













ORIGINAL RESEARCH

Interaction of Blood Pressure and Glycemic Status in Developing Cardiovascular Disease: Analysis of a Nationwide Real-World Database

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BACKGROUND: Hypertension and diabetes frequently coexist. However, little is known about the interaction between high blood pressure (BP) and hyperglycemia in the development of cardiovascular disease (CVD).

METHODS AND RESULTS: We conducted an observational cohort study that included 3336363 patients (median age, 43 years old; men, 57.2%). People taking BP- or glucose-lowering medications or those with prior history of CVD were excluded. We defined stage 1 hypertension as having systolic BP of 130 to 139 mmHg or diastolic BP of 80 to 89 mmHg and stage 2 hypertension as having systolic BP of ≥ 140 mmHg or diastolic BP of ≥ 90 mmHg. We defined prediabetes as having fasting plasma glucose of 100 to 125 mg/dL and diabetes as having fasting plasma glucose of ≥ 126 mg/dL. Over a mean follow-up period of 1185 ± 942 days, 5665 myocardial infarction, 52475 angina pectoris, 25436 stroke, 54508 heart failure, and 12932 atrial fibrillation events occurred. The BP and fasting plasma glucose categories additively increased the risk of myocardial infarction, angina pectoris, stroke, heart failure, and atrial fibrillation. However, the relative risk of stage 1 and stage 2 hypertension developing into CVD was attenuated with deteriorating glycemic status. Similarly, the relative risk of prediabetes and diabetes developing into CVD was attenuated with increasing BP. For example, the relative risk reduction of stage 2 hypertension for heart failure was 53.5% in individuals with normal fasting plasma glucose, 46.4% in those with prediabetes, and 37.2% in those with diabetes. The robustness of our findings was confirmed using a multitude of sensitivity analyses.

CONCLUSIONS: Although hypertension and hyperglycemia additively increase the risk of developing CVD, the relative contribution of hypertension to the development of CVD decreased with deteriorating glycemic status and that of hyperglycemia was attenuated with increasing BP. Our results indicate a potential interaction between hypertension and hyperglycemia in the development of CVD.

Key Words: cardiovascular disease ■ diabetes ■ epidemiology ■ hypertension

Hypertension and hyperglycemia both increase the risk of developing cardiovascular disease (CVD), and these 2 conditions frequently coexist.¹⁻⁶ However, the combined effect and interaction of hypertension and hyperglycemia in the development of CVD have yet to

be fully elucidated. In particular, 3 major points should be further investigated. First, the threshold of blood pressure (BP) values for diagnosing hypertension was lowered from 140/90 mmHg to 130/80 mmHg in the latest American College of Cardiology/American Heart

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CLINICAL PERSPECTIVE

What Is New?

- Hypertension (stage 1 and stage 2 hypertension) and hyperglycemia (prediabetes and diabetes) additively increased the risk of cardiovascular events.
- The relative risk reduction of stage 1 and stage 2 hypertension for cardiovascular events was attenuated with deteriorating glycemic status.
- Similarly, the relative association of prediabetes and diabetes with incident cardiovascular disease was also attenuated with increasing blood pressure.

What Are the Clinical Implications?

- Although hypertension and hyperglycemia additively increase the risk of developing cardiovascular disease, their relative contribution was attenuated in the presence of either, suggesting that preventive efforts for hypertension or hyperglycemia could provide a greater benefit before they coexist.

Nonstandard Abbreviations and Acronyms

AP	angina pectoris
RRR	relative risk reduction

Association BP guideline, with hypertension currently categorized into 2 groups: stage 1 hypertension (systolic BP [SBP] of 130–139 mmHg or diastolic BP [DBP] of 80–89 mmHg) and stage 2 hypertension (SBP \geq 140 mmHg or DBP \geq 90 mmHg).⁷ Further, recent studies have shown that prediabetes and not just diabetes increase the risk of CVD.^{8,9} Therefore, as hyperglycemic states, prediabetes and diabetes need to be studied separately. In general, data on the combination of stage 1 or stage 2 hypertension and prediabetes or diabetes remain scarce. Second, previous studies on the association of high BP and hyperglycemia with incident CVD have mainly analyzed their relationship with atherosclerotic CVD (eg, coronary artery disease, stroke).^{10–13} However, their association with heart failure (HF) and atrial fibrillation (AF) is also of interest as the prevalence and clinical importance of HF and AF have been increasing. Third, the contribution of hypertension to CVD development can be modified by the presence of diabetes and vice versa. Nevertheless, the interaction between hypertension and diabetes in the development of CVD has been scarcely investigated. Using a large-scale health checkup and administrative claims data set, we examined (1) whether hypertension (stage 1 and stage 2 hypertension) and hyperglycemia

(prediabetes and diabetes) additively increased the risk of developing CVD, including myocardial infarction (MI), angina pectoris (AP), stroke, HF, and AF, and (2) whether the contributions of hypertension and hyperglycemia to the risk of developing CVD interact with each other.

METHODS

Data Availability

The JMDC Claims Database used in this study is available for anyone who purchases it from JMDC Inc., a health care venture company in Japan (<https://www.jmdc.co.jp/en/in>).

Study Population

This was a retrospective observational cohort study based on the JMDC Claims Database (JMDC Inc., Tokyo, Japan), a health checkup and administrative claims database in Japan.^{5,14} Most individuals registered in this database are employees working for relatively large companies in Japan. This database includes records of individuals' annual health checkup data (eg, BP, fasting plasma glucose [FPG], body mass index [BMI], self-reported questionnaires regarding lifestyles) and administrative claims data recorded using the *International Classification of Diseases, 10th Revision (ICD-10)* coding. Among the 4 534 334 individuals with available health data, including physical examination and blood test data, we excluded those who met any of the following criteria: (1) <20 years old (n=6868); (2) with history of CVD, including MI, AP, stroke, HF, and AF (n=200 244); (3) with history of renal disease or dialysis (n=1092); (4) taking BP- or glucose-lowering medications (n=399 036); (5) missing data on cigarette smoking (n=261 724); and (6) missing data on alcohol consumption (n=329 007). Considering these, the final study population included 3 336 363 participants (Figure S1).

Ethics

The Ethical Committee of the University of Tokyo approved this study (No. 2018-10862), which was conducted in accordance with the Declaration of Helsinki. Provided that all data contained in the JMDC Claims Database were anonymized after combining individual health checkups and administrative claims records, the requirement for informed consent was waived.

Measurements and Definitions

Data on the following items were collected using standardized protocols during health checkups: BP, BMI, and FPG. In the Japanese health checkup system, trained health care professionals measured BP at least twice after 5 minutes rest, and the average of these

BP values were recorded based on the recommendations of the Ministry of Health, Labour and Welfare, and the Japanese Society of Cardiovascular Disease Prevention.⁵ Detailed methods regarding BP measurement are presented in Data S1. Consistent with the aforementioned guidelines, stage 1 hypertension was defined as having SBP of 130 to 139 mmHg or DBP of 80 to 89 mmHg, and stage 2 hypertension was defined as having SBP \geq 140 mmHg or DBP \geq 90 mmHg. On the other hand, we defined prediabetes as having FPG of 100 to 125 mg/dL and diabetes as having FPG \geq 126 mg/dL.¹⁵ Overweight or obesity was defined as having BMI of \geq 25 kg/m². Dyslipidemia was defined as having low-density lipoprotein cholesterol level of \geq 140 mg/dL, high-density lipoprotein cholesterol level of $<$ 40 mg/dL, and triglyceride level of \geq 150 mg/dL, or reporting the use of lipid-lowering medications.¹⁶ We obtained information on cigarette smoking (current, noncurrent) and alcohol consumption (everyday, not everyday) from self-reported questionnaires included in the health checkups.

Outcomes

Outcomes were collected between January 2005 and April 2021. The primary outcomes included MI, AP, stroke, HF, and AF. The *ICD-10* codes used in the present study are shown in Data S2.

Statistical Analysis

Continuous variables and categorical variables are presented as medians (Q1–Q3) and numbers (percentages), respectively. We assessed the statistical significance of the differences between groups using analysis of variance for continuous variables and chi-square tests for categorical variables.

Study participants were categorized into 9 groups according to a combination of BP classification (normal/elevated BP, stage 1 hypertension, stage 2 hypertension) and glycemic status (normal FPG, prediabetes, diabetes). We conducted multivariable Cox regression analyses to identify the association of each combination of BP category and glycemic status with incident CVD. We adjusted the hazard ratio (HR) of each combination of BP category and glycemic status for age, sex, BMI, dyslipidemia, cigarette smoking, and alcohol consumption.

To compare the association of BP category with incident CVD according to glycemic status, we categorized the study population into 3 groups (normal FPG, prediabetes, diabetes). We conducted Cox regression analyses to identify the association between BP category and the incidence of CVD. Model 1 included BP category alone (unadjusted model) and Model 2 included BP category, age, and sex. Multivariable Cox regression analyses (forced entry model) were

conducted for the latter. For Model 3, we added conventional CVD risk factors, including BMI, FPG, dyslipidemia, cigarette smoking, and alcohol consumption, to Model 2 and also performed multivariable Cox regression analyses (forced entry model). The *P* values for multiplicative interactions between each disease and the 3 glycemic categories were calculated.

To compare the association of glycemic status with incident CVD according to BP categories, we categorized the study population into 3 groups (normal/elevated BP, stage 1 hypertension, stage 2 hypertension). We conducted Cox regression analyses to identify the association between glycemic status and the incidence of CVD. Model 1 included glycemic status alone (unadjusted model), and Model 2 included glycemic status, age, and sex. Multivariable Cox regression analyses (forced entry model) were conducted for the latter. For Model 3, we added conventional CVD risk factors, including BMI, SBP, dyslipidemia, cigarette smoking, and alcohol consumption, to Model 2 and also performed multivariable Cox regression analyses (forced entry model). The *P* values for multiplicative interactions between each disease and the 3 BP categories were calculated.

We estimated the relative risk reduction (RRR) with its corresponding 95% CI adjusted for the covariates included in the multivariable Cox regression model. We calculated the RRR using the following formula: $(HR-1)/HR$. We approximated HR to relative risk by assuming that changes over time would be small.

We also assessed for any associations of SBP and FPG (as continuous variables) with the risk of developing CVD using a restricted cubic spline regression model.^{17,18} We used 4 cutoff points for SBP and FPG (5th, 35th, 65th, and 95th percentiles) with the reference point set at 120 mmHg for SBP and 100 mg/dL for FPG. We fitted 3 cubic spline models using 3, 4, and 5 knots, and the model with 4 knots was selected as it had the lowest Akaike's information criterion. HRs and 95% CIs for incident CVD were calculated and adjusted for the same covariates used in the multivariable Cox regression analyses.

Nine sensitivity analyses were also conducted to confirm the interaction between BP and FPG in the development of CVD. First, we conducted multiple imputations for missing data.⁵ Second, considering death can be a competing risk factor for CVD events, we conducted cause-specific Cox proportional hazard modeling as a competing risks analysis.⁵ Third, we added individuals taking BP-lowering medications to stage 2 hypertension and those taking glucose-lowering medications to diabetes. Fourth, we extracted individuals with available data on estimated glomerular filtration rate and added the estimated glomerular filtration rate to the covariates. Fifth, we conducted subgroup analyses that were stratified by sex. Sixth, dyslipidemia was

redefined as having a total cholesterol level of ≥ 200 mg/dL or reporting the use of lipid-lowering medications. Seventh, we redefined glycemic status using hemoglobin A1c (HbA1c) as follows: normal group (HbA1c level of $< 5.7\%$), group with prediabetes (HbA1c level of $\geq 5.7\%$ and $\leq 6.4\%$), and group with diabetes (HbA1c level of $\geq 6.5\%$). Eighth, to consider that the association between the glycemic status and the development of CVD is nonlinear, we categorized individuals into normal FPG/prediabetes and diabetes. Ninth, we set the induction period of 1 year and included participants with a follow-up period of ≥ 365 days.

Statistical significance was set at $P < 0.05$. We set statistical significance for interactions at $P < 0.20$.¹⁹ All statistical analyses were conducted using STATA version 17 (StataCorp LLC, College Station, TX).

RESULTS

Baseline Characteristics

The baseline characteristics of the study participants are summarized in Table 1. The median age of the study individuals was 43 (36–51) years old, and 1 907 065 individuals (57.2%) were men. In terms of BP, the median SBP and DBP were 117 (106–127) mmHg and 72

Table 1. Baseline Characteristics

Characteristics	
Age, y	43 (36–51)
Men, n (%)	1 907 065 (57.2)
Body mass index, kg/m ²	22.2 (20.1–24.6)
Overweight/obesity, n (%)	736 677 (22.1)
Systolic blood pressure, mmHg	117 (106–127)
Diastolic blood pressure, mmHg	72 (64–80)
Blood pressure classification	
Normal blood pressure, n (%)	1 807 169 (54.2)
Elevated blood pressure, n (%)	495 489 (14.9)
Stage 1 hypertension, n (%)	675 919 (20.3)
Stage 2 hypertension, n (%)	357 786 (10.7)
Fasting plasma glucose, mg/dL	91 (85–97)
Glycemic status	
Normal fasting plasma glucose, n (%)	2 719 830 (81.5)
Prediabetes, n (%)	563 573 (16.9)
Diabetes, n (%)	52 960 (1.6)
Low-density lipoprotein cholesterol, mg/dL	118 (98–140)
High-density lipoprotein cholesterol, mg/dL	62 (52–74)
Triglycerides, mg/dL	78 (55–117)
Dyslipidemia, n (%)	1 230 099 (36.9)
Cigarette smoking, n (%)	851 243 (25.5)
Alcohol consumption, n (%)	716 298 (21.5)

Data are expressed as number (percentage) or median (Q1–Q3).

(64–80) mmHg, respectively. Stage 1 was observed in 20.3%, and stage 2 hypertension was observed in 10.7%. In terms of glycemic status, the median FPG level was 91 (85–97) mg/dL. Prediabetes and diabetes were observed in 16.9% and 1.6%, respectively. The comparison of baseline characteristics between the 9 groups according to combination of BP category and glycemic status is shown in Table S1.

Association Between Combination of BP Category and Glycemic Status and Incident CVD

The risks of MI, AP, stroke, HF, and AF increased with both BP category and glycemic status (Figure 1). For example, compared with normal/elevated BP and normal FPG, the HRs (95% CI) of stage 2 hypertension alone, diabetes alone, and both stage 2 hypertension and diabetes for MI were 1.92 (1.76–2.10), 2.44 (2.00–2.98), and 3.20 (2.71–3.79), respectively.

Association of BP Category With Incident CVD According to Glycemic Status

Figure 2 summarizes the association of BP category with incident CVD according to glycemic status. The incidences of MI, AP, stroke, HF, and AF increased with glycemic status. In contrast, the HRs of stage 1 or stage 2 hypertension for developing CVD decreased with glycemic status. P for interactions was significant for MI ($P=0.1746$), AP ($P=0.0449$), and HF ($P<0.001$). However, it was not significant for AF ($P=0.5712$). The HRs of stage 1 or stage 2 hypertension for all-cause death decreased with glycemic status (P value for interaction=0.0228) (Figure S2). The RRR of stage 1 or stage 2 hypertension for MI, AP, HF, and AF decreased with glycemic status (Figure 3, Table S2). For example, the RRR of stage 2 hypertension for MI was 48.1% in individuals with normal FPG, 41.7% in those with prediabetes, and 29.6% in those with diabetes. On the other hand, the HR and RRR for stroke of stage 1 and stage 2 decreased from the group with normal FPG to the group with prediabetes but increased from the group with prediabetes to the group with diabetes. The P value for the interaction was 0.0077, suggesting that this association was statistically significant. The restricted cubic spline showed that the increased risks of MI, AP, and HF associated with increased BP was attenuated with increased FPG. However, this association was not evident for stroke or AF (Figure S3).

Association of Glycemic Status With Incident CVD According to BP Categories

Figure 4 summarizes the association between glycemic status and incident CVD according to the BP categories. The incidences of MI, AP, stroke, HF, and

A Myocardial Infarction				B Angina Pectoris				C Stroke			
	Normal FPG	Prediabetes	Diabetes		Normal FPG	Prediabetes	Diabetes		Normal FPG	Prediabetes	Diabetes
Normal/Elevated BP	1.00 (Reference)	1.13 (1.03–1.25)	2.44 (2.00–2.98)	Normal/Elevated BP	1.00 (Reference)	1.03 (1.00–1.07)	1.48 (1.36–1.62)	Normal/Elevated BP	1.00 (Reference)	1.05 (1.00–1.10)	1.23 (1.07–1.42)
Stage 1 Hypertension	1.37 (1.27–1.48)	1.47 (1.33–1.63)	2.60 (2.14–3.16)	Stage 1 Hypertension	1.19 (1.16–1.25)	1.21 (1.17–1.25)	1.59 (1.46–1.73)	Stage 1 Hypertension	1.36 (1.31–1.41)	1.32 (1.25–1.39)	1.70 (1.50–1.92)
Stage 2 Hypertension	1.92 (1.76–2.10)	2.01 (1.81–2.23)	3.20 (2.71–3.79)	Stage 2 Hypertension	1.53 (1.49–1.58)	1.54 (1.48–1.59)	1.88 (1.75–2.03)	Stage 2 Hypertension	2.23 (2.15–2.32)	2.05 (1.95–2.16)	2.73 (2.49–3.00)

D Heart Failure				E Atrial Fibrillation				F Sample Size			
	Normal FPG	Prediabetes	Diabetes		Normal FPG	Prediabetes	Diabetes		Normal FPG	Prediabetes	Diabetes
Normal/Elevated BP	1.00 (Reference)	1.10 (1.07–1.14)	1.73 (1.59–1.88)	Normal/Elevated BP	1.00 (Reference)	1.08 (1.02–1.15)	1.32 (1.11–1.57)	Normal/Elevated BP	1,997,260	287,625	17,773
Stage 1 Hypertension	1.30 (1.27–1.33)	1.31 (1.27–1.36)	1.82 (1.67–1.97)	Stage 1 Hypertension	1.15 (1.10–1.21)	1.21 (1.13–1.30)	1.46 (1.23–1.72)	Stage 1 Hypertension	500,060	159,589	16,270
Stage 2 Hypertension	2.13 (2.07–2.19)	2.12 (2.05–2.20)	2.67 (2.50–2.86)	Stage 2 Hypertension	1.54 (1.45–1.63)	1.55 (1.45–1.67)	1.79 (1.56–2.06)	Stage 2 Hypertension	222,510	116,359	18,917

Figure 1. Combination of BP category and glycemic status in developing CVD.

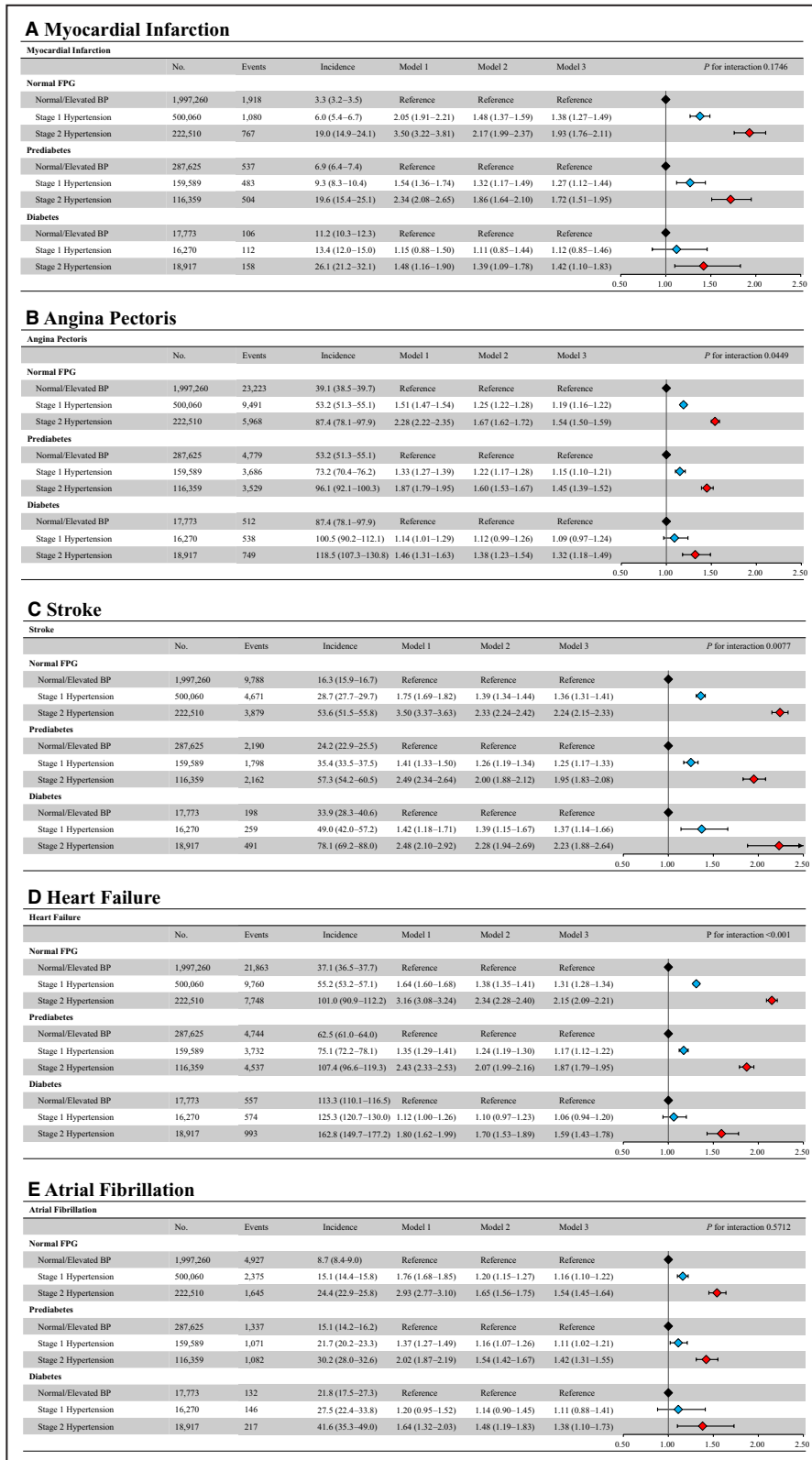
Study participants were categorized into 9 groups according to a combination of blood pressure classification (normal/elevated blood pressure, stage 1 hypertension, stage 2 hypertension) and glycemic status (normal fasting plasma glucose, prediabetes, diabetes). We conducted multivariable Cox regression analyses to identify the association of each combination of blood pressure category and glycemic status with incident cardiovascular disease: (A) myocardial infarction, (B) angina pectoris, (C) stroke, (D) heart failure, and (E) atrial fibrillation. We adjusted the hazard ratio of each combination of blood pressure category and glycemic status for age, sex, body mass index, dyslipidemia, cigarette smoking, and alcohol consumption. (F) shows the sample size of each combination. BP indicates blood pressure; CVD, cardiovascular disease; and FPG, fasting plasma glucose.

AF increased according to BP category. On the other hand, the HRs of prediabetes or diabetes for developing CVD decreased according to BP category. Note that *P* value for interaction was significant for MI (*P*=0.0029), AP (*P*=0.0056), stroke (*P*=0.0307), and HF (*P*<0.001). However, it was not significant for AF (*P*=0.4632). The HRs of prediabetes or diabetes for all-cause death decreased according to BP category (*P* value for interaction=0.0029) (Figure S4). The RRRs of diabetes for MI, AP, stroke, HF, and AF decreased according to BP category (Figure 5, Table S2). For example, the RRR of diabetes for MI was 61.0% in individuals with normal/elevated BP, 44.4% in those with stage 1 hypertension, and 34.3% in those with stage 2 hypertension. The restricted cubic spline showed that the increased risks of MI, AP, and HF associated with increased FPG was attenuated with increased BP. However, this association was not evident for stroke or AF (Figure S5).

Sensitivity Analyses

Nine sensitivity analyses were performed to validate our findings. First, we analyzed 3927094 individuals after multiple imputations for missing data. In this population, HRs of BP category for incident CVD, excluding stroke, decreased with glycemic status, and HRs of glycemic status for incident CVD decreased

with BP category (Table S3). Second, in the cause-specific analysis, the interaction between BP category and glycemic status was unchanged (Table S4). Third, we included 349290 individuals who were taking BP-lowering or glucose-lowering medications. In this population, HRs according to BP category for each CVD event decreased with glycemic status, and HRs of glycemic status for each CVD event decreased with BP category (Table S5). Fourth, we analyzed 1671614 individuals with available data on estimated glomerular filtration rate, and the interaction of BP category and glycemic status in developing CVD was consistent after adding estimated glomerular filtration rate to the covariates (Table S6). Fifth, the interaction between BP category and glycemic status in the risk of developing CVD was similar regardless of sex (Table S7). Sixth, the interaction between BP category and glycemic status in the risk of developing CVD was not changed if we defined dyslipidemia as a total cholesterol level of ≥200 mg/dL or reporting the use of lipid-lowering medications (Table S8). Seventh, the interaction between the BP category and glycemic status category defined using HbA1c in the risk of developing CVD was similar (Table S9). Eighth, we recategorized individuals into normal FPG/prediabetes and diabetes. The risk for developing CVD in diabetes compared with normal FPG/



prediabetes was lower with increasing BP (Table S10). Ninth, we extracted 2 694 211 participants with a follow-up period of ≥365 days. Even in this population, the interaction between BP category and glycemic status in the risk of developing CVD was similar (Table S11).

DISCUSSION

Our analysis, which included more than 3 million individuals without prior history of CVD, demonstrated that hypertension (stage 1 hypertension, stage 2

Figure 2. Association of BP category with incident CVD according to glycemic status.

We categorized the study population into 3 groups (normal fasting plasma glucose, prediabetes, diabetes). We conducted Cox regression analyses to identify the association between blood pressure category and the incidence of cardiovascular disease: (A) myocardial infarction; (B) angina pectoris; (C) stroke; (D) heart failure; and (E) atrial fibrillation. Model 1 included blood pressure category alone (unadjusted model) and Model 2 included blood pressure category, age, and sex. Multivariable Cox regression analyses (forced entry model) were conducted for the latter. For Model 3, we added conventional cardiovascular disease risk factors, including body mass index, fasting plasma glucose, dyslipidemia, cigarette smoking, and alcohol consumption to Model 2 and also performed multivariable Cox regression analyses (forced entry model). We estimated the hazard ratios in stage 1 hypertension and stage 2 hypertension compared with normal/elevated blood pressure by fasting plasma glucose category. The *P* for interaction represented the *P* value of the interaction term between the blood pressure category and the fasting plasma glucose category. The interaction term was tested in a model including the blood pressure category, the fasting plasma glucose category, and the interaction term, separate from the model used in the primary analysis. The incidence rate was per 10000 person-years. BP indicates blood pressure; CVD, cardiovascular disease; and FPG, fasting plasma glucose.

hypertension) and hyperglycemia (prediabetes, diabetes) additively increased the risk of developing CVD, including MI, AP, stroke, HF, and AF. However, the contribution of hypertension to subsequent CVD events decreased with increasing FPG levels, and the association between hyperglycemia and incident CVD was attenuated with increasing BP. The RRRs of stage 1 or stage 2 hypertension for CVD events was greater in individuals with normal FPG levels than in those with prediabetes or diabetes. Similarly, HRs of prediabetes or diabetes for CVD events decreased in individuals with stage 1 and 2 hypertension. These associations were prominent in the groups with MI, AP, and HF. To the best of our knowledge, this is the first investigation to demonstrate the potential interaction of hypertension and hyperglycemia with the risk of developing broad-range CVD using large-scale and real-world data.

Although various studies have investigated the combined effect of hypertension and hyperglycemia, analyzing CVD outcomes of hypertension or hyperglycemia stratified by baseline BP or glycemic status, the results of these previous studies have been inconsistent. For example, an analysis of a prospective population-based cohort in China showed that a BP of 130 to 139/80 to 89 mmHg did not increase the risk of developing CVD in people who had normal blood sugar or were considered to be prediabetes but increased in those with diabetes.¹⁰ However, another recent study showed that the risk of developing CVD increased with SBP and DBP irrespective of glycemic status.¹¹ Although an analysis of the Jackson Heart Study reported that prediabetes was not related to risk of developing CVD regardless of the presence of hypertension,²⁰ another cohort study demonstrated that prediabetes increased the risk of developing CVD when complicated with hypertension.¹² These inconsistencies could be attributable to insufficient statistical power (ie, small sample, small event size) and differences in their definitions of hypertension, diabetes, and analyzed end point. Therefore, we analyzed a large-scale, real-world database, which included more than 3 million participants without prior history of CVD, and conducted comprehensive analyses to identify the

combined effect of hypertension and hyperglycemia and the interaction between hypertension and hyperglycemia in the development of CVD.

The present study is distinguishable from previous studies in the following aspects: We categorized our study population into 9 groups based on combination of BP category (normal/elevated BP, stage 1 hypertension, stage 2 hypertension) and glycemic status (normal FPG, prediabetes, diabetes) and showed the additive association of both BP and glycemic category with the risk of developing wide-range CVD events (ie, not only atherosclerotic CVD but also HF and AF), confirming the independent prognostic roles of stage 2 hypertension and diabetes as well as stage 1 hypertension and prediabetes. It should be noted that even prediabetes increases the risk of developing CVD in individuals with stage 1 or stage 2 hypertension. Despite the additive influence of hypertension and hyperglycemia on the subsequent risk of developing CVD, the association between hypertension and incident CVD was attenuated with increasing FPG. Additionally, the association between diabetes and incident CVD also decreased with increasing BP. We confirmed the interaction between hypertension and hyperglycemia in the development of CVD using a multitude of sensitivity analyses. However, this interaction appeared to be inconsistent across specific CVD events. For example, considering *P* values for interaction, association was statistically significant for MI, AP, stroke, and HF but not for AF. Furthermore, in terms of stroke, the association of hypertension with incident stroke decreased from individuals with normal FPG to those with prediabetes but increased from those with prediabetes to those with diabetes. Further investigations using other independent data sets must be done to fully validate these findings.

This study suggested several clinical implications. Our results on the RRRs suggested that the potential benefit of treatment for hypertension would be greater in individuals with normal FPG than in those with prediabetes or diabetes. Similarly, the potential benefit of treatment for hyperglycemia would also be greater in individuals without hypertension than in those with

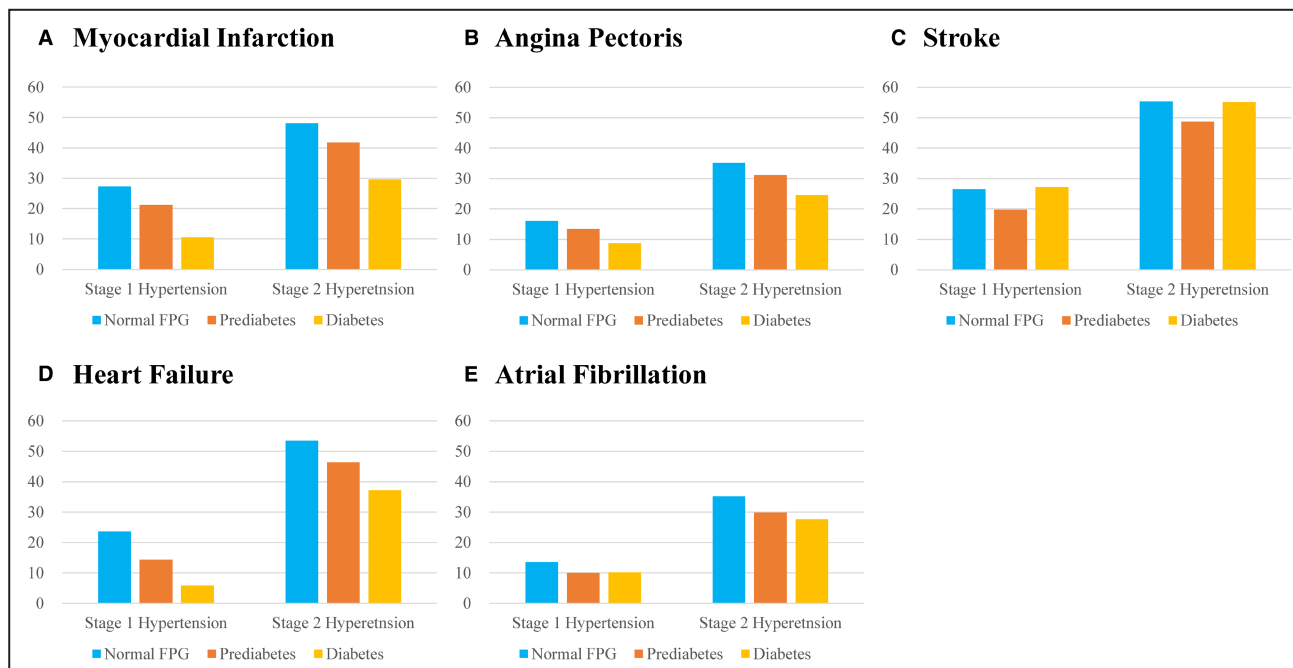


Figure 3. Relative risk reduction of stage 1 or stage 2 hypertension stratified by glycemic status.

Relative risk reduction of stage 1 or stage 2 hypertension for myocardial infarction (A), angina pectoris (B), stroke (C), heart failure (D), and atrial fibrillation (E) stratified by glycemic status. FPG indicates fasting plasma glucose.

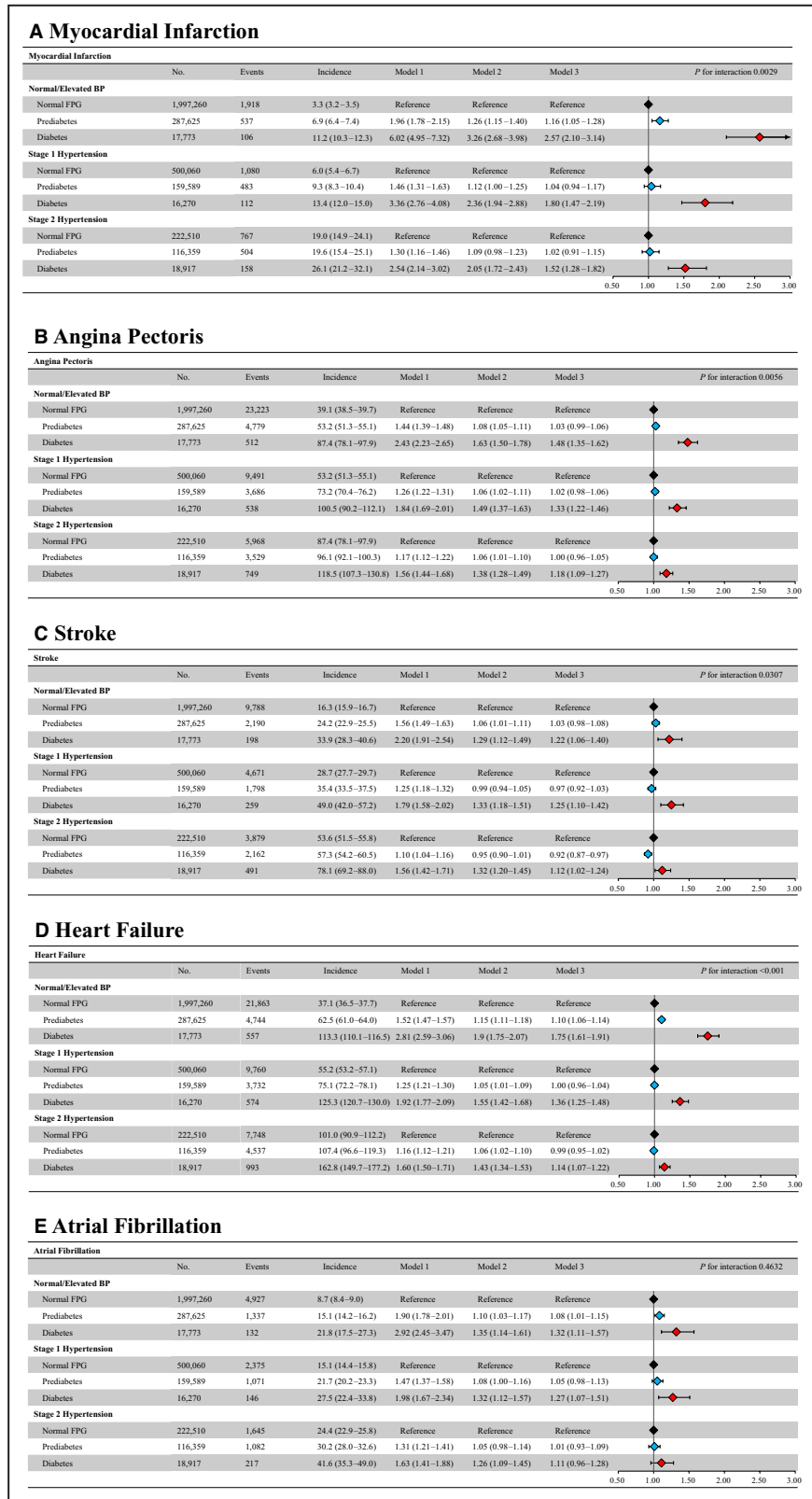
stage 1 or stage 2 hypertension. These results remind us of the different results exhibited by the SPRINT (The Systolic Blood Pressure Intervention Trial)²¹ study and the ACCORD-BP (Action to Control Cardiovascular Disease in Diabetes Blood Pressure) trial.²² SPRINT showed that intensive BP treatment targeting SBP <120mmHg decreased composite CVD events and all-cause mortality more than standard BP treatment targeting SBP <140mmHg, supporting aggressive BP management in patients with hypertension.²¹ On the other hand, ACCORD-BP did not demonstrate any reduction in CVD events after intensive BP treatment in patients with hypertension complicated with diabetes.²² Recently, the STEP (Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients) study, including old Chinese patients (60 to 80years of age) with hypertension (mean SBP of 146.1 mmHg), demonstrated that the incidence of CVD events was

lower in intensive BP treatment (targeting SBP of 110 to <130mmHg) than in standard treatment (targeting SBP of <150mmHg).²³ In the STEP trial, approximately 19% of study participants had diabetes, and prespecified subgroup analyses showed that the point estimate for HR of intensive BP control was similar between individuals with and without diabetes, but the beneficial impact of intensive BP control did not reach statistical significance in those with diabetes.

The difference in the results of these 2 trials suggests the potential attenuation of the therapeutic benefit of BP lowering in patients with diabetes. We consider that the significant interaction between BP and FPG for MI, AP, stroke, and HF detected in this study also backs up that hypothesis. Nevertheless, it should be noted that our results never negate the significance of treatment in individuals with hypertension and diabetes. As shown in our results, hypertension and hyperglycemia

Figure 4. Association of glycemic status with incident CVD according to BP category.

We categorized the study population into 3 groups (normal/elevated blood pressure, stage 1 hypertension, stage 2 hypertension). We conducted Cox regression analyses to identify the association between glycemic status and the incidence of cardiovascular disease: (A) myocardial infarction; (B) angina pectoris; (C) stroke; (D) heart failure; and (E) atrial fibrillation. Model 1 included glycemic status alone (unadjusted model), and Model 2 included glycemic status, age, and sex. Multivariable Cox regression analyses (forced entry model) were conducted for the latter. For Model 3, we added conventional cardiovascular disease risk factors, including body mass index, systolic blood pressure, dyslipidemia, cigarette smoking, and alcohol consumption to Model 2 and also performed multivariable Cox regression analyses (forced entry model). We estimated the hazard ratios in prediabetes and diabetes compared with normal fasting plasma glucose by blood pressure category. The *P* for interaction represented the *P* value of the interaction term between the blood pressure category and the fasting plasma glucose category. The interaction term was tested in a model including the blood pressure category, the fasting plasma glucose category, and the interaction term, separate from the model used in the primary analysis. The incidence rate was per 10000 person-years. BP indicates blood pressure; CVD, cardiovascular disease; and FPG, fasting plasma glucose.



were additively associated with an elevated risk of developing CVD, rather emphasizing the requirement of both BP-lowering and glucose-lowering treatments. Herein, what is important to note is that when starting

BP-lowering treatment for an individual with hypertension but normal FPG levels, we also need to prevent the progression of normoglycemia to prediabetes or diabetes. Similarly, when initiating glucose-lowering

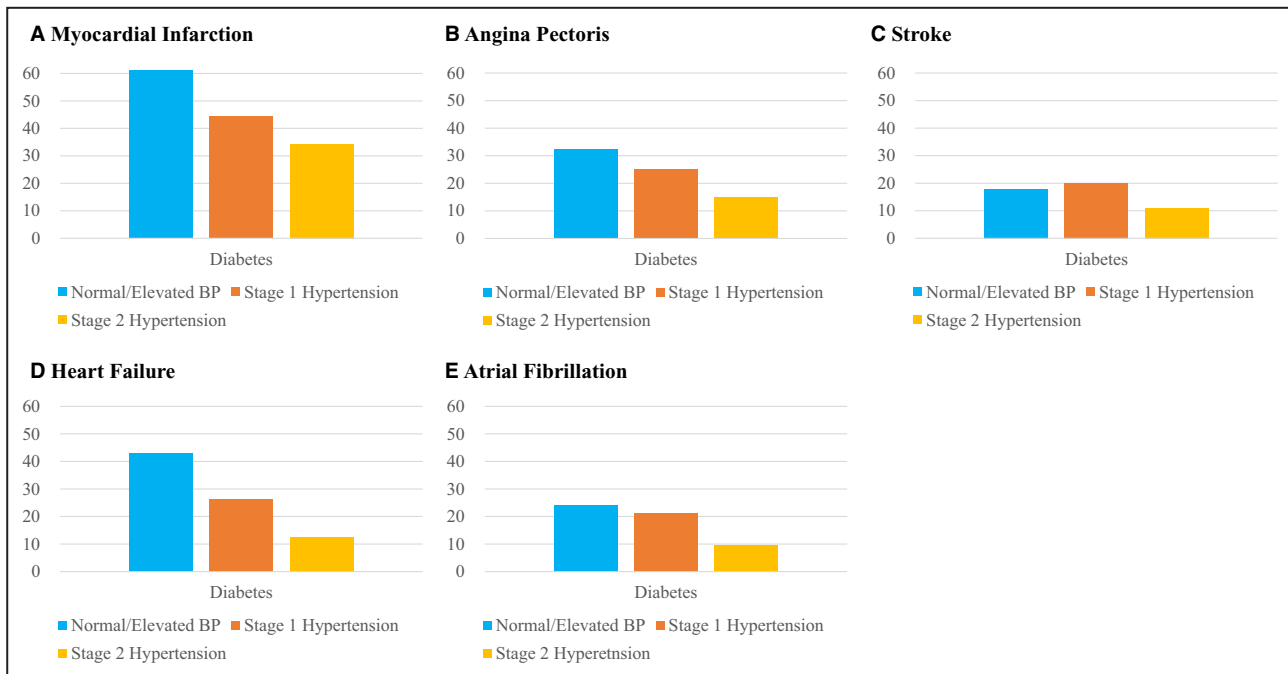


Figure 5. Relative risk reduction of diabetes stratified by BP category.

Relative risk reduction of diabetes for myocardial infarction (A), angina pectoris (B), stroke (C), heart failure (D), and atrial fibrillation (E) stratified by BP category. BP indicates blood pressure.

interventions for patients with prediabetes or diabetes but normal BP, it is also important to prevent the development of hypertension. Hypertension and diabetes often have a common background. For example, obesity is the most frequent comorbidity of both hypertension and diabetes. This finding may confirm the importance of optimizing modifiable risk factors (eg, obesity) and lifestyle in the treatment of hypertension or hyperglycemia.

We acknowledge the following limitations in this study, mainly the use of a health checkup and administrative claims database.^{5,14,24} The measurements of BP and FPG during a single health checkup cannot fully represent the phenotype of BP or glycemic status of study participants. Although the incidence of CVD in our database is comparable to other epidemiological data in Japan,^{25,26} we should consider that the diagnoses recorded in claims databases are less validated than those recorded in prospective registries. CVD diagnoses recorded in both inpatient and outpatient settings were counted in the JMDC Claims Database. Unfortunately, our database does not allow us to completely distinguish between diagnoses made in the inpatient and outpatient settings. Further, our data set primarily includes the working-age population in Japan and whether our primary results could be generalized remains unclear. Our findings need to be validated in other independent data sets. Multivariable Cox regression analyses were performed. However, we could not eliminate

the possibility of unmeasured confounders and residual biases. For example, although socioeconomic status could have influenced our results, our data set did not include information on socioeconomic status. Furthermore, it was not possible to obtain sufficient information on the facility's location. Because the follow-up period in this study was relatively short, further investigations with a long-term follow-up period are needed to confirm our findings. Multiple statistical tests were performed in this study, and it is not possible to completely control for multiplicity. Although we examined the association of the baseline BP and FPG with CVD in this study, the serial change of BP and FPG could influence the results. Finally, the cause of death (CVD death, non-CVD death) was not available in the JMDC Claims Database.

CONCLUSIONS

Our analysis of a large-scale, real-world database, which included more than 3 million adults without prior history of CVD, demonstrated that hypertension and hyperglycemia additively increased the subsequent risk of developing CVD. However, the relative contribution of hypertension to the development of CVD decreased with deteriorating glycemic status and that of hyperglycemia was attenuated with increasing BP, suggesting a potential interaction between hypertension and hyperglycemia in the development of CVD.

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Supplemental Material

Data S1
Data S2
Tables S1–S11
Figure S1–S5

REFERENCES

- Collaborators GBD. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390:1345–1422. doi: [10.1016/S0140-6736\(17\)32366-8](https://doi.org/10.1016/S0140-6736(17)32366-8)
- Lawes CM, Vander Hoorn S, Rodgers A. International Society of Hypertension. Global burden of blood-pressure-related disease, 2001. *Lancet*. 2008;371:1513–1518.
- Flint AC, Conell C, Ren X, Banki NM, Chan SL, Rao VA, Melles RB, Bhatt DL. Effect of systolic and diastolic blood pressure on cardiovascular outcomes. *N Engl J Med*. 2019;381:243–251. doi: [10.1056/NEJMoat803180](https://doi.org/10.1056/NEJMoat803180)
- Emerging Risk Factors C, Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio E, Ingelsson E, Lawlor DA, Selvin E, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. *Lancet*. 2010;375:2215–2222. doi: [10.1016/S0140-6736\(10\)60484-9](https://doi.org/10.1016/S0140-6736(10)60484-9)
- Kaneko H, Yano Y, Itoh H, Morita K, Kiriya H, Kamon T, Fujii K, Michihata N, Jo T, Takeda N, et al. Association of blood pressure classification using the 2017 American College of Cardiology/American Heart Association blood pressure guideline with risk of heart failure and atrial fibrillation. *Circulation*. 2021;143:2244–2253. doi: [10.1161/CIRCULATIONAHA.120.052624](https://doi.org/10.1161/CIRCULATIONAHA.120.052624)
- Kaneko H, Itoh H, Kiriya H, Kamon T, Fujii K, Morita K, Michihata N, Jo T, Takeda N, Morita H, et al. Fasting plasma glucose and subsequent cardiovascular disease among young adults: analysis of a nationwide epidemiological database. *Atherosclerosis*. 2021;319:35–41. doi: [10.1016/j.atherosclerosis.2020.12.024](https://doi.org/10.1016/j.atherosclerosis.2020.12.024)
- Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2018;138:e484–e594. doi: [10.1161/CIR.0000000000000596](https://doi.org/10.1161/CIR.0000000000000596)
- Ali MK, Bullard KM, Saydah S, Imperatore G, Gregg EW. Cardiovascular and renal burdens of prediabetes in the USA: analysis of data from serial cross-sectional surveys, 1988–2014. *Lancet Diabetes Endocrinol*. 2018;6:392–403. doi: [10.1016/S2213-8587\(18\)30027-5](https://doi.org/10.1016/S2213-8587(18)30027-5)
- Cai X, Zhang Y, Li M, Wu JH, Mai L, Li J, Yang Y, Hu Y, Huang Y. Association between prediabetes and risk of all cause mortality and cardiovascular disease: updated meta-analysis. *BMJ*. 2020;370:m2297.
- Tian J, Sheng CS, Sun W, Song X, Wang H, Li Q, Li W, Wang W. Effects of high blood pressure on cardiovascular disease events among Chinese adults with different glucose metabolism. *Diabetes Care*. 2018;41:1895–1900. doi: [10.2337/dc18-0918](https://doi.org/10.2337/dc18-0918)
- Yamada MH, Fujihara K, Kodama S, Sato T, Osawa T, Yaguchi Y, Yamamoto M, Kitazawa M, Matsubayashi Y, Yamada T, et al. Associations of systolic blood pressure and diastolic blood pressure with the incidence of coronary artery disease or cerebrovascular disease according to glucose status. *Diabetes Care*. 2021;44:2124–2131. doi: [10.2337/dc20-2252](https://doi.org/10.2337/dc20-2252)
- Qiu M, Shen W, Song X, Ju L, Tong W, Wang H, Zheng S, Jin Y, Wu Y, Wang W, et al. Effects of prediabetes mellitus alone or plus hypertension on subsequent occurrence of cardiovascular disease and diabetes mellitus: longitudinal study. *Hypertension*. 2015;65:525–530. doi: [10.1161/HYPERTENSIONAHA.114.04632](https://doi.org/10.1161/HYPERTENSIONAHA.114.04632)
- Kokubo Y, Okamura T, Watanabe M, Higashiyama A, Ono Y, Miyamoto Y, Furukawa Y, Kamide K, Kawanishi K, Okayama A, et al. The combined impact of blood pressure category and glucose abnormality on the incidence of cardiovascular diseases in a Japanese urban cohort: the Suita study. *Hypertens Res*. 2010;33:1238–1243. doi: [10.1038/hr.2010.174](https://doi.org/10.1038/hr.2010.174)
- Kaneko H, Itoh H, Yotsumoto H, Kiriya H, Kamon T, Fujii K, Morita K, Michihata N, Jo T, Takeda N, et al. Association of isolated diastolic hypertension based on the cutoff value in the 2017 American College of Cardiology/American Heart Association blood pressure guidelines with subsequent cardiovascular events in the general population. *J Am Heart Assoc*. 2020;9:e017963. doi: [10.1161/JAHA.120.017963](https://doi.org/10.1161/JAHA.120.017963)
- American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. *Diabetes Care*. 2021;44:S15–S33.
- Kinoshita M, Yokote K, Arai H, Iida M, Ishigaki Y, Ishibashi S, Umemoto S, Egusa G, Ohmura H, Okamura T, et al. Japan Atherosclerosis Society (JAS) guidelines for prevention of atherosclerotic cardiovascular diseases 2017. *J Atheroscler Thromb*. 2018;25:846–984. doi: [10.5551/jat.2017](https://doi.org/10.5551/jat.2017)
- Itoh H, Kaneko H, Okada A, Yano Y, Morita K, Seki H, Kiriya H, Kamon T, Fujii K, Matsuoka S, et al. Fasting plasma glucose and incident colorectal cancer: analysis of a nationwide epidemiological database. *J Clin Endocrinol Metab*. 2021;106:e4448–e4458. doi: [10.1210/clinem/dgab466](https://doi.org/10.1210/clinem/dgab466)
- Shiozawa M, Kaneko H, Itoh H, Morita K, Okada A, Matsuoka S, Kiriya H, Kamon T, Fujii K, Michihata N, et al. Association of body mass index with ischemic and hemorrhagic stroke. *Nutrients*. 2021;13. doi: [10.3390/nu13072343](https://doi.org/10.3390/nu13072343)
- Thiese MS, Ronna B, Ott U. P value interpretations and considerations. *J Thorac Dis*. 2016;8:E928–E931. doi: [10.21037/jtd.2016.08.16](https://doi.org/10.21037/jtd.2016.08.16)
- Hubbard D, Colantonio LD, Tanner RM, Carson AP, Sakhuja S, Jaeger BC, Carey RM, Cohen LP, Shimbo D, Butler M, et al. Prediabetes and risk for cardiovascular disease by hypertension status in black adults: the Jackson heart study. *Diabetes Care*. 2019;42:2322–2329. doi: [10.2337/dc19-1074](https://doi.org/10.2337/dc19-1074)
- Group SR, Wright JT Jr, Williamson JD, Whelton PK, Snyder JK, Sink KM, Rocco MV, Reboussin DM, Rahman M, Oparil S, et al. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103–2116. doi: [10.1056/NEJMoat511939](https://doi.org/10.1056/NEJMoat511939)
- Group AS, Cushman WC, Evans GW, Byington RP, Goff DC Jr, Grimm RH Jr, Cutler JA, Simons-Morton DG, Basile JN, Corson MA, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med*. 2010;362:1575–1585. doi: [10.1056/NEJMoat1001286](https://doi.org/10.1056/NEJMoat1001286)
- Zhang W, Zhang S, Deng Y, Wu S, Ren J, Sun G, Yang J, Jiang Y, Xu X, Wang TD, et al. Trial of intensive blood-pressure control in older patients

-
- with hypertension. *N Engl J Med.* 2021;385:1268–1279. doi: [10.1056/NEJMoa2111437](https://doi.org/10.1056/NEJMoa2111437)
24. Matsuoka S, Kaneko H, Okada A, Morita K, Itoh H, Michihata N, Jo T, Takeda N, Morita H, Fujii K, et al. Age modified relationship between modifiable risk factors and the risk of atrial fibrillation. *Circ Arrhythm Electrophysiol.* 2022;15:e010409. doi: [10.1161/CIRCEP.121.010409](https://doi.org/10.1161/CIRCEP.121.010409)
25. Saito I, Yamagishi K, Kokubo Y, Yatsuya H, Iso H, Sawada N, Inoue M, Tsugane S. Association between mortality and incidence rates of coronary heart disease and stroke: the Japan Public Health Center-based prospective (JPHC) study. *Int J Cardiol.* 2016;222:281–286. doi: [10.1016/j.ijcard.2016.07.222](https://doi.org/10.1016/j.ijcard.2016.07.222)
26. Fujihara K, Yamada-Harada M, Matsubayashi Y, Kitazawa M, Yamamoto M, Yaguchi Y, Seida H, Kodama S, Akazawa K, Sone H. Accuracy of Japanese claims data in identifying diabetes-related complications. *Pharmacoepidemiol Drug Saf.* 2021;30:594–601. doi: [10.1002/pds.5213](https://doi.org/10.1002/pds.5213)

SUPPLEMENTAL MATERIAL

Data S1. Methods of Blood Pressure Measurement

1. The auscultation method should use an accurately calibrated mercury or aneroid sphygmomanometer. A calibrated electronic sphygmomanometer can also be used.
2. Healthcare professionals should choose the correct cuff size and wrap the cuff around the arm, with the center of the cuff bladder over the brachial artery. The stethoscope, standard sphygmomanometers, and cuff and bulb should be checked regularly to ensure that BP measurements have a standardized high level of accuracy and precision. The appropriate BP cuff size should be determined by measuring the participant's arm circumference at the mid-point between the acromion and olecranon. A cuff with a bladder 13 cm wide and 22–24 cm long should be used for the auscultation method. A pediatric cuff should be used for a brachial girth less than 27 cm, and a large adult cuff for an arm girth ≥ 34 cm.
3. Caffeine, eating, heavy physical activity, smoking, and talking should be avoided before measurement.
4. Research staff should measure right-arm brachial artery blood pressure two times after the participant had been sitting in a quiet room for 5 minutes in a seated position on a chair with back support and the participant's legs uncrossed. The inner aspect of the bend at the elbow (cubital fossa) should be maintained at heart level.
5. Measurement: The cuff should rapidly be inflated while palpating the radial or brachial artery, and the stethoscope should be used after blood pressure has risen to 20-30 mmHg or more above the pulse rate disappearing level. The cuff should be slowly deflated (2 mmHg per second). Staff should record the 1st and 5th Korotkoff sounds, rounding the pressure in mmHg to the nearest even number and recording it.
6. The measurements should be performed two times at an interval of ≥ 1 min, and the mean value of two measurements that provide stable values (difference in the values: < 5 mmHg) should be used for the analyses.

Data S2. ICD-10 Codes

Myocardial Infarction: I210–I214, and I219

Angina Pectoris: I200, I201, I208, and I209

Stroke: I630, I631–I636, I638, I639, I600–I611, I613–I616, I619, I629, and G459

Heart Failure: I500, I501, I509, and I110

Table S1. Baseline characteristics in accordance with BP category and FPG Category

	Normal or Elevated BP			Stage 1 Hypertension			Stage 2 Hypertension		
	Normal FPG	Prediabetes	Diabetes	Normal FPG	Prediabetes	Diabetes	Normal FPG	Prediabetes	Diabetes
Number	1,997,260	287,625	17,773	500,060	159,589	16,270	222,510	116,359	18,917
Age, years	41 (33-48)	47 (40-54)	50 (42-57)	45 (39-52)	50 (43-56)	50 (44-57)	49 (42-55)	52 (45-58)	52 (45-58)
Men, n (%)	959,755 (48.1)	196,892 (68.5)	13,651 (76.8)	341,582 (68.3)	124,218 (77.8)	13,537 (83.2)	152,816 (68.7)	89,269 (76.7)	15,345 (81.1)
Body mass index, kg/m ²	21.3 (19.5-23.4)	22.9 (20.9-25.1)	24.2 (21.9-27.1)	23.2 (21.1-25.5)	24.2 (22.1-26.7)	25.8 (23.2-28.8)	24.0 (21.7-26.8)	24.8 (22.5-27.7)	26.7 (23.8-30.2)
Obesity, n (%)	267,296 (13.4)	76,766 (26.7)	7,645 (43.0)	151,316 (30.3)	65,243 (40.9)	9,456 (58.1)	89,867 (40.4)	56,760 (48.8)	12,328 (65.2)
Systolic blood pressure, mmHg	110 (102-118)	114 (107-121)	117 (110-123)	129 (122-133)	129 (124-134)	130 (125-134)	144 (138-151)	145 (140-154)	148 (141-158)
Diastolic blood pressure, mmHg	67 (61-72)	70 (65-75)	71 (66-76)	82 (80-85)	82 (80-85)	82 (80-86)	92 (88-97)	93 (89-98)	94 (89-100)
Fasting plasma glucose, mg/dL	88 (83-93)	104 (101-108)	140 (131-167)	90 (86-94)	105 (102-110)	142 (131-172)	91 (87-95)	106 (102-111)	144 (132-178)
Low-density lipoprotein	113 (94-134)	125 (104-147)	131 (109-155)	123 (103-145)	131 (110-152)	136 (113-159)	127 (106-149)	133 (112-155)	138 (115-163)

cholesterol, mg/dL													
High-density lipoprotein cholesterol, mg/dL	64 (54-76)	59 (50-71)	53 (44-64)	60 (50-72)	57 (48-69)	52 (44-62)	60 (50-73)	58 (49-70)	52 (44-63)				
Triglycerides, mg/dL	69 (50-99)	91 (65-134)	122 (83-187)	89 (63-133)	108 (75-161)	141 (96-218)	100 (69-149)	115 (80-171)	148 (100-225)				
Dyslipidemia, n (%)	553,715 (27.7)	135,983 (47.3)	11,300 (63.6)	222,138 (44.4)	92,759 (58.1)	11,726 (72.1)	115,762 (52.0)	72,589 (62.4)	14,127 (74.7)				
Cigarette smoking, n (%)	457,734 (22.9)	86,826 (30.2)	7,555 (42.5)	139,527 (27.9)	47,653 (29.9)	6,500 (40.0)	64,897 (29.2)	33,742 (29.0)	6,809 (36.0)				
Alcohol consumption, n (%)	314,400 (15.7)	78,167 (27.2)	4,398 (24.7)	133,846 (26.8)	57,116 (35.8)	4,962 (30.5)	71,523 (32.1)	45,550 (39.1)	6,336 (33.5)				

Data are expressed as number (percentage) or median (Q1-Q3).

Table S2. Relative Risk Reduction for Each Cardiovascular Event

	Normal FPG (n=2,719,830)	Prediabetes (n=563,573)	Diabetes (n=52,960)	P for interactio n		Normal/Elevate d BP (n=2,302,658)	Stage 1 Hypertension (n=675,919)	Stage 2 Hypertension (n=357,786)	P for interactio n
Myocardial Infarction									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.1746	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0029
Stage 1 Hypertension	27.3% (21.5%-32.7%)	21.2% (10.7%-30.4%)	10.5% (-16.8%-31.4%)		Prediabetes	13.7% (4.7%-21.9%)	4.3% (-6.7%-14.2%)	2.2% (-9.7%-12.8%)	
Stage 2 Hypertension	48.1% (43.3%-52.6%)	41.7% (33.8%-48.7%)	29.6% (9.2%-45.4%)		Diabetes	61.0% (52.4%-68.1%)	44.4% (32.2%-54.4%)	34.3% (21.7%-45.0%)	
Angina Pectoris									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0449	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0056
Stage 1 Hypertension	16.0% (13.8%-18.0%)	13.4% (9.5%-17.1%)	8.7% (-3.2%-19.1%)		Prediabetes	2.5% (-0.8%-5.6%)	1.8% (-2.1%-5.6%)	0.5% (-3.9%-4.6%)	
Stage 2 Hypertension	35.2% (33.2%-37.2%)	31.1% (27.9%-34.2%)	24.5% (15.1%-32.9%)		Diabetes	32.4% (26.1%-38.1%)	25.0% (18.1%-31.4%)	15.0% (8.1%-21.4%)	
Stroke									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0077	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0307
Stage 1 Hypertension	26.5% (23.8%-29.2%)	19.8% (14.5%-24.7%)	27.2% (12.2%-39.6%)		Prediabetes	2.7% (-2.1%-7.3%)	-2.6% (-8.5%-2.9%)	-9.1% (-15.1%-3.4%)	

Stage 2 Hypertension	55.3% (53.5%-57.1%)	48.8% (45.5%-51.9%)	55.1% (46.7%-62.2%)		Diabetes	17.8% (5.2%-28.7%)	20.1% (9.4%-29.7%)	11.1% (2.1%-19.3%)	
Heart Failure									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	< 0.001	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	< 0.001
Stage 1 Hypertension	23.6% (21.7%-25.5%)	14.4% (10.5%-18.0%)	5.9% (-5.8%-16.3%)		Prediabetes	9.0% (6.0%-12.0%)	-0.2% (-4.1%-3.7%)	-1.3% (-5.2%-2.4%)	
Stage 2 Hypertension	53.5% (52.2%-54.8%)	46.4% (44.0%-48.7%)	37.2% (30.1%-43.7%)		Diabetes	43.0% (37.9%-47.6%)	26.5% (19.9%-32.5%)	12.5% (6.3%-18.3%)	
Atrial Fibrillation									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.5712	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.4632
Stage 1 Hypertension	13.5% (9.0%-17.8%)	10.0% (2.4%-17.1%)	10.2% (-13.9%-29.2%)		Prediabetes	7.0% (0.9%-12.7%)	4.9% (-2.4%-11.7%)	1.0% (-7.1%-8.5%)	
Stage 2 Hypertension	35.2% (31.2%-39.0%)	29.8% (23.7%-35.5%)	27.7% (9.9%-41.9%)		Diabetes	24.2% (9.6%-36.4%)	21.4% (6.8%-33.7%)	9.5% (-4.6%-21.7%)	

FPG=fasting plasma glucose, BP=blood pressure. Hazard ratios (95% confidence interval) of stage 1 or stage 2 hypertension were adjusted for age, sex, body mass index, fasting plasma glucose, dyslipidemia, cigarette smoking, and alcohol consumption. Hazard ratios (95% confidence interval) of prediabetes or diabetes were adjusted for age, sex, body mass index, systolic blood pressure, dyslipidemia, cigarette smoking, and alcohol consumption. Relative risk reduction was calculated from hazard ratios.

Table S3. Association of Blood Pressure and Glycemic Status with Incident Cardiovascular Disease (Multiple Imputations for Missing Data)

	Normal FPG (n=3,208,830)	Prediabetes (n=655,883)	Diabetes (n=62,381)	P for interactio n		Normal/Elevate d BP (n=2,715,653)	Stage 1 Hypertension (n=795,789)	Stage 2 Hypertension (n=415,652)	P for interactio n
Myocardial Infarction									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.2566	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0175
Stage 1 Hypertension	1.38 (1.29- 1.48)	1.26 (1.12- 1.41)	1.16 (0.90- 1.48)		Prediabetes	1.12 (1.02- 1.23)	1.02 (0.92- 1.13)	1.03 (0.93- 1.14)	
Stage 2 Hypertension	1.90 (1.75- 2.06)	1.71 (1.52- 1.92)	1.52 (1.20- 1.92)		Diabetes	2.36 (1.96- 2.85)	1.75 (1.46- 2.10)	1.58 (1.34- 1.85)	
Angina Pectoris									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0311	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0069
Stage 1 Hypertension	1.19 (1.16- 1.21)	1.15 (1.10- 1.20)	1.10 (0.98- 1.23)		Prediabetes	1.03 (1.00- 1.06)	1.02 (0.98- 1.05)	1.00 (0.96- 1.04)	
Stage 2 Hypertension	1.55 (1.51- 1.59)	1.45 (1.39- 1.52)	1.35 (1.22- 1.50)		Diabetes	1.48 (1.36- 1.60)	1.34 (1.24- 1.45)	1.21 (1.12- 1.29)	
Stroke									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0040	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0124
Stage 1 Hypertension	1.35 (1.31- 1.40)	1.25 (1.18- 1.33)	1.35 (1.14- 1.60)		Prediabetes	1.03 (0.98- 1.07)	0.98 (0.93- 1.03)	0.92 (0.87- 0.96)	
Stage 2 Hypertension	2.23 (2.15- 2.32)	1.95 (1.84- 2.07)	2.20 (1.89- 2.57)		Diabetes	1.25 (1.10- 1.42)	1.26 (1.12- 1.41)	1.13 (1.03- 1.23)	
Heart Failure									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	< 0.001	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	<0.001

Stage 1 Hypertension	1.31 (1.28-1.34)	1.17 (1.13-1.22)	1.11 (0.99-1.23)		Prediabetes	1.10 (1.06-1.13)	1.00 (0.96-1.03)	0.99 (0.95-1.02)	
Stage 2 Hypertension	2.17 (2.11-2.22)	1.88 (1.81-1.96)	1.62 (1.46-1.78)		Diabetes	1.70 (1.57-1.84)	1.38 (1.28-1.49)	1.14 (1.07-1.21)	
Atrial Fibrillation									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.1162	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.1479
Stage 1 Hypertension	1.18 (1.12-1.23)	1.08 (1.00-1.17)	1.13 (0.91-1.41)		Prediabetes	1.08 (1.02-1.15)	1.02 (0.96-1.10)	1.00 (0.94-1.08)	
Stage 2 Hypertension	1.58 (1.49-1.66)	1.42 (1.31-1.53)	1.36 (1.10-1.68)		Diabetes	1.28 (1.09-1.51)	1.23 (1.06-1.44)	1.04 (0.91-1.19)	

FPG=fasting plasma glucose, BP=blood pressure. Hazard ratios (95% confidence interval) of stage 1 or stage 2 hypertension were adjusted for age, sex, body mass index, fasting plasma glucose, dyslipidemia, cigarette smoking, and alcohol consumption. Hazard ratios (95% confidence interval) of prediabetes or diabetes were adjusted for age, sex, body mass index, systolic blood pressure, dyslipidemia, cigarette smoking, and alcohol consumption.

Table S4. Association of Blood Pressure and Glycemic Status with Incident Cardiovascular Disease (Cause-Specific Analysis)

	Normal FPG (n=2,719,830)	Prediabetes (n=563,573)	Diabetes (n=52,960)	P for interactio n		Normal/Elevate d BP (n=2,302,658)	Stage 1 Hypertension (n=675,919)	Stage 2 Hypertension (n=357,786)	P for interactio n
Myocardial Infarction									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.1746	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0029
Stage 1 Hypertension	1.38 (1.27-1.49)	1.27 (1.12-1.44)	1.12 (0.85-1.46)		Prediabetes	1.16 (1.05-1.28)	1.04 (0.94-1.17)	1.02 (0.91-1.15)	
Stage 2 Hypertension	1.93 (1.76-2.11)	1.72 (1.51-1.95)	1.42 (1.10-1.83)		Diabetes	2.57 (2.10-3.14)	1.80 (1.47-2.19)	1.52 (1.28-1.82)	
Angina Pectoris									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0449	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0056
Stage 1 Hypertension	1.19 (1.16-1.22)	1.15 (1.10-1.21)	1.09 (0.97-1.24)		Prediabetes	1.03 (0.99-1.06)	1.02 (0.98-1.06)	1.00 (0.96-1.05)	
Stage 2 Hypertension	1.54 (1.50-1.59)	1.45 (1.39-1.52)	1.32 (1.18-1.49)		Diabetes	1.48 (1.35-1.62)	1.33 (1.22-1.46)	1.18 (1.09-1.27)	
Stroke									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0077	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0307
Stage 1 Hypertension	1.36 (1.31-1.41)	1.25 (1.17-1.33)	1.37 (1.14-1.66)		Prediabetes	1.03 (0.98-1.08)	0.97 (0.92-1.03)	0.92 (0.87-0.97)	
Stage 2 Hypertension	2.24 (2.15-2.33)	1.95 (1.83-2.08)	2.23 (1.88-2.64)		Diabetes	1.22 (1.06-1.40)	1.25 (1.10-1.42)	1.12 (1.02-1.24)	
Heart Failure									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	<0.001	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	<0.001

BP				FPG					
Stage 1 Hypertension	1.31 (1.28-1.34)	1.17 (1.12-1.22)	1.06 (0.94-1.20)		Prediabetes	1.10 (1.06-1.14)	1.00 (0.96-1.04)	0.99 (0.95-1.02)	
Stage 2 Hypertension	2.15 (2.09-2.21)	1.87 (1.79-1.95)	1.59 (1.43-1.78)		Diabetes	1.75 (1.61-1.91)	1.36 (1.25-1.48)	1.14 (1.07-1.22)	
Atrial Fibrillation									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.5712	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.4632
Stage 1 Hypertension	1.16 (1.10-1.22)	1.11 (1.02-1.21)	1.11 (0.88-1.41)		Prediabetes	1.08 (1.01-1.15)	1.05 (0.98-1.13)	1.01 (0.93-1.09)	
Stage 2 Hypertension	1.54 (1.45-1.64)	1.42 (1.31-1.55)	1.38 (1.10-1.73)		Diabetes	1.32 (1.11-1.57)	1.27 (1.07-1.51)	1.11 (0.96-1.28)	

FPG=fasting plasma glucose, BP=blood pressure. Hazard ratios (95% confidence interval) of stage 1 or stage 2 hypertension were adjusted for age, sex, body mass index, fasting plasma glucose, dyslipidemia, cigarette smoking, and alcohol consumption. Hazard ratios (95% confidence interval) of prediabetes or diabetes were adjusted for age, sex, body mass index, systolic blood pressure, dyslipidemia, cigarette smoking, and alcohol consumption.

Table S5. Association of Blood Pressure and Glycemic Status with Incident Cardiovascular Disease (Adding Individuals Taking Any Blood Pressure or Glucose-Lowering Medications)

	Normal FPG (n=2,868,581)	Prediabetes (n=661,643)	Diabetes (n=155,429)	P for interactio n		Normal/Elevate d BP (n=2,326,139)	Stage 1 Hypertension (n=690,589)	Stage 2 Hypertension (n=668,925)	P for interactio n
Myocardial Infarction									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0020	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	< 0.0001
Stage 1 Hypertension	1.38 (1.28-1.49)	1.29 (1.14-1.46)	1.31 (1.09-1.56)		Prediabetes	1.16 (1.05-1.28)	1.05 (0.94-1.17)	1.00 (0.92-1.09)	
Stage 2 Hypertension	2.06 (1.91-2.22)	1.76 (1.57-1.97)	1.52 (1.31-1.77)		Diabetes	2.40 (2.08-2.77)	1.98 (1.71-2.29)	1.52 (1.38-1.67)	
Angina Pectoris									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	< 0.001	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	< 0.0001
Stage 1 Hypertension	1.20 (1.17-1.23)	1.17 (1.12-1.22)	1.05 (0.97-1.14)		Prediabetes	1.03 (0.99-1.06)	1.02 (0.98-1.06)	1.01 (0.98-1.04)	
Stage 2 Hypertension	1.73 (1.69-1.77)	1.59 (1.53-1.65)	1.37 (1.29-1.46)		Diabetes	1.62 (1.53-1.71)	1.42 (1.33-1.52)	1.27 (1.23-1.32)	
Stroke									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	<0.001	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0034
Stage 1 Hypertension	1.37 (1.33-1.42)	1.26 (1.18-1.34)	1.25 (1.11-1.41)		Prediabetes	1.03 (0.98-1.08)	0.98 (0.92-1.03)	0.93 (0.90-0.97)	
Stage 2 Hypertension	2.20 (2.12-2.27)	1.90 (1.80-2.01)	1.84 (1.67-2.03)		Diabetes	1.35 (1.24-1.48)	1.29 (1.18-1.42)	1.17 (1.11-1.23)	
Heart Failure									

Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	< 0.001	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	< 0.0001
Stage 1 Hypertension	1.32 (1.29-1.35)	1.18 (1.13-1.23)	1.08 (1.00-1.17)		Prediabetes	1.10 (1.06-1.14)	1.00 (0.96-1.04)	1.00 (0.98-1.03)	
Stage 2 Hypertension	2.29 (2.24-2.35)	1.98 (1.91-2.06)	1.63 (1.53-1.74)		Diabetes	1.70 (1.61-1.81)	1.38 (1.30-1.47)	1.18 (1.14-1.22)	
Atrial Fibrillation									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.6154	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.7949
Stage 1 Hypertension	1.16 (1.10-1.22)	1.11 (1.02-1.20)	1.09 (0.92-1.30)		Prediabetes	1.08 (1.01-1.15)	1.05 (0.98-1.13)	1.05 (0.99-1.10)	
Stage 2 Hypertension	1.72 (1.64-1.81)	1.63 (1.52-1.75)	1.56 (1.36-1.80)		Diabetes	1.09 (0.96-1.23)	1.08 (0.94-1.24)	1.01 (0.94-1.08)	

FPG=fasting plasma glucose, BP=blood pressure. Hazard ratios (95% confidence interval) of stage 1 or stage 2 hypertension were adjusted for age, sex, body mass index, fasting plasma glucose, dyslipidemia, cigarette smoking, and alcohol consumption. Hazard ratios (95% confidence interval) of prediabetes or diabetes were adjusted for age, sex, body mass index, systolic blood pressure, dyslipidemia, cigarette smoking, and alcohol consumption.

Table S6. Association of Blood Pressure and Glycemic Status with Incident Cardiovascular Disease (Adding Estimated Glomerular Filtration Rate to Covariates)

	Normal FPG (n=1,366,336)	Prediabetes (n=280,702)	Diabetes (n=24,576)	P for interactio n		Normal/Elevate d BP (n=1,163,328)	Stage 1 Hypertension (n=335,160)	Stage 2 Hypertension (n=173,126)	P for interactio n
Myocardial Infarction									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.7699	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.2711
Stage 1 Hypertension	1.32 (1.18-1.48)	1.28 (1.06-1.54)	1.16 (0.74-1.79)		Prediabetes	1.12 (0.97-1.30)	1.03 (0.88-1.21)	1.13 (0.95-1.35)	
Stage 2 Hypertension	1.74 (1.52-1.99)	1.79 (1.48-2.16)	1.34 (0.88-2.05)		Diabetes	2.08 (1.50-2.89)	1.48 (1.07-2.04)	1.33 (0.99-1.78)	
Angina Pectoris									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0930	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0673
Stage 1 Hypertension	1.22 (1.18-1.27)	1.12 (1.05-1.19)	1.17 (0.97-1.42)		Prediabetes	1.06 (1.01-1.11)	0.98 (0.93-1.04)	1.01 (0.95-1.08)	
Stage 2 Hypertension	1.54 (1.47-1.62)	1.42 (1.33-1.52)	1.36 (1.13-1.63)		Diabetes	1.42 (1.23-1.64)	1.33 (1.16-1.52)	1.16 (1.02-1.31)	
Stroke									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0283	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.1450
Stage 1 Hypertension	1.34 (1.27-1.41)	1.26 (1.15-1.38)	1.26 (0.92-1.72)		Prediabetes	1.04 (0.97-1.12)	1.03 (0.94-1.12)	0.92 (0.85-1.00)	
Stage 2 Hypertension	2.22 (2.09-2.36)	1.88 (1.71-2.07)	2.45 (1.86-3.24)		Diabetes	1.06 (0.84-1.34)	1.04 (0.84-1.30)	1.15 (0.99-1.34)	
Heart Failure									

Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	< 0.0001	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	< 0.0001
Stage 1 Hypertension	1.33 (1.28-1.38)	1.17 (1.10-1.25)	1.07 (0.88-1.28)		Prediabetes	1.12 (1.07-1.18)	1.00 (0.94-1.06)	0.99 (0.93-1.04)	
Stage 2 Hypertension	2.19 (2.10-2.29)	1.85 (1.73-1.97)	1.57 (1.32-1.86)		Diabetes	1.70 (1.48-1.94)	1.32 (1.15-1.50)	1.12 (1.01-1.25)	
Atrial Fibrillation									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.5352	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.6290
Stage 1 Hypertension	1.15 (1.06-1.24)	1.13 (1.00-1.28)	1.59 (1.07-2.38)		Prediabetes	1.06 (0.96-1.16)	1.05 (0.93-1.17)	1.03 (0.91-1.16)	
Stage 2 Hypertension	1.47 (1.35-1.62)	1.40 (1.23-1.60)	1.66 (1.12-2.47)		Diabetes	0.95 (0.69-1.30)	1.25 (0.96-1.62)	0.97 (0.76-1.24)	

FPG=fasting plasma glucose, BP=blood pressure. Hazard ratios (95% confidence interval) of stage 1 or stage 2 hypertension were adjusted for age, sex, body mass index, fasting plasma glucose, dyslipidemia, cigarette smoking, and alcohol consumption. Hazard ratios (95% confidence interval) of prediabetes or diabetes were adjusted for age, sex, body mass index, systolic blood pressure, dyslipidemia, cigarette smoking, and alcohol consumption.

Table S7. Association of Blood Pressure and Glycemic Status with Incident Cardiovascular Disease (Subgroup Analyses)

Men									
	Normal FPG (n=1,454,153)	Prediabetes (n=410,379)	Diabetes (n=42,533)	P for interactio n		Normal/Elevate d BP (n=1,170,298)	Stage 1 Hypertension (n=479,337)	Stage 2 Hypertension (n=257,430)	P for interactio n
Myocardial Infarction									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0868	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0249
Stage 1 Hypertension	1.47 (1.34-1.60)	1.29 (1.13-1.47)	1.17 (0.88-1.56)		Prediabetes	1.18 (1.06-1.32)	1.05 (0.93-1.18)	1.01 (0.89-1.14)	
Stage 2 Hypertension	2.06 (1.87-2.28)	1.72 (1.51-1.97)	1.50 (1.14-1.97)		Diabetes	2.29 (1.84-2.85)	1.71 (1.39-2.11)	1.47 (1.23-1.77)	
Angina Pectoris									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.4951	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0955
Stage 1 Hypertension	1.18 (1.14-1.21)	1.17 (1.12-1.23)	1.17 (1.02-1.34)		Prediabetes	1.02 (0.98-1.06)	1.03 (0.98-1.07)	1.02 (0.97-1.07)	
Stage 2 Hypertension	1.56 (1.50-1.62)	1.50 (1.42-1.58)	1.43 (1.25-1.62)		Diabetes	1.40 (1.27-1.55)	1.34 (1.22-1.47)	1.18 (1.09-1.29)	
Stroke									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.2322	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.2840
Stage 1 Hypertension	1.39 (1.32-1.45)	1.30 (1.21-1.40)	1.43 (1.17-1.76)		Prediabetes	1.04 (0.98-1.10)	0.99 (0.93-1.05)	0.95 (0.90-1.01)	
Stage 2 Hypertension	2.37 (2.26-2.49)	2.14 (2.00-2.30)	2.32 (1.92-2.80)		Diabetes	1.21 (1.03-1.42)	1.26 (1.10-1.45)	1.13 (1.02-1.26)	
Heart Failure									

Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	< 0.001	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	< 0.0001
Stage 1 Hypertension	1.31 (1.27-1.35)	1.19 (1.13-1.25)	1.08 (0.95-1.22)		Prediabetes	1.09 (1.05-1.14)	1.01 (0.97-1.05)	0.98 (0.94-1.02)	
Stage 2 Hypertension	2.19 (2.12-2.27)	1.89 (1.80-1.98)	1.60 (1.42-1.80)		Diabetes	1.70 (1.55-1.87)	1.36 (1.24-1.49)	1.13 (1.05-1.21)	
Atrial Fibrillation									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.7333	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.7545
Stage 1 Hypertension	1.12 (1.06-1.19)	1.09 (1.00-1.19)	1.15 (0.90-1.48)		Prediabetes	1.06 (0.99-1.13)	1.04 (0.96-1.12)	1.00 (0.92-1.08)	
Stage 2 Hypertension	1.49 (1.39-1.59)	1.38 (1.26-1.51)	1.44 (1.13-1.82)		Diabetes	1.24 (1.03-1.49)	1.27 (1.06-1.51)	1.13 (0.97-1.31)	
Women									
	Normal FPG (n=1,265,677)	Prediabetes (n=153,194)	Diabetes (n=10,427)	P for interaction		Normal/Elevated BP (n=1,132,360)	Stage 1 Hypertension (n=196,582)	Stage 2 Hypertension (n=100,356)	P for interaction
Myocardial Infarction									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.7067	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.4304
Stage 1 Hypertension	1.12 (0.93-1.35)	1.10 (0.73-1.65)	0.84 (0.37-1.92)		Prediabetes	0.97 (0.75-1.24)	0.98 (0.67-1.42)	1.16 (0.80-1.68)	
Stage 2 Hypertension	1.40 (1.11-1.78)	1.73 (1.17-2.55)	0.97 (0.45-2.09)		Diabetes	4.02 (2.42-6.67)	2.96 (1.48-5.91)	2.12 (1.16-3.90)	
Angina Pectoris									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0027	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0174
Stage 1 Hypertension	1.22 (1.17-	1.11 (1.01-	0.80 (0.59-		Prediabetes	1.04 (0.98-	0.99 (0.90-	0.95 (0.87-	

Hypertension	1.27)	1.22)	1.10)		Diabetes	1.10)	1.08)	1.05)	
Stage 2	1.48 (1.40-	1.29 (1.17-	0.95 (0.71-			1.72 (1.42-	1.19 (0.93-	1.11 (0.91-	
Hypertension	1.56)	1.43)	1.26)			2.08)	1.53)	1.37)	
Stroke									
Normal/Elevated	1 [Reference]	1 [Reference]	1 [Reference]	0.0005	Normal	1 [Reference]	1 [Reference]	1 [Reference]	0.0220
BP					FPG				
Stage 1	1.34 (1.26-	1.13 (0.99-	1.16 (0.72-		Prediabetes	1.00 (0.92-	0.92 (0.82-	0.78 (0.69-	
Hypertension	1.43)	1.29)	1.86)			1.09)	1.04)	0.88)	
Stage 2	1.99 (1.85-	1.42 (1.24-	1.96 (1.30-		Diabetes	1.16 (0.84-	1.10 (0.77-	1.09 (0.85-	
Hypertension	2.13)	1.63)	2.96)			1.60)	1.56)	1.39)	
Heart Failure									
Normal/Elevated	1 [Reference]	1 [Reference]	1 [Reference]	0.0019	Normal	1 [Reference]	1 [Reference]	1 [Reference]	0.0114
BP					FPG				
Stage 1	1.33 (1.28-	1.11 (1.01-	1.00 (0.73-		Prediabetes	1.09 (1.03-	0.95 (0.87-	1.03 (0.95-	
Hypertension	1.39)	1.22)	1.36)			1.15)	1.03)	1.12)	
Stage 2	2.03 (1.93-	1.81 (1.66-	1.57 (1.20-		Diabetes	1.64 (1.35-	1.23 (0.97-	1.17 (0.99-	
Hypertension	2.14)	1.98)	2.05)			2.00)	1.56)	1.38)	
Atrial Fibrillation									
Normal/Elevated	1 [Reference]	1 [Reference]	1 [Reference]	0.6125	Normal	1 [Reference]	1 [Reference]	1 [Reference]	0.3691
BP					FPG				
Stage 1	1.31 (1.16-	1.28 (1.01-	0.80 (0.35-		Prediabetes	1.12 (0.96-	1.13 (0.91-	1.12 (0.90-	
Hypertension	1.46)	1.61)	1.85)			1.30)	1.40)	1.39)	
Stage 2	1.75 (1.53-	1.80 (1.43-	0.97 (0.45-		Diabetes	1.76 (1.06-	1.10 (0.57-	0.81 (0.47-	
Hypertension	2.01)	2.27)	2.08)			2.94)	2.15)	1.40)	

FPG=fasting plasma glucose, BP=blood pressure. Hazard ratios (95% confidence interval) of stage 1 or stage 2 hypertension were adjusted for age, sex, body mass index, fasting plasma glucose, dyslipidemia, cigarette smoking, and alcohol consumption. Hazard ratios (95% confidence interval) of prediabetes or diabetes were adjusted for age, sex, body mass index, systolic blood pressure, dyslipidemia, cigarette smoking, and alcohol consumption. In a subgroup analysis stratified by sex, sex was excluded from covariates.

Table S8. Association of Blood Pressure and Glycemic Status with Incident Cardiovascular Disease (Changing the Definition of Dyslipidemia)

	Normal FPG (n=2,719,830)	Prediabetes (n=563,573)	Diabetes (n=52,960)	P for interacti on		Normal/Elevate d BP (n=2,302,658)	Stage 1 Hypertension (n=675,919)	Stage 2 Hypertension (n=357,786)	P for interactio n
Myocardial Infarction									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.2039	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0030
Stage 1 Hypertension	1.38 (1.27-1.49)	1.27 (1.12-1.44)	1.13 (0.86-1.48)		Prediabetes	1.17 (1.06-1.30)	1.05 (0.94-1.18)	1.03 (0.92-1.16)	
Stage 2 Hypertension	1.93 (1.76-2.11)	1.72 (1.52-1.95)	1.44 (1.11-1.86)		Diabetes	2.63 (2.16-3.22)	1.84 (1.51-2.25)	1.57 (1.31-1.87)	
Angina Pectoris									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0401	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0043
Stage 1 Hypertension	1.19 (1.16-1.22)	1.16 (1.11-1.21)	1.10 (0.97-1.24)		Prediabetes	1.03 (1.00-1.07)	1.03 (0.99-1.07)	1.01 (0.97-1.05)	
Stage 2 Hypertension	1.55 (1.50-1.60)	1.45 (1.39-1.52)	1.33 (1.18-1.49)		Diabetes	1.50 (1.37-1.64)	1.35 (1.24-1.48)	1.19 (1.10-1.29)	
Stroke									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0070	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0297
Stage 1 Hypertension	1.36 (1.31-1.41)	1.25 (1.17-1.33)	1.38 (1.15-1.67)		Prediabetes	1.03 (0.98-1.08)	0.98 (0.92-1.03)	0.92 (0.87-0.97)	
Stage 2 Hypertension	2.24 (2.15-2.33)	1.95 (1.84-2.08)	2.25 (1.89-2.66)		Diabetes	1.23 (1.06-1.41)	1.26 (1.11-1.43)	1.13 (1.03-1.25)	
Heart Failure									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	< 0.0001	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	< 0.0001

BP				FPG					
Stage 1 Hypertension	1.31 (1.28-1.35)	1.17 (1.12-1.22)	1.06 (0.94-1.20)		Prediabetes	1.11 (1.07-1.14)	1.00 (0.96-1.04)	0.99 (0.95-1.03)	
Stage 2 Hypertension	2.16 (2.10-2.22)	1.87 (1.79-1.95)	1.59 (1.43-1.78)		Diabetes	1.77 (1.63-1.93)	1.37 (1.26-1.49)	1.14 (1.07-1.23)	
Atrial Fibrillation									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.5761	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.3985
Stage 1 Hypertension	1.16 (1.10-1.22)	1.11 (1.03-1.21)	1.11 (0.88-1.41)		Prediabetes	1.08 (1.01-1.15)	1.05 (0.97-1.13)	1.01 (0.93-1.09)	
Stage 2 Hypertension	1.55 (1.46-1.64)	1.43 (1.31-1.55)	1.38 (1.10-1.72)		Diabetes	1.31 (1.10-1.56)	1.26 (1.06-1.49)	1.09 (0.94-1.26)	

FPG=fasting plasma glucose, BP=blood pressure. Hazard ratios (95% confidence interval) of stage 1 or stage 2 hypertension were adjusted for age, sex, body mass index, fasting plasma glucose, dyslipidemia, cigarette smoking, and alcohol consumption. Hazard ratios (95% confidence interval) of prediabetes or diabetes were adjusted for age, sex, body mass index, systolic blood pressure, dyslipidemia, cigarette smoking, and alcohol consumption. Dyslipidemia was redefined as having total cholesterol level of ≥ 200 mg/dL or reporting the use of lipid-lowering medications.

Table S9. Association of Blood Pressure and Glycemic Status with Incident Cardiovascular Disease (Redefining Hyperglycemia using HbA1c)

	Normal (n=2,371,995)	Prediabetes (n=558,061)	Diabetes (n=49,286)	P for interacti on		Normal/Elevate d BP (n=2,059,741)	Stage 1 Hypertension (n=601,533)	Stage 2 Hypertension (n=318,068)	P for interactio n
Myocardial Infarction									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.5805	Normal	1 [Reference]	1 [Reference]	1 [Reference]	0.1542
Stage 1 Hypertension	1.28 (1.17-1.40)	1.42 (1.25-1.61)	1.24 (0.94-1.62)		Prediabetes	1.11 (1.01-1.23)	1.21 (1.07-1.36)	1.07 (0.94-1.22)	
Stage 2 Hypertension	1.84 (1.67-2.03)	1.80 (1.57-2.07)	1.71 (1.31-2.23)		Diabetes	2.37 (1.92-2.93)	1.97 (1.60-2.42)	1.73 (1.44-2.09)	
Angina Pectoris									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0666	Normal	1 [Reference]	1 [Reference]	1 [Reference]	0.2285
Stage 1 Hypertension	1.18 (1.15-1.22)	1.17 (1.12-1.22)	1.13 (1.00-1.28)		Prediabetes	1.06 (1.02-1.09)	1.07 (1.03-1.12)	1.04 (0.99-1.09)	
Stage 2 Hypertension	1.56 (1.51-1.61)	1.45 (1.38-1.52)	1.39 (1.24-1.57)		Diabetes	1.46 (1.34-1.60)	1.41 (1.29-1.54)	1.28 (1.18-1.39)	
Stroke									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.3950	Normal	1 [Reference]	1 [Reference]	1 [Reference]	0.8056
Stage 1 Hypertension	1.35 (1.29-1.40)	1.33 (1.25-1.42)	1.43 (1.19-1.73)		Prediabetes	0.99 (0.94-1.03)	1.01 (0.95-1.07)	0.99 (0.93-1.05)	
Stage 2 Hypertension	2.23 (2.14-2.33)	2.08 (1.94-2.22)	2.21 (1.85-2.64)		Diabetes	1.18 (1.02-1.36)	1.30 (1.14-1.48)	1.19 (1.07-1.32)	
Heart Failure									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	< 0.0001	Normal	1 [Reference]	1 [Reference]	1 [Reference]	< 0.0001

BP									
Stage 1 Hypertension	1.31 (1.27-1.34)	1.22 (1.17-1.27)	1.16 (1.03-1.31)		Prediabetes	1.08 (1.05-1.12)	1.06 (1.01-1.10)	0.98 (0.94-1.03)	
Stage 2 Hypertension	2.24 (2.17-2.31)	1.81 (1.73-1.90)	1.76 (1.57-1.97)		Diabetes	1.55 (1.42-1.69)	1.37 (1.26-1.50)	1.19 (1.11-1.28)	
Atrial Fibrillation									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0852	Normal	1 [Reference]	1 [Reference]	1 [Reference]	0.3347
Stage 1 Hypertension	1.16 (1.10-1.23)	1.09 (0.99-1.18)	1.11 (0.86-1.44)		Prediabetes	1.02 (0.96-1.09)	0.99 (0.92-1.08)	0.94 (0.86-1.03)	
Stage 2 Hypertension	1.56 (1.47-1.67)	1.36 (1.23-1.49)	1.27 (0.99-1.63)		Diabetes	1.12 (0.93-1.35)	1.14 (0.94-1.37)	0.93 (0.78-1.10)	

BP=blood pressure. FPG=fasting plasma glucose, BP=blood pressure. Hazard ratios (95% confidence interval) of stage 1 or stage 2 hypertension were adjusted for age, sex, body mass index, fasting plasma glucose, dyslipidemia, cigarette smoking, and alcohol consumption.

Hazard ratios (95% confidence interval) of prediabetes or diabetes were adjusted for age, sex, body mass index, systolic blood pressure, dyslipidemia, cigarette smoking, and alcohol consumption. We defined prediabetes as having HbA1c of 5.7-6.4%, and diabetes as having HbA1c \geq 6.5%. We excluded 357,021 individuals with missing HbA1c data.

Table S10. Association of Blood Pressure and Glycemic Status with Incident Cardiovascular Disease (Changing the Categorization of Glycemic Status)

	Normal FPG/Prediabetes (n=3,283,403)	Diabetes (n=52,960)	P for interaction		Normal/Elevate d BP (n=2,302,658)	Stage 1 Hypertension (n=675,919)	Stage 2 Hypertension (n=357,786)	P for interactio n
Myocardial Infarction								
Normal/Elevated BP	1 [Reference]	1 [Reference]	0.1399	Normal FPG/Prediabetes	1 [Reference]	1 [Reference]	1 [Reference]	0.0011
Stage 1 Hypertension	1.34 (1.26-1.43)	1.12 (0.85-1.46)		Diabetes	2.45 (2.01-2.99)	1.77 (1.46-2.15)	1.51 (1.27-1.79)	
Stage 2 Hypertension	1.85 (1.72-1.99)	1.42 (1.10-1.83)						
Angina Pectoris								
Normal/Elevated BP	1 [Reference]	1 [Reference]	0.0938	Normal FPG/Prediabetes	1 [Reference]	1 [Reference]	1 [Reference]	0.0007
Stage 1 Hypertension	1.18 (1.15-1.21)	1.09 (0.97-1.24)		Diabetes	1.47 (1.34-1.60)	1.33 (1.21-1.45)	1.17 (1.09-1.27)	
Stage 2 Hypertension	1.51 (1.48-1.55)	1.32 (1.18-1.49)						
Stroke								
Normal/Elevated BP	1 [Reference]	1 [Reference]	0.9272	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.6122
Stage 1 Hypertension	1.33 (1.29-1.38)	1.37 (1.14-1.66)		Diabetes	1.21 (1.05-1.39)	1.26 (1.11-1.43)	1.17 (1.06-1.28)	
Stage 2 Hypertension	2.15 (2.08-2.23)	2.23 (1.88-2.64)						
Heart Failure								
Normal/Elevated BP	1 [Reference]	1 [Reference]	< 0.0001	Normal	1 [Reference]	1 [Reference]	1 [Reference]	< 0.0001

BP				FPG/Prediabetes				
Stage 1 Hypertension	1.27 (1.25-1.30)	1.06 (0.94-1.20)		Diabetes	1.71 (1.57-1.86)	1.36 (1.25-1.48)	1.15 (1.08-1.23)	
Stage 2 Hypertension	2.07 (2.02-2.12)	1.59 (1.43-1.78)						
Atrial Fibrillation								
Normal/Elevated BP	1 [Reference]	1 [Reference]	0.7523	Normal FPG/Prediabetes	1 [Reference]	1 [Reference]	1 [Reference]	0.3111
Stage 1 Hypertension	1.14 (1.10-1.20)	1.11 (0.88-1.41)		Diabetes	1.29 (1.08-1.53)	1.25 (1.06-1.48)	1.10 (0.96-1.27)	
Stage 2 Hypertension	1.50 (1.43-1.58)	1.38 (1.10-1.73)						

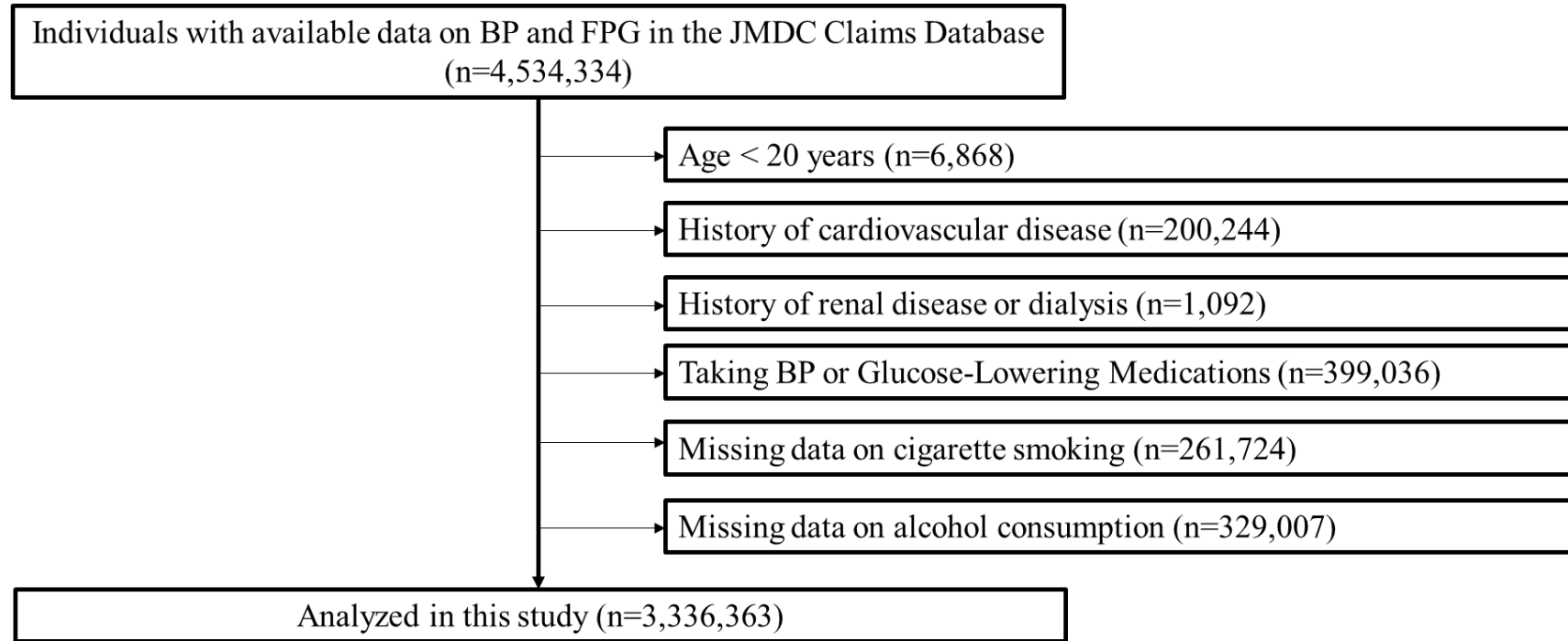
FPG=fasting plasma glucose, BP=blood pressure. FPG=fasting plasma glucose, BP=blood pressure. Hazard ratios (95% confidence interval) of stage 1 or stage 2 hypertension were adjusted for age, sex, body mass index, fasting plasma glucose, dyslipidemia, cigarette smoking, and alcohol consumption. Hazard ratios (95% confidence interval) of diabetes were adjusted for age, sex, body mass index, systolic blood pressure, dyslipidemia, cigarette smoking, and alcohol consumption.

Table S11. Association of Blood Pressure and Glycemic Status with Incident Cardiovascular Disease (Induction Period of One Year)									
	Normal FPG (n=2,190,921)	Prediabetes (n=460,943)	Diabetes (n=42,347)	P for interactio n		Normal/Elevate d BP (n=1,856,234)	Stage 1 Hypertension (n=553,180)	Stage 2 Hypertension (n=284,797)	P for interactio n
Myocardial Infarction									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.1240	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0098
Stage 1 Hypertension	1.43 (1.31-1.57)	1.28 (1.10-1.48)	1.16 (0.85-1.58)		Prediabetes	1.16 (1.04-1.31)	1.01 (0.89-1.15)	0.99 (0.86-1.13)	
Stage 2 Hypertension	1.98 (1.78-2.19)	1.68 (1.44-1.95)	1.37 (1.01-1.86)		Diabetes	2.53 (2.00-3.21)	1.81 (1.44-2.27)	1.47 (1.19-1.82)	
Angina Pectoris									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0061	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0015
Stage 1 Hypertension	1.20 (1.17-1.24)	1.2 (1.14-1.26)	1.07 (0.92-1.23)		Prediabetes	1.01 (0.97-1.05)	1.03 (0.98-1.07)	0.99 (0.94-1.04)	
Stage 2 Hypertension	1.52 (1.47-1.57)	1.42 (1.35-1.50)	1.18 (1.02-1.36)		Diabetes	1.48 (1.34-1.65)	1.29 (1.17-1.44)	1.10 (1.00-1.21)	
Stroke									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.0191	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.0948
Stage 1 Hypertension	1.40 (1.34-1.46)	1.31 (1.21-1.41)	1.43 (1.15-1.78)		Prediabetes	1.02 (0.96-1.08)	0.98 (0.92-1.05)	0.91 (0.85-0.97)	
Stage 2 Hypertension	2.23 (2.13-2.34)	1.91 (1.78-2.06)	2.11 (1.72-2.60)		Diabetes	1.17 (0.99-1.39)	1.24 (1.07-1.43)	1.08 (0.96-1.22)	
Heart Failure									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	<0.001	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	<0.001

Stage 1 Hypertension	1.33 (1.29-1.37)	1.19 (1.13-1.25)	1.03 (0.90-1.19)		Prediabetes	1.1 (1.06-1.14)	0.99 (0.95-1.04)	0.96 (0.92-1.01)	
Stage 2 Hypertension	2.12 (2.05-2.19)	1.79 (1.70-1.88)	1.45 (1.28-1.65)		Diabetes	1.71 (1.55-1.89)	1.29 (1.17-1.43)	1.08 (0.99-1.17)	
Atrial Fibrillation									
Normal/Elevated BP	1 [Reference]	1 [Reference]	1 [Reference]	0.6551	Normal FPG	1 [Reference]	1 [Reference]	1 [Reference]	0.5866
Stage 1 Hypertension	1.17 (1.10-1.24)	1.14 (1.04-1.26)	1.04 (0.79-1.38)		Prediabetes	1.04 (0.97-1.12)	1.04 (0.95-1.13)	0.99 (0.90-1.08)	
Stage 2 Hypertension	1.56 (1.46-1.67)	1.45 (1.31-1.60)	1.33 (1.02-1.73)		Diabetes	1.33 (1.09-1.63)	1.20 (0.98-1.48)	1.08 (0.91-1.28)	

FPG=fasting plasma glucose, BP=blood pressure. Hazard ratios (95% confidence interval) of stage 1 or stage 2 hypertension were adjusted for age, sex, body mass index, fasting plasma glucose, dyslipidemia, cigarette smoking, and alcohol consumption. Hazard ratios (95% confidence interval) of prediabetes or diabetes were adjusted for age, sex, body mass index, systolic blood pressure, dyslipidemia, cigarette smoking, and alcohol consumption.

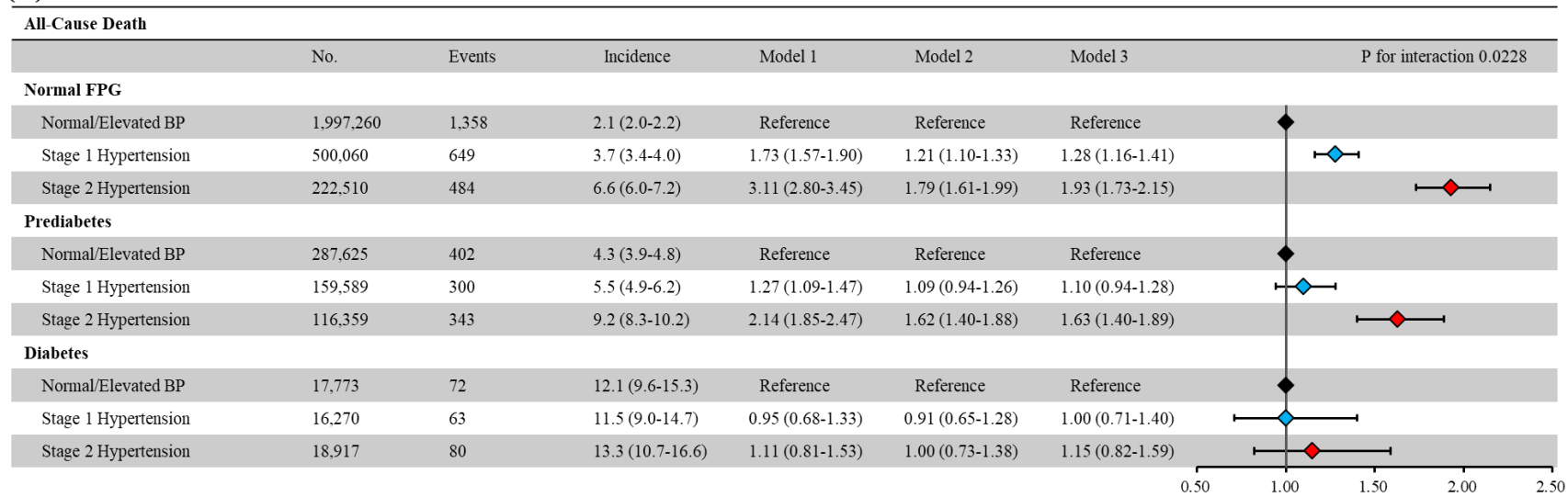
Figure S1. Flowchart



FPG=fasting plasma glucose, BP=blood pressure.

Figure S2. Association of BP Category with All-Cause Mortality according to Glycemic Status

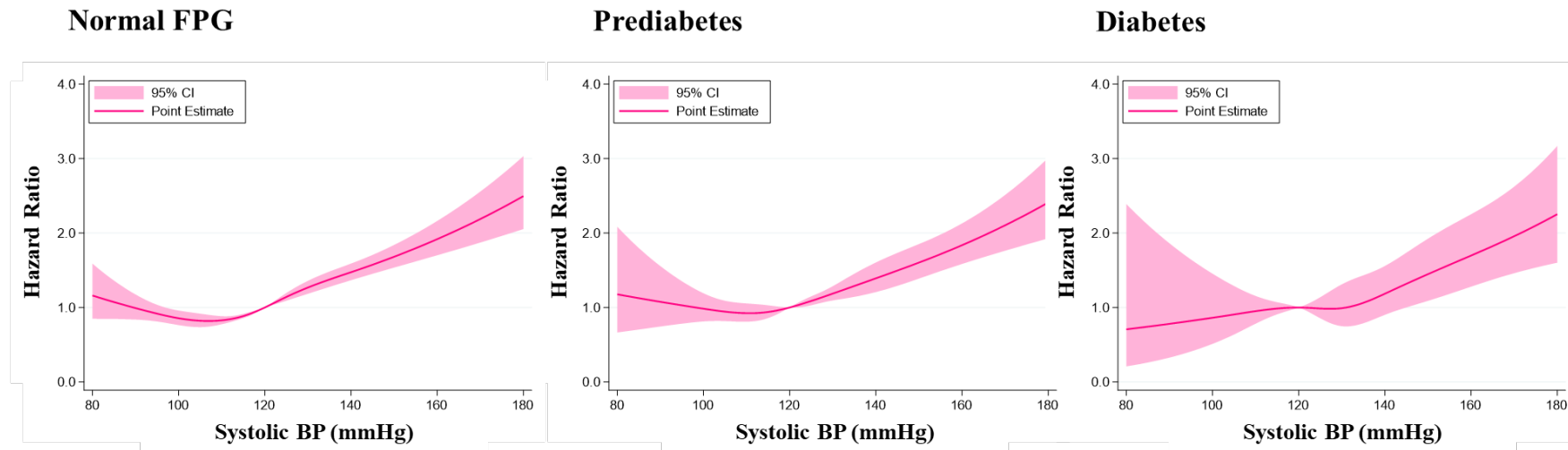
(F) All-Cause Death



FPG=fasting plasma glucose, BP=blood pressure.

Figure S3. Restricted Cubic Spline

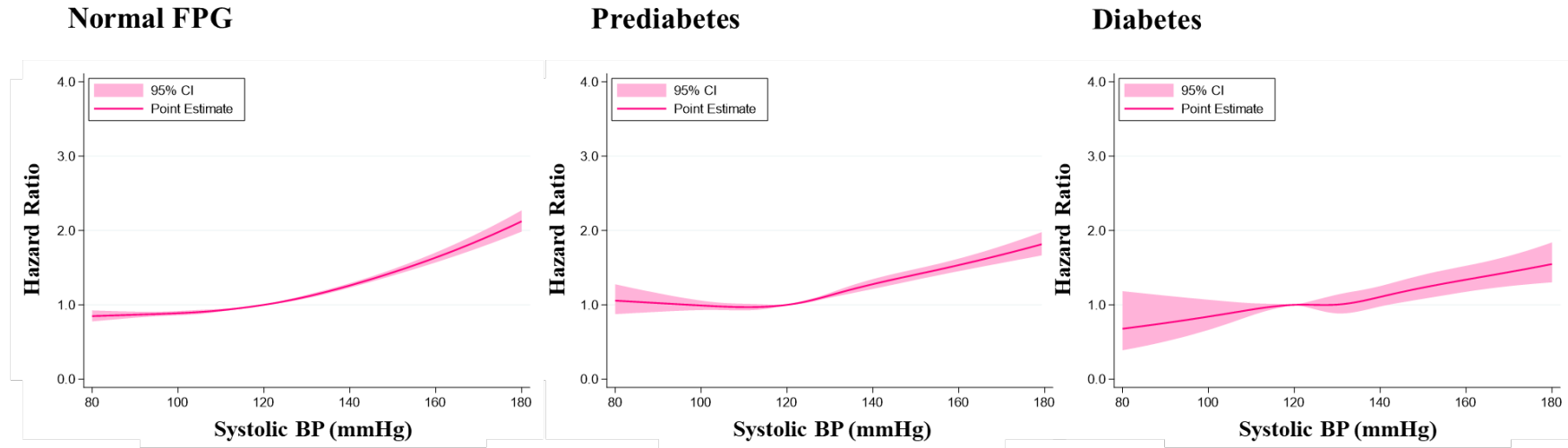
(A) Myocardial Infarction



FPG=fasting plasma glucose, BP=blood pressure.

Figure S3. Restricted Cubic Spline

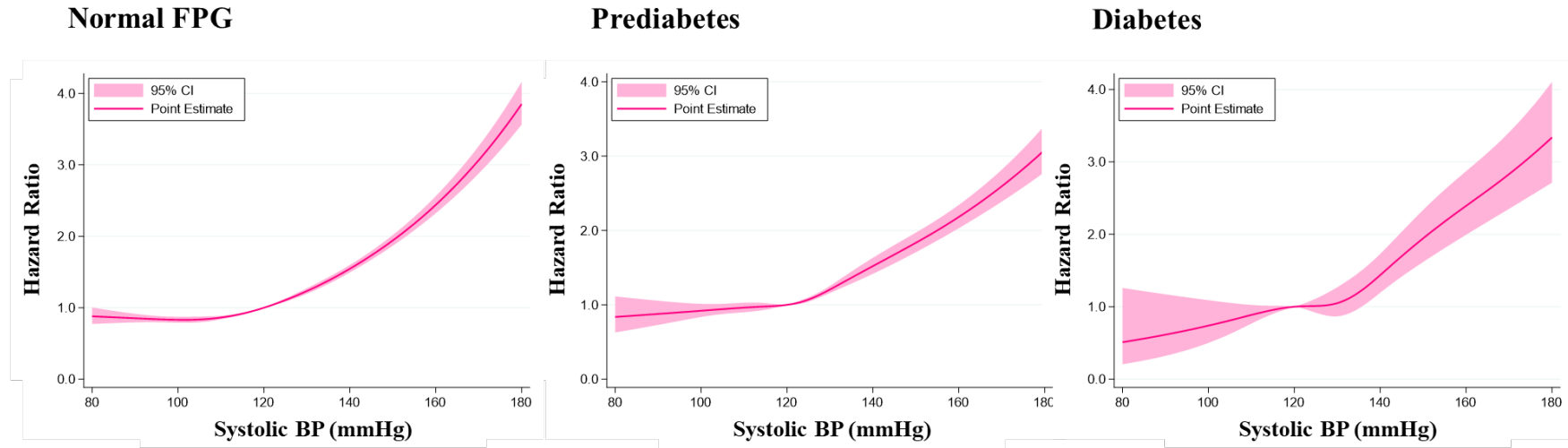
(B) Angina Pectoris



FPG=fasting plasma glucose, BP=blood pressure.

Figure S3. Restricted Cubic Spline

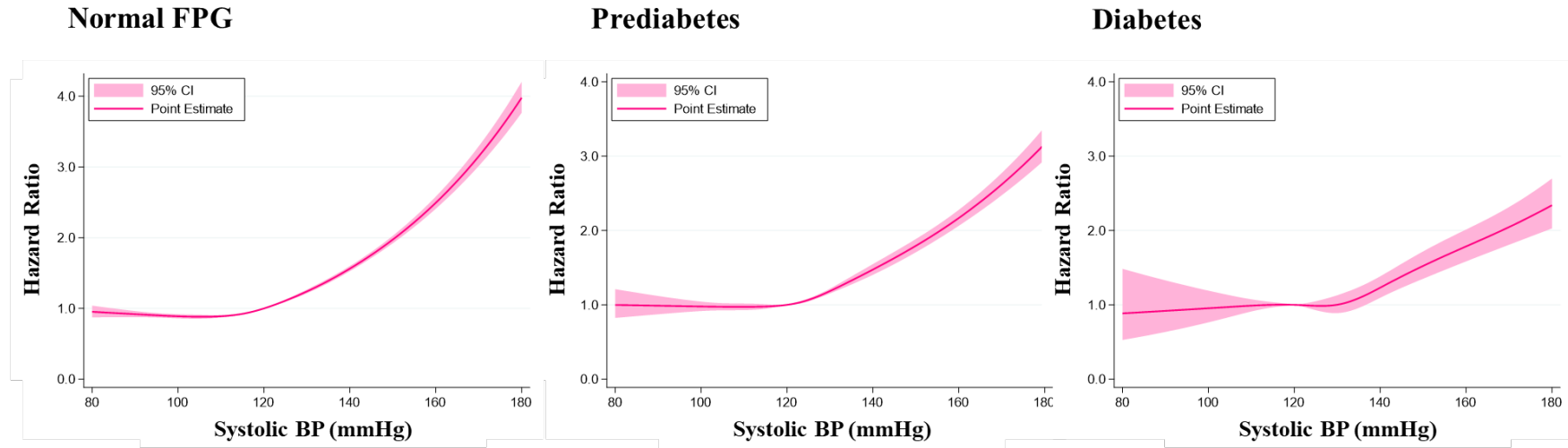
(C) Stroke



FPG=fasting plasma glucose, BP=blood pressure.

Figure S3. Restricted Cubic Spline

(D) Heart Failure

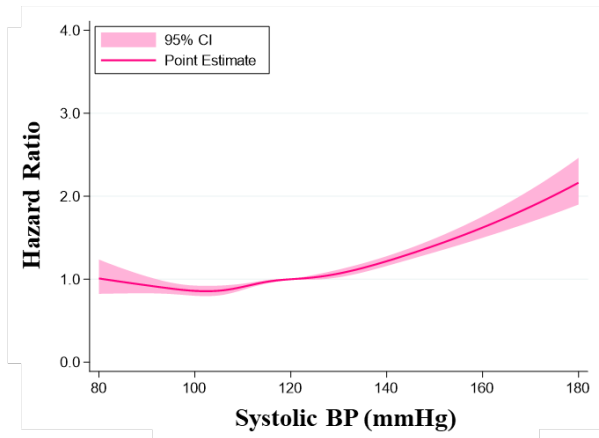


FPG=fasting plasma glucose, BP=blood pressure.

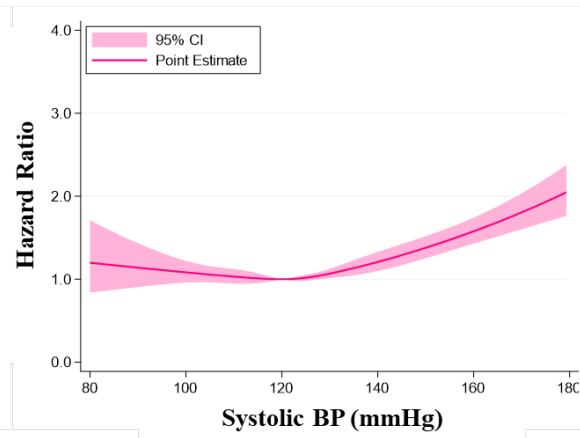
Figure S3. Restricted Cubic Spline

(E) Atrial Fibrillation

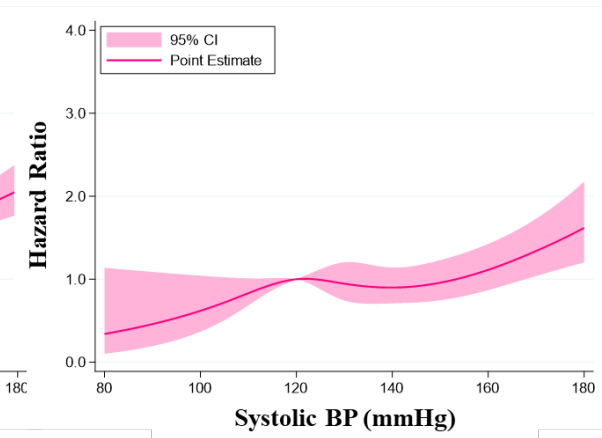
Normal FPG



Prediabetes



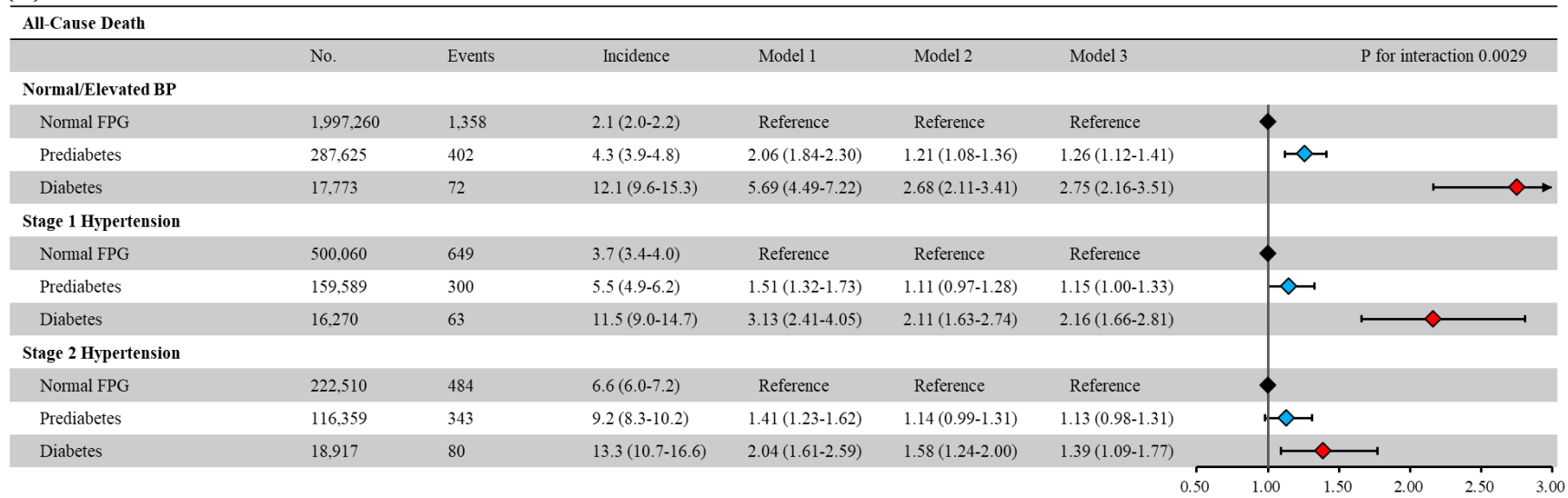
Diabetes



FPG=fasting plasma glucose, BP=blood pressure.

Figure S4. Association of Glycemic Status with All-Cause Mortality according to BP Category

(F) All-Cause Death



FPG=fasting plasma glucose, BP=blood pressure.

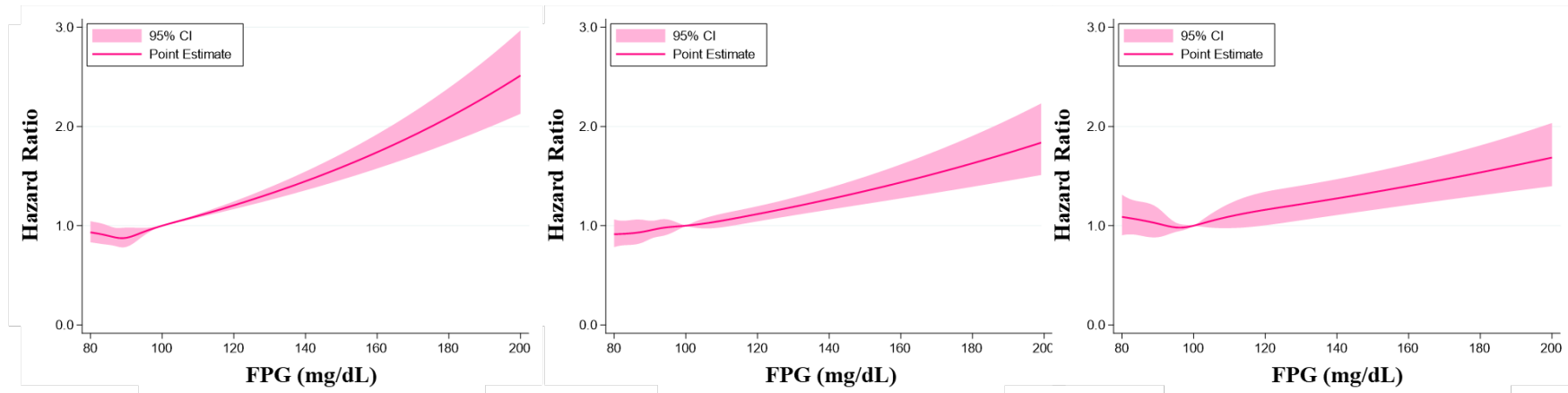
Figure S5. Restricted Cubic Spline

(A) Myocardial Infarction

Normal/Elevated BP

Stage 1 Hypertension

Stage 2 Hypertension



FPG=fasting plasma glucose, BP=blood pressure.

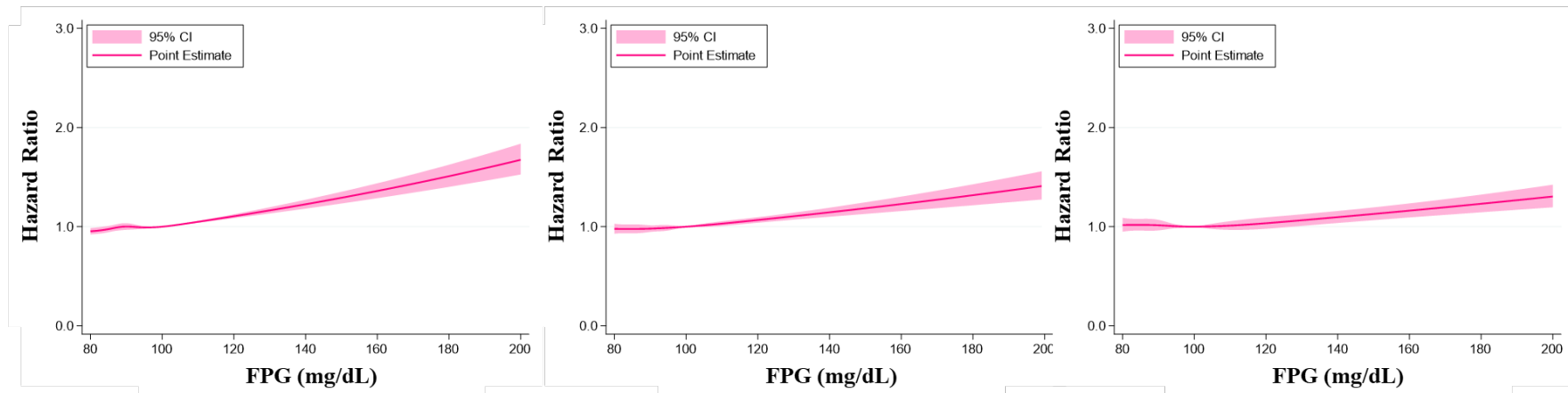
Figure S5. Restricted Cubic Spline

(B) Angina Pectoris

Normal/Elevated BP

Stage 1 Hypertension

Stage 2 Hypertension



FPG=fasting plasma glucose, BP=blood pressure.

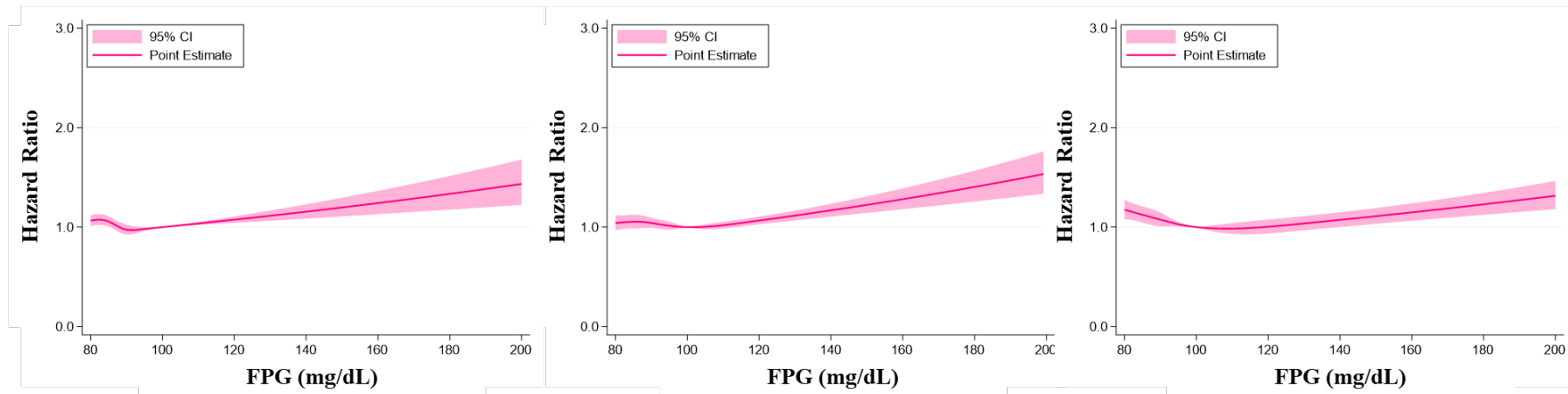
Figure S5. Restricted Cubic Spline

(C) Stroke

Normal/Elevated BP

Stage 1 Hypertension

Stage 2 Hypertension



FPG=fasting plasma glucose, BP=blood pressure.

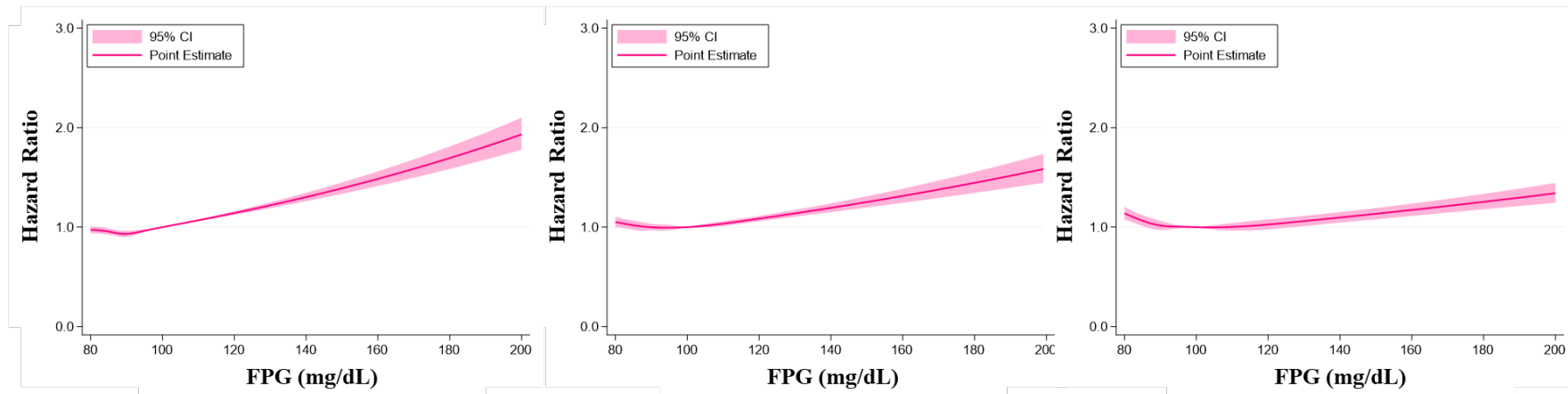
Figure S5. Restricted Cubic Spline

(D) Heart Failure

Normal/Elevated BP

Stage 1 Hypertension

Stage 2 Hypertension



FPG=fasting plasma glucose, BP=blood pressure.

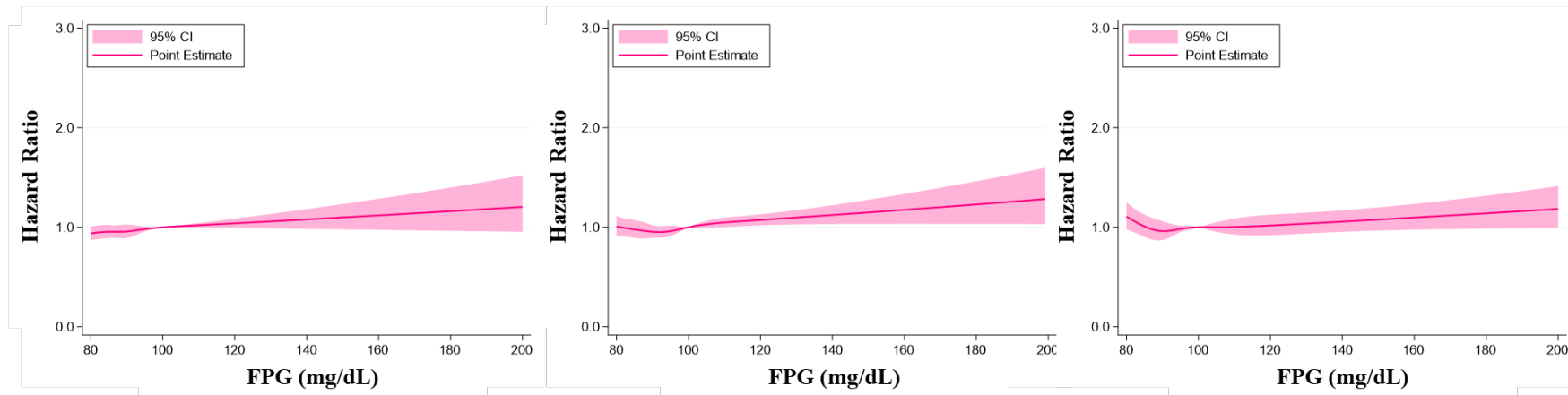
Figure S5. Restricted Cubic Spline

(E) Atrial Fibrillation

Normal/Elevated BP

Stage 1 Hypertension

Stage 2 Hypertension



FPG=fasting plasma glucose, BP=blood pressure.