2 Age1 + \beta_3 Age1^2 + \beta_4 Female + \beta_5 t1 + \beta_6 BMI + \beta_7 HDL \\ & + \beta_8 LDL + \beta_9 Triglyceride + \beta_{10} ALT + \beta_{11} AST + \beta_{12} GGP + \beta_{13} B\_Sugar \\ & + \beta_{14} HbA1c + \beta_{15} U\_Sugar + \beta_{16} U\_Protein + \beta_{17} Weight\_1 \\ & + \beta_{18} Weight\_20 + \beta_{19} Eat\_fast + \beta_{20} Late\_supper + \beta_{21} No\_breakfast \\ & + \beta_{22} Exercise + \beta_{23} Activity + \beta_{24} Walk\_fast + \beta_{25} Sleep \\ & + \beta_{26} Alcohol\_freq + \beta_{27} Alcohol\_amount + \beta_{28} Smoke + u_i . \end{aligned} \quad (2)$$

The definition and summary of these variables are given in Table 3. A total of 4,620,677 observations that have no missing values for any of the explanatory variables are used. The results of the estimation are given under "Model 1B" in Table 2. As before, all the variables are significant at any reasonable level; even the largest p-value is less than 10^{-6}. For age, the estimate of *Age*1 is negative and that of $Age1^2$ is positive. Since both of *Age*1 and $Age1^2$ are functions of age, they must evaluate simultaneously (the estimate of *Age*1 determines the age which minimizes SBP). From these estimates, we can calculate that the SBP takes the minimum value at age around 25, and it increases by 3.0 mmHg from age 40 to 50 and 4.6 mmHg from age 50 to 60, respectively. For gender and the time trend, we get the similar results as those of Model 1A and these variables are quite important even after various characteristics of individuals are considered. For the variables measured at the medical checkups, the estimates of *BMI*, *HDL LDL*, *Triglyceride*, *AST*, *GGP*, *B_Sugar* and *U_Protein* are positive, and those of *ALT*, *HbA1c* and *U_Sugar* are negative. For the weight changes, the estimate of *Weight_*1 is positive but that of *Weight_*20 is negative. For eating habits and physical conditions, the estimates of *No_breakfast*, *Activity* and *Sleep* are positive but those of *Eat_fast*, *Late_supper*, *Exercise* and Speed are negative. For alcohol drinking, the estimate of *Alcohol_freq* is positive but that of *Alcohol_amount* becomes negative. The estimate of *Smoke* becomes negative.

Table 3. Definitions and summaries of explanatory variables.

Variable	Definition	Summary	
		Average	SD
age		47.9	9.73
Female	1: Female; 0: otherwise	1: 39.5%; 0: 60.5%	
Family	1: Famlly member; 0: otherwise	1: 22.2%; 0: 77.8%	
BMI	body mass index = height (m)/weight (kg)^2	23.0	3.67
HDL	high density lipoprotein cholesterol blood, mg/dL	63.6	16.85
LDL	low-density lipoprotein cholesterol, mg/dL	121.7	30.98
Triglyceride	mg/dL	108.1	85.84
ALT	alanine aminotransferase, U/L	22.3	10.68
AST	aspartate aminotransferase, U/L	23.2	17.68
GGP	γ-glutamyl transferase, units per lite	95.6	18.49
B_Sugar	blood sugar, mg/dL	38.1	45.46
HbA1c	hemoglobin A1c, %	5.5	0.61
U_Sugar	urine sugar, integers of 1 - 5; 1: undetected, 2: around 50 mg/dL, 3: around 100 mg/dL, 4: around 250 mg/dL and 5: around 500 mg/dL or over; 1 is normal, 5 is worst	1: 97.82%; 2: 0.47%; 3: 0.53%; 4: 0.39%; 5: 0.79%	
U_Protein	urine protein, integers of 1 - 5; 1: undetected, 2: around 15 mg/dL, 3: around 30 mg/dL, 4: around 100 mg/dL and 5: around 250 mg/dL or over; 1 is normal, 5 is worst	1: 88.96%; 2: 7.91%; 3: 2.38%; 4: 0.59%; 5: 0.15%	
Weight_1	1: weight changed by 3 kg or more in a year; 0: otherwise	1: 26.5%; 0: 73.5%	
Weight_20	weight increased by 10 kg or more from age 20	1: 35.3%; 0: 64.7%	
Eat_fast	1: eating faster than other people; 0: otherwise	1: 32.5%; 0: 67.5%	
Late_supper	1: eating supper within two hours before bedtime three times or more in a week; 0: otherwise,	1: 32.1%; 0: 67.9%	
No_breakfast	1: not eating breakfast three times or more in a week; 0: otherwise	1: 18.1%; 0: 81.9%	
Exercise	1: doing exercise for 30 minutes or more twice or more in a week for more than a year; 0 otherwise	1: 21.7%; 0: 78.3%	
Activity	1: doing physical activities (walking or equivalent) for one hour or more daily, 0: otherwise	1: 35.7%; 0: 64.3%	
Speed	1: walking faster than other people of a similar age and the same gender; 0: otherwise	0: 45.1%; 0: 54.9%	
Sleep	1: sleeping well; 0: otherwise	1: 45.1%; 0: 54.9%	
Alcohol_freq	0: not drinking alcoholic drinks, 1: sometimes, 2: everyday	0: 40.9%; 1: 33.8%; 2: 25.4%	
Alcohol_amount	0: not drinking; 1: drinking less than 180 ml of Japanese sake wine (with an alcohol percentage of about 15%) or equivalent alcohol in a day when drinking; 2: drinking 180 - 360 ml; 3: drinking 360 - 540 ml; 4: drinking 540 ml or more,	0: 40.9%; 1: 22.2%; 2: 22.6%; 3: 10.6%; 4: 3.7%	
Smoke	1: smoking; 0: otherwise	1: 25.1%; 2: 74.9%	
Antihypertensive	1: taking antihypertensive drugs, 0: otherwise	1: 11.7%; 0: 88.3%	

SD: Standard deviation; *GGP*, *AST* and *ALT* are mainly related to liver functions.

For BP, taking the antihypertensive drugs or not is an important factor. However, whether an individual takes antihypertensive drugs depends on the BP level. In other words, an individual with higher BP is more likely to take antihypertensive drugs. So, we cannot directly use *Antihypertensive* (taking antihypertensive drugs: 1; 0: otherwise) dummy because of the endogeneity problem (actually, if we directly use *Antihypertensive* in the regression equation, its estimate becomes + 4.80 mmHg). Nawata, Sekizawa and Kimura [34] suggested a method to take the expected value of the variable to solve the endogeneity problem, the following model evaluating the effect of *Antihypertensive*. (Model 1C):

$$SBP_i = x_i'\beta + \gamma E\left(Antihypertensive\right) + v_i, \tag{3}$$

where x_i and β are vectors of the explanatory variables and parameters in Model 1B, respectively. The model evaluates the net effects of variables including *Antihypertensive.* Note that the error terms become heteroscedastic, White's method [70] is used to calculate the standard error. A total of 4,615,346 observations that have no missing values for any of the explanatory variables are used. Although the number of observations is 0.12% fewer than the previous model, the values of explanatory variables are very similar. In terms of averages, the largest relative error is 0.036%. So, I do not present the summaries of variables for this model to avoid unnecessary duplications. E (*Antihypertensive*) is estimated by the probit model and the results of the probit estimation are given in Table 4. The results of estimation are given under "Model 1C" in Table 2. The results show the very similar tendency to those of Model 1B for the estimates of

Table 4. Results of estimation: Probit model.

Variable	Estimates	SE	Variable	Estimates	SE
Constant	−6.2393	0.0165	*U_Sugar*	−0.0058	0.0019
*Age*1	0.1358	0.0008	*U_Protein*	0.1728	0.0016
$Age1^2$	−0.0009	0.0000	*Weight_*1	−0.1456	0.0022
Female	−0.1174	0.0031	*Weight_*20	0.0438	0.0017
Family	0.0045	0.0034	*Eat_fast*	0.0446	0.0011
*t*1	−0.0104	0.0005	*Late_supper*	0.0582	0.0019
BMI	0.0918	0.0003	*No_breakfast*	−0.0215	0.0021
HDL	−0.0019	0.0001	*Exercise*	−0.0867	0.0027
LDL	−0.0064	0.0000	*Activity*	−0.0231	0.0022
Triglyceride	0.0001	0.0000	*Speed*	−0.0158	0.0020
ALT	0.0041	0.0001	*Sleep*	−0.0722	0.0019
AST	0.0025	0.0001	*Alcohol_freq*	0.0111	0.0021
GGP	−0.0014	0.0001	*Alcohol_amount*	0.0566	0.0022
B_Sugar	0.0013	0.0000	*Smoke*	−0.008199	0.001869
HbA1c	0.0194	0.0020			
Log likelihood	−1243885				

SE: Standard error.

x_i . Except *LDL* and *Alcohol_amount*, the estimates have the same signs. For the estimate of $E(Antihypertensive)$, representing the reduction of SBP by taking antihypertensive drugs, is −13.3 mmHg and significant reduction of SBP is admitted by taking antihypertensive drugs.

3.2. DBP

DBP is analyzed using the same three models as before. The models are:

Model 2A:

$$DBP_i = \beta_1 + \beta_2 Age1 + \beta_3 Age1^2 + \beta_4 Family + \beta_5 Female + \beta_6 t1 + u_i . \quad (4)$$

Model 2B:

$$\begin{aligned} DBP_i = {} & \beta_1 + \beta_2 Age1 + \beta_3 Age1^2 + \beta_4 Female + \beta_5 t1 + \beta_6 BMI + \beta_7 HDL \\ & + \beta_8 LDL + \beta_9 Triglyceride + \beta_{10} ALT + \beta_{11} AST + \beta_{12} GGP + \beta_{13} B\_Sugar \\ & + \beta_{14} HbA1c + \beta_{15} U\_Sugar + \beta_{16} U\_Protein + \beta_{17} Weight\_1 \\ & + \beta_{18} Weight\_20 + \beta_{19} Eat\_fast + \beta_{20} Late\_supper + \beta_{21} No\_breakfast \\ & + \beta_{22} Exercise + \beta_{23} Activity + \beta_{24} Walk\_fast + \beta_{25} Sleep \\ & + \beta_{26} Alcohol\_freq + \beta_{27} Alcohol\_amount + \beta_{28} Smoke + u_i . \end{aligned} \quad (5)$$

Model 2C:

$$DBP_i = x_i'\beta + \gamma E\left(Antihypertensive\right) + v_i . \quad (6)$$

The numbers of the observations are the same as the SBP case. The results of the estimation are given in Table 5. As the SBP case, almost variables are significant at any reasonable. The p-values are quite small except *Eat_fast* in Model B (the p-value is 0.0011) and *Speed* in Moles 2B and 2C (p-values are 0.0001 and 0.0013, respectively). The estimates of $Age1^2$ become negative in Models 2A and 2C. In Model 2A, in which the gross effect of age is evaluated, DBP increases by 3.2 mmHg from age 40 to 50 and 1.9 mmHg from age 50 to 60, respectively. The effects of most other variables affecting DBP are similar to those in the SBP models. The signs of estimates are the same as those of the SBP models except *ALT* in Models 2B and 2C, and *Activity* and *Alcohol_amount* in Model 2B. For the estimate of E (*Antihypertensive*), representing the reduction of DBP by taking antihypertensive drugs, is −7.8 mmHg and significant reduction of DBP is also admitted by taking antihypertensive drugs.

Table 5. Results of estimation: DBP equations.

	Model 2A		Model 2B		Model 2C	
Variable	Estimates	SE	Estimates	SE	Estimates	SE
Constant	77.3782	0.0321	49.9643	0.0878	42.7498	0.1210
*Age*1	0.6639	0.0011	−0.1176	0.0032	0.4283	0.0023
$Age1^2$	−0.0062	0.0000	0.0076	0.0001	−0.0021	0.0000
Female	−5.7849	0.0082	−3.5992	0.0150	−3.6802	0.0150
Family	−1.5058	0.0106	−0.5272	0.0159	−0.5713	0.0160

Continued

*t*1	−0.0474	0.0011	−0.0721	0.0024	−0.0844	0.0023
BMI			0.8064	0.0018	0.9294	0.0023
HDL			0.0451	0.0004	0.0430	0.0004
LDL			0.0154	0.0002	0.0057	0.0002
Triglyceride			0.0103	0.0001	0.0105	0.0001
ALT			0.0095	0.0005	0.0090	0.0006
AST			0.0142	0.0008	0.0175	0.0009
GGP			0.0135	0.0001	0.0161	0.0002
B_Sugar			0.0643	0.0004	0.0724	0.0005
HbA1c			−1.3314	0.0126	−1.2238	0.0134
U_Sugar			−0.4520	0.0135	−0.4073	0.0140
U_Protein			0.6776	0.0102	0.9851	0.0118
*Weight_*1			−0.4665	0.0114	−0.4841	0.0113
*Weight_*20			0.4440	0.0125	0.5490	0.0128
Eat_fast			−0.0346	0.0106	0.0341	0.0106
Late_supper			−0.1322	0.0111	−0.1798	0.0110
No_breakfast			0.5804	0.0132	0.4815	0.0133
Exercise			−0.3097	0.0124	−0.3771	0.0125
Activity			−0.1203	0.0106	−0.1412	0.0106
Speed			−0.0401	0.0100	−0.1511	0.0101
Sleep			0.2808	0.0099	0.2790	0.0099
Alcohol_freq			0.9026	0.0095	0.9394	0.0095
Alcohol_amount			0.2350	0.0064	0.2891	0.0065
Smoke			−1.0514	0.0120	−1.2649	0.0123
E(*Antihypertensive*)					−7.8403	0.0895
R^2	0.1254		0.2504		0.2517	
No. of Observations	12,877,653		4,620,677		4,615,346	

SE: Standard error.

4. Discussion

Age is a very important variable affecting both SBP and DBP as previous studies. The quadric terms of age are significant, and the effects of age may not be a linear function. Moreover, the effects of age are a little different between different SBP and DBP. The estimates of quadric terms of age are positive for SBP. SBP increases rapidly as age increases. However, for DBP, the estimates of quadric terms are negative in Models 2A and 2C. In these models, DBP becomes higher as an individual becomes older; however, the increasing rate becomes smaller. Miura Nagai and Ohkubo [71] reported that SBP had been declining for 50 years for all ages and genders; however, for DBP, the same trend was observed for fe-

males but not males. Therefore, the effects of age should be carefully revised to get more precise evaluations for both SBP and DBP.

A large difference between males and females is admitted both in SBP and DBP in all models. As pointed out before [32], this fact raises the question of whether the same BP criterion should be used for hypertension regardless of gender. Being a family member makes SBP higher in Models 1B and 1C, and DBP lower in Models 2A, 2B and 2C. But the effects are rather small (0.3 mmHg and −0.6 mmHg in Models 1C and 2C, respectively). The declining time trends of both SBP and DBP are observed in all models; that is consistent to the previous study [72].

For the evaluation of modifiable variables, not only values of estimates but also dispersions of variables become important. The results of Models 1C and 2C are used in the following analysis. For quantitative variables, the effect of a variable is measured by a product of its estimate and SD. The values of *BMI* and *B_sugar* become 4.8 mmHg and 5.5 mmHg for SBP and 3.0 mmHg and 2.9 mmHg for DBP. This means that *BMI* and *B_sugar* are very important to control BP, and these variables are related to obesity and preventing obesity may improve the BP conditions. The absolute values of other variables are at most 1.2 mmHg for SBP and 0.9 mmHg for DBP. The effects of qualitative variables are measured by their estimates except *U_Protein*, *Alcohol_freq* and *Alcohol_amount*. (Although *U_Sugar* takes from 1 to 5, the most of observations take 1 or 2.) The effect of Smoke is −1.0 mmHg and −1.3 mmHg for SBP and DBP, however, other negative effects of smoking are not considered in this study. The effects of other variables are relatively small and the absolute effects are less than 0.6 mmHg for both SBP and DBP. SBP and DBP increase by 1.3 mmHg and 1.0 mmHg if *U_Protein* increases by 1. Since the percentages of observations for *U_Protein* of 2, 3, 4 and 5 are 7.9%, 2.4%, 0.4% and 0.8%, respectively, *U_Protein* is also an important variable to control BP. In case of alcohol drinking, the SBP and DBP of heavy drinkers (who drink 540 ml or more every day) are 2.2 mmHg and 3.0 mmHg higher than those of non-alcohol drinkers.

The taking antihypertensive drugs make SBP and DBP 13.4 mmHg and 7.8 mmHg lower, and significant reduction is admitted. Note that if we directly use the *Antihypertensive* dummy in the regression equations, the estimates become +4.8 mmHg and +3.3 mmHg; that shows the importance and usefulness of the method used in this study.

5. Conclusions

In this paper, BP in Japan is evaluated using the JMDC Claims Database containing 13,157,681 medical checkup observations obtained from 3,233,271 individuals from January, 2005 to September, 2019. I first evaluate the BP distributions of 12,877,653 observations in which the BP data are available. The averages and SD of all observations are 120.4 mmHg and 15.9 mmHg for SBP and 74.2 mmHg and 11.3 mmHg for DBP, respectively. For 140/90 and 130/90 mmHg

criteria, 14.0% and 38.0% are classified as hypertension.

Then, the factors that may affect BP are evaluated using regression models. Age is a very important variable affecting both SBP and DBP. The quadric terms of age are significant, and the effects of age may not be a linear function. The effects of age are a little bit different between SBP and DBP. The estimates of quadric term of age are positive for SBP but negative for DBP in all models except Model 2B. SBP increases rapidly as age increases. DBP becomes higher as an individual becomes older; however, the increasing rate becomes smaller in Models 2A and 2C. BP of females is significantly lower than that of males in all models; that fact raises a question that the gender should be considered in the hypertension criteria. Declining trends are admitted in both SBP and DBP.

Among modifiable factors, BMI and blood sugar level are very important factors. These are related to obesity and preventing obesity might improve the BP conditions. BP of heavy alcohol drinkers is significantly higher than nonalcohol drinkers. Taking antihypertensive drugs makes SBP and DBP 13.4 mmHg and 7.8 mmHg lower, and significant reduction is admitted. If we directly use the *Antihypertensive* dummy in the regression equations, the estimates become positive and the importance and usefulness of the method used in this study are clearly showed.

In this study, the distributions and factors affecting BP are analyzed. The criteria of BP should be carefully determined considering age and gender of individuals. The effects of BP on other diseases are not evaluated. Although there are various types of treatment methods and antihypertension drugs, their effects are not evaluated, either. These are subjects to be studied in the future.

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Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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