

Online Supplement- McEvoy et al.

Supplemental Methods

Criteria for Sprint-eligible subsample

This included only participants who were older than 50 years, without diabetes, and with SBP ≥ 130 mmHg and who had any one of the following; estimated Framingham CVD 10-year Risk $\geq 15\%$, or LVH by EKG, or ankle-brachial index < 0.9 , or estimated glomerular filtration rate between 20-59 mL/min/1.73 m². After exclusions, this subsample comprised of 1,403 participants.

High-sensitivity troponin-T Measurement at ARIC visits 2,4 and 5

Visit 2 hs-cTnT was measured in stored serum samples at the University of Minnesota in 2012-2013 using a sandwich immunoassay method with a Roche Elecsys 2010 Analyzer (Roche Diagnostics, Indianapolis, Indiana). Intra-assay coefficients of variation (CVs) were 2.1% at a mean hs-cTnT concentration of 26 ng/L and 1.0% at 1990 ng/L. Inter-assay CVs were 6.0% at a mean hs-cTnT concentration of 25 ng/L and 3.7% at 1940 ng/L.

Visit 4 hs-cTnT was measured in stored plasma samples at Baylor College of Medicine in 2010 using an electrochemiluminescence immunoassay implemented on a Roche Cobas e411 analyzer. Intra-assay coefficients of variation (CVs) were 2.1% at a mean hs-cTnT concentration of 29ng/L and 0.76% at 2378ng/L. Inter-assay CVs were 6.9% and 2.6% at mean cTnT concentrations of 29 ng/L and 2378 ng/L.

Visit 5 hs-cTnT was measured in stored plasma samples at Baylor College of Medicine in 2013 using an electrochemiluminescence immunoassay implemented on a Roche Cobas e411 analyzer. Intra-assay coefficients of variation (CVs) were 1.8% at a mean hs-cTnT concentration of 29 ng/L and 1.9% at 2227 ng/L. Inter-assay CVs were 6.4% and 5.6% at mean cTnT concentrations of 29 ng/L and 2227 ng/L.

Heart Failure ascertainment

Heart failure hospitalization cases were identified from diagnosis codes and HF death (as well as all-cause mortality) from hospital discharge records for inpatient deaths and death certificates for deaths occurring outside the hospital. Beginning in 2005, the ARIC study conducted retrospective surveillance and adjudication of hospitalized HF events. Hospitalized medical records indicating signs or symptoms of HF were fully abstracted and reviewed. ¹

Supplemental Tables

eTable 1. Exclusion process for the primary analysis sample

Exclusion process	Excluded	Sample
Visit 2 Participants		14348
Prevalent CVD or HF at visit 2	1651	12697
Missing hs-cTnT at visit 2	789	11908
Missing DBP at visit 2	1	11907
Missing other covariates	265	11642
Other race and Minneapolis & Washington County blacks	77	11565

eTable 2- Characteristics of the SPRINT-eligible subsample, Overall and According to categories of diastolic blood pressure (mmHg) at baseline (1990-1992)

	Overall	DBP <60	DBP 60-69	DBP 70-79	DBP 80-89	DBP 90-99	DBP ≥100	P Value
N	1403	26 (1.9%)	140 (10.0%)	456 (32.5%)	524 (37.3%)	210 (15.0%)	47 (3.3%)	
Age (years)	60.6 (4.6)	62.8 (4.2)	62.2 (3.9)	61.6 (4.2)	60.0 (4.7)	59.0 (4.9)	57.8 (4.5)	<0.001
Female, %	34.4	42.3	49.3	39.7	29.4	24.8	34	<0.001
Black, %	27.4	11.5	26.4	21.3	27.5	36.7	57.4	<0.001
Smoking status, %								0.212
Never smoking, %	33.3	38.5	31.4	31.8	34.9	31.4	40.4	
Current smoker, %	25.7	15.4	32.1	25.4	24.4	24.3	36.2	
Former smoker, %	41	46.2	36.4	42.8	40.6	44.3	23.4	
Drinking status, %								0.635
Never drinking, %	21.2	30.8	25	22.8	20.2	17.6	17	
Current drinker, %	58.3	57.7	53.6	56.4	60.5	60	59.6	
Former drinker, %	20.5	11.5	21.4	20.8	19.3	22.4	23.4	
SBP (mmHg)	145.8 (11.8)	144.8 (11.1)	142.3 (10.7)	142.9 (10.0)	145.6 (11.4)	151.7 (12.1)	161.9 (12.7)	<0.001
Antihypertensive Med Use, %	49.5	46.2	54.3	46.5	47.1	57.1	57.4	0.067
BMI (kg/m ²)	28.9 (5.4)	28.6 (6.2)	29.0 (5.5)	28.7 (5.3)	28.9 (5.2)	29.2 (5.5)	29.6 (6.8)	0.845
LDL-cholesterol (mg/dL)	142.7 (37.7)	142.7 (35.3)	140.2 (35.4)	142.9 (38.5)	143.2 (36.7)	143.3 (40.8)	140.5 (35.8)	0.969
HDL-cholesterol (mg/dL)	45.0 (14.4)	47.7 (14.0)	47.3 (14.8)	43.8 (13.8)	44.4 (14.3)	45.8 (14.9)	51.0 (15.5)	0.004
Triglycerides (mg/dL)	146.0 (70.6)	149.4 (64.7)	140.2 (59.1)	148.9 (68.2)	147.4 (74.6)	143.6 (72.9)	127.8 (71.9)	0.377
Lipid medication, %	5.1	11.5	5.7	5.9	5.5	1.9	2.1	0.135
eGFR (ml/min/1.73 m ²)	92.2 (16.1)	85.8 (21.7)	91.1 (16.8)	90.5 (15.6)	94.2 (15.4)	92.0 (15.9)	93.4 (20.0)	0.002

Estimates are mean (SD) or %. BMI= body mass index, DBP= Diastolic Blood Pressure, LDL= Low Density Lipoprotein, HDL= High Density Lipoprotein, eGFR= estimated Glomerular Filtration Rate.

eTable 3- Adjusted* Odds Ratios† (95% confidence intervals) for prevalent baseline Elevated Hs-cTnT in the SPRINT-eligible subsample, according to baseline categories of diastolic blood pressure (mmHg) (N=1,403)

	Cross-Sectional Analysis for Elevated Hs-cTnT (≥ 14 ng/L)		
Visit 2 Diastolic BP	n/N	Odds Ratio (95% CI)	p-value
<60 mm Hg	3/26	1.67 (0.45-6.24)	0.444
60-69 mm Hg	12/140	1.23 (0.57-2.65)	0.596
70-79 mm Hg	28/456	0.84 (0.48-1.47)	0.538
80-89 mm Hg	40/524	1 (reference)	.
90-99 mm Hg	18/210	0.66 (0.35-1.24)	0.198
≥ 100 mm Hg	4/47	0.41 (0.12-1.43)	0.163

*Adjusted for: age (years), race-center, gender, body mass index in kg/m², smoking (current; former; never), alcohol intake (current; former; never), systolic BP (in mmHg), hypertension medication use (yes, no), diagnosed diabetes (yes, no), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), current use of cholesterol-lowering medication (yes or no), and estimated glomerular filtration rate in mL/min/1.73m².

† Logistic model for cross-sectional association between diastolic BP and baseline elevated hs-cTnT

eTable 4 – Adjusted* Hazards Ratios (95% confidence intervals), for sub-component Incident Coronary Heart Disease (CHD) events over prospective follow-up (N=11,565)

Visit 2 Diastolic BP	Fatal CHD			MI			Cardiac procedure		
	n/N	HR (95% CI)	p-value	n/N	HR (95% CI)	p-value	n/N	HR (95% CI)	p-value
<60 mm Hg	20/1087	1.88 (1.01-3.49)	0.046	97/1087	1.60 (1.19-2.14)	0.002	48/1087	1.19 (0.81-1.75)	0.382
60-69 mm Hg	53/3728	1.13 (0.72-1.79)	0.586	283/3728	1.20 (0.96-1.48)	0.103	211/3728	1.28 (0.99-1.67)	0.061
70-79 mm Hg	62/4247	0.87 (0.58-1.29)	0.483	383/4247	1.17 (0.97-1.41)	0.102	307/4247	1.34 (1.07-1.68)	0.01
80-89 mm Hg	47/1902	1 (reference)	.	183/1902	1 (reference)	.	120/1902	1 (reference)	.
90-99 mm Hg	13/487	0.67 (0.36-1.26)	0.213	55/487	0.95 (0.69-1.29)	0.721	36/487	1.01 (0.69-1.48)	0.951
≥ 100 mm Hg	4/112	0.47 (0.16-1.40)	0.176	17/112	0.96 (0.57-1.61)	0.864	4/112	0.49 (0.18-1.36)	0.17

*Cox Model adjusted for: age (years), race-center, gender, body mass index in kg/m², smoking (current; former; never), alcohol intake (current; former; never), systolic BP (in mmHg), hypertension medication use (yes, no), diagnosed diabetes (yes, no), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), current use of cholesterol-lowering medication (yes or no), and estimated glomerular filtration rate in mL/min/1.73m². Significant values in bold. Abbreviations as per Table 1

eTable 5- Adjusted* Hazards Ratios (95% confidence intervals), for Incident Heart Failure according to baseline DBP categories (N=11,565)

Visit 2 Diastolic BP	Heart Failure		
	n/N	HR (95% CI)	p-value
<60 mm Hg	154/ 1087	1.48 (1.18-1.85)	<0.001
60-69 mm Hg	519/ 3728	1.26 (1.08-1.48)	0.004
70-79 mm Hg	641/ 4247	1.17 (1.01-1.35)	0.032
80-89 mm Hg	315/ 1902	1.00 (1.00-1.00)	.
90-99 mm Hg	108/ 487	1.02 (0.82-1.28)	0.839
≥ 100 mm Hg	29/ 112	0.94 (0.63-1.40)	0.774

*Cox Model adjusted for: age (years), race-center, gender, body mass index in kg/m², smoking (current; former; never), alcohol intake (current; former; never), systolic BP (in mmHg), hypertension medication use (yes, no), diagnosed diabetes (yes, no), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), current use of cholesterol-lowering medication (yes or no), and estimated glomerular filtration rate in mL/min/1.73m². Significant values in bold. Abbreviations as per Table 1.

eTable 6 -Adjusted* Hazards Ratios (95% confidence intervals), among the SPRINT-eligible subsample, for Incident Coronary Heart Disease (CHD), Stroke, or Mortality events over prospective follow-up (N=1,403)

Visit 2 Diastolic BP	CHD			Stroke			Mortality		
	n/N	HR (95% CI)	p-value	n/N	HR (95% CI)	p-value	n/N	HR (95% CI)	p-value
<60 mm Hg	9/26	2.01 (1.01-4.00)	0.048	1/26	0.44 (0.06-3.23)	0.421	16/26	1.42 (0.84-2.39)	0.187
60-69 mm Hg	38/ 140	1.21 (0.84-1.76)	0.309	16/ 139	0.98 (0.56-1.74)	0.955	76/ 140	1.02 (0.78-1.34)	0.863
70-79 mm Hg	132/ 455	1.15 (0.90-1.48)	0.26	56/ 455	1.05 (0.72-1.54)	0.783	204/ 455	0.86 (0.71-1.05)	0.134
80-89 mm Hg	135/ 524	1 (reference)	.	62/ 520	1 (reference)	.	246/ 524	1 (reference)	.
90-99 mm Hg	51/ 210	0.86 (0.62-1.20)	0.372	24/ 209	0.84 (0.52-1.37)	0.493	93/ 210	0.81 (0.63-1.04)	0.105
≥ 100 mm Hg	13/47	1.05 (0.58-1.91)	0.874	9/47	1.27 (0.60-2.68)	0.535	23/47	0.98 (0.62-1.54)	0.93

*Cox Model adjusted for: age (years), race-center, gender, body mass index in kg/m², smoking (current; former; never), alcohol intake (current; former; never), systolic BP (in mmHg), hypertension medication use (yes, no), diagnosed diabetes (yes, no), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), current use of cholesterol-lowering medication (yes or no), and estimated glomerular filtration rate in mL/min/1.73m². Significant values in bold. Abbreviations as per Table 1.

eTable 7. Adjusted* Hazards Ratios (95% confidence intervals) for Incident Coronary Heart Disease (CHD), Stroke, or Mortality events over prospective follow-up (N=11,565), with Diastolic BP modeled as a time-varying exposure and adjusted for systolic BP, anti-hypertensive medication use and eGFR as time-varying confounders.

Time-varying Diastolic BP at visits 2, 3, and 4	CHD		Stroke		Mortality	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
<60 mm Hg	1.35 (1.15-1.59)	<0.001	1.35 (1.04-1.75)	0.03	1.28 (1.14-1.45)	<0.001
60-69 mm Hg	1.10 (0.98-1.23)	0.11	1.03 (0.84-1.25)	0.80	1.20 (1.10-1.31)	<0.001
70-79 mm Hg	0.89 (0.78-1.03)	0.10	0.91 (0.73-1.14)	0.40	1.10 (0.99-1.23)	0.07
80-89 mm Hg	1 (reference)	.	1 (reference)	.	1 (reference)	.
90-99 mm Hg	0.84 (0.66-1.07)	0.15	1.41 (1.02-1.95)	0.04	1.39 (1.17-1.67)	<0.001
≥ 100 mm Hg	0.88 (0.60-1.30)	0.53	2.47 (1.61-3.78)	<0.001	1.51 (1.12-2.02)	0.006

*Cox Model adjusted for: visit 2 age (years), race-center, gender, visit 2 body mass index in kg/m², visit 2 smoking status (current; former; never), visit 2 alcohol intake (current; former; never), systolic BP (in mmHg, updated as a time-varying exposure at visits 2, 3 and 4), hypertension medication use (yes or no, updated as a time-varying exposure at visits 2, 3 and 4), visit 2 diagnosed diabetes (yes or no), visit 2 LDL-cholesterol (mg/dL), visit 2 HDL-cholesterol (mg/dL), visit 2 triglycerides (mg/dL), current use of cholesterol-lowering medication at visit 2 (yes or no), and estimated glomerular filtration rate in mL/min/1.73m² (updated as a time-varying exposure at visits 2, 3 and 4).

Significant values in bold. Abbreviations as per Table 1.

eTable 8- Adjusted* Hazard Ratios† for Events, according to categories of diastolic BP after stratification by anti-hypertensive treatment status or by hs-cTnT (ng/L) or by presence of LVH by EKG. (N=11,565)

Visit 2 Diastolic BP	Visit 2	n/N	CHD HR (95% CI)	p-value	n/N	Mortality HR (95% CI)	p-value
<60 mm Hg	Not on BP Medication	116/ 889	1.49 (1.14-1.95)	0.004	252/ 889	1.13 (0.93-1.38)	0.22
60-79 mm Hg		847/ 5945	1.22 (1.03-1.44)	0.023	1386/ 5945	0.95 (0.83-1.08)	0.44
80-89 mm Hg		199/ 1181	1 (reference)	.	332/ 1181	1 (reference)	.
≥90 mm Hg		55/ 307	0.77 (0.57-1.05)	0.098	107/ 307	1.21 (0.97-1.51)	0.10
<60 mm Hg	On BP Medication	49/ 198	1.56 (1.09-2.25)	0.016	93/ 198	1.58 (1.21-2.07)	<0.001
60-79 mm Hg		452/ 2030	1.20 (0.98-1.47)	0.074	773/ 2029	1.12 (0.96-1.30)	0.15
80-89 mm Hg		151/ 721	1 (reference)	.	265/ 721	1 (reference)	.
≥90 mm Hg		74/ 292	1.10 (0.82-1.48)	0.509	131/ 292	0.93 (0.75-1.16)	0.51
<60 mm Hg	hs-cTnT <14 ng/L	146/ 1048	1.33 (1.06-1.67)	0.01	319/ 1048	1.21 (1.03-1.43)	0.02
60-79 mm Hg		1219/ 7711	1.20 (1.05-1.37)	0.01	1990/ 7710	1.01 (0.91-1.12)	0.88
80-89 mm Hg		321/ 1800	1 (reference)	.	527/ 1800	1 (reference)	.
≥90 mm Hg		108/ 549	0.87 (0.69-1.09)	0.21	201/ 549	1.07 (0.91-1.27)	0.42
<60 mm Hg	hs-cTnT ≥14 ng/L	19/39	2.59 (1.34-4.99)	0.01	26/39	1.25 (0.75-2.07)	0.38
60-79 mm Hg		80/ 264	0.99 (0.63-1.58)	0.98	169/ 264	0.96 (0.70-1.31)	0.81
80-89 mm Hg		29/ 102	1 (reference)	.	70/ 102	1 (reference)	.
≥90 mm Hg		21/50	1.27 (0.67-2.41)	0.46	37/50	0.87 (0.56-1.34)	0.53
<60 mm Hg	No LVH by EKG	159/ 1072	1.41 (1.13-1.75)	0.002	338/ 1072	1.24 (1.06-1.46)	0.008
60-79 mm Hg		1257/ 7789	1.19 (1.04-1.36)	0.01	2076/ 7788	1.00 (0.90-1.10)	0.95
80-89 mm Hg		331/ 1828	1 (reference)	.	564/ 1828	1 (reference)	.
≥90 mm Hg		112/ 542	0.89 (0.71-1.11)	0.28	207/ 542	1.02 (0.86-1.20)	0.85
<60 mm Hg	LVH by EKG	5/12	3.32 (0.92-11.95)	0.06	6/12	1.52 (0.54-4.32)	0.43
60-79 mm Hg		29/ 127	1.05 (0.52-2.11)	0.90	63/ 127	1.39 (0.83-2.31)	0.21
80-89 mm Hg		18/60	1 (reference)	.	32/60	1 (reference)	.
≥90 mm Hg		16/53	0.85 (0.38-1.90)	0.70	30/53	1.05 (0.59-1.86)	0.87

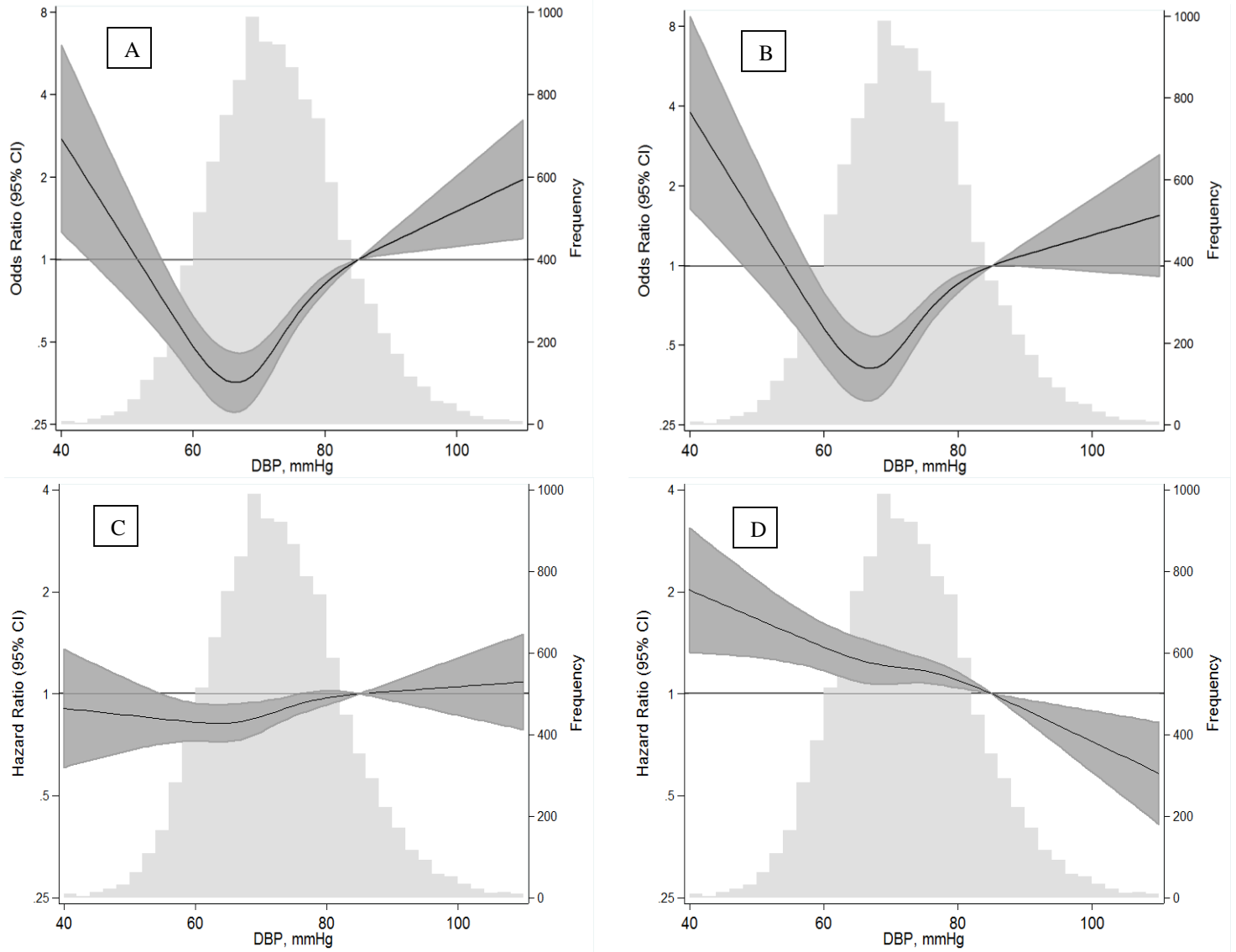
*Adjusted for: age (years), race-center, gender, body mass index in kg/m², smoking (current; former; never), alcohol intake (current; former; never), systolic BP (in mmHg), diagnosed diabetes (yes, no), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), current use of cholesterol-lowering medication (yes or no), and estimated glomerular filtration rate in mL/min/1.73m².

†Cox model for prospective association between diastolic BP and incident events

CHD=coronary heart disease, Hs-cTnT= high-sensitivity Troponin T, other abbreviations as per Table 1.

Supplemental Figures

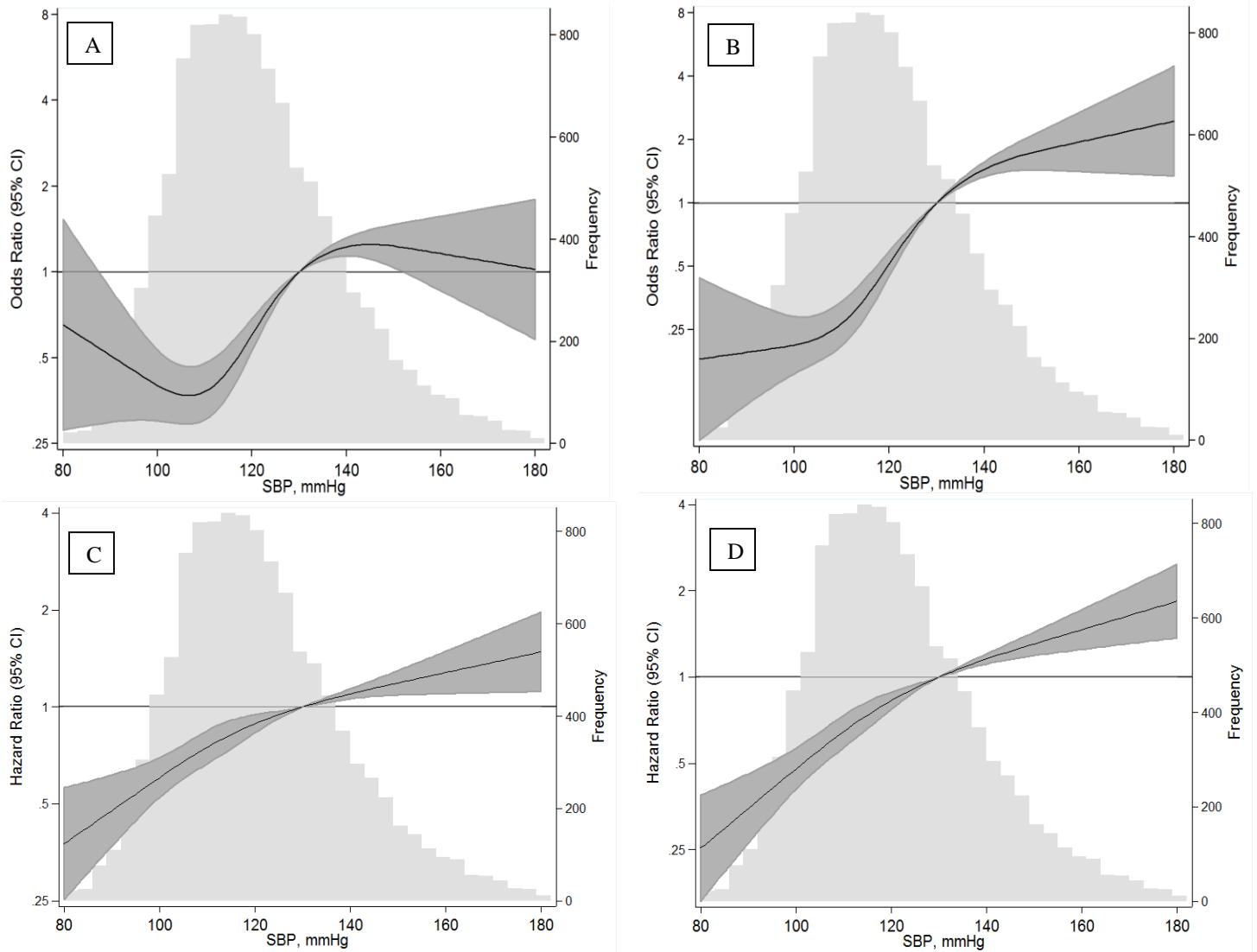
eFigure 1-Adjusted* Odds Ratio (95% confidence interval) for Prevalent Elevated hs-cTnT (≥ 14 ng/L) and Hazard Ratio (95% confidence interval) for incident CHD, according to baseline Diastolic Blood Pressure (DBP) with background histogram of DBP distribution in the sample; with and without adjustment for SBP



- A- OR of hs-cTnT ≥ 14 ng/L according to baseline DBP, adjusted for base model
- B- OR of hs-cTnT ≥ 14 ng/L according to baseline DBP, adjusted for base model and baseline SBP in mmHg
- C- HR of incident CHD according to baseline DBP, adjusted for base model
- D- HR of incident CHD according to baseline DBP, adjusted for base model and baseline SBP in mmHg

*Base model adjusted for: age (years), race-center, gender, body mass index in kg/m^2 , smoking (current; former; never), alcohol intake (current; former; never), hypertension medication use (yes, no), diagnosed diabetes (yes, no), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), current use of cholesterol-lowering medication (yes or no), and estimated glomerular filtration rate in $\text{mL}/\text{min}/1.73\text{m}^2$. **Restricted Cubic Spline with background distributional histogram of baseline Diastolic BP. Note that the "frequency" axis label identifies the number ARIC participants at each point on this background histogram. The shaded area around the regression line represents the 95% confidence interval**

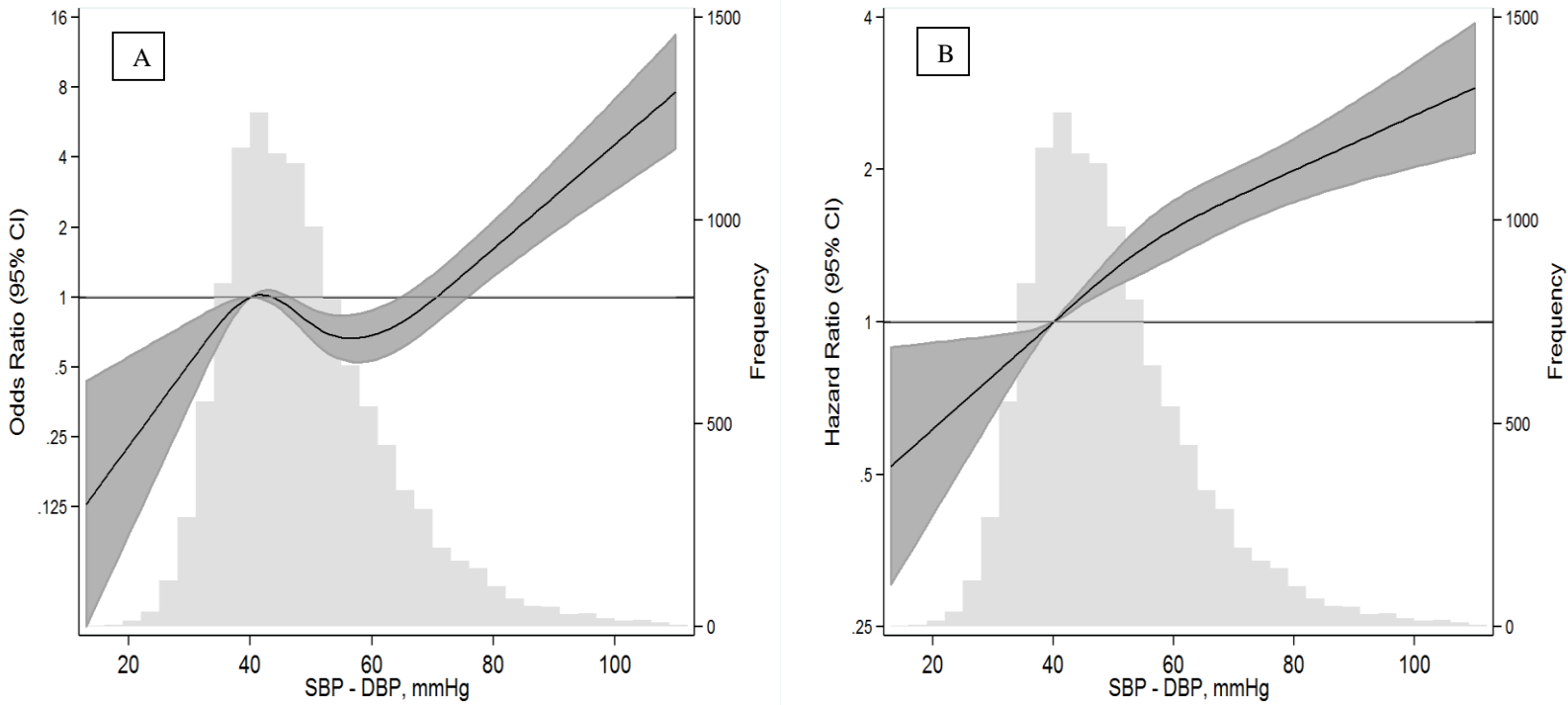
eFigure 2-Adjusted* Odds Ratio (95% confidence interval) for Prevalent Elevated hs-cTnT (≥ 14 ng/L) and Hazard Ratio (95% confidence interval) for incident CHD, according to baseline Systolic Blood Pressure (SBP) with background histogram of SBP distribution in the sample; with and without adjustment for DBP



- A- OR of hs-cTnT ≥ 14 ng/L according to baseline SBP, adjusted for base model
- B- OR of hs-cTnT ≥ 14 ng/L according to baseline SBP, adjusted for base model and baseline DBP in mmHg
- C- HR of incident CHD according to baseline SBP, adjusted for base model
- D- HR of incident CHD according to baseline SBP, adjusted for base model and baseline DBP in mmHg

*Base model adjusted for: age (years), race-center, gender, body mass index in kg/m^2 , smoking (current; former; never), alcohol intake (current; former; never), hypertension medication use (yes, no), diagnosed diabetes (yes, no), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), current use of cholesterol-lowering medication (yes or no), and estimated glomerular filtration rate in $\text{mL}/\text{min}/1.73\text{m}^2$. **Restricted Cubic Spline with background distributional histogram of baseline Systolic BP. Note that the "frequency" axis label identifies the number ARIC participants at each point on this background histogram. The shaded area around the regression line represents the 95% confidence interval**

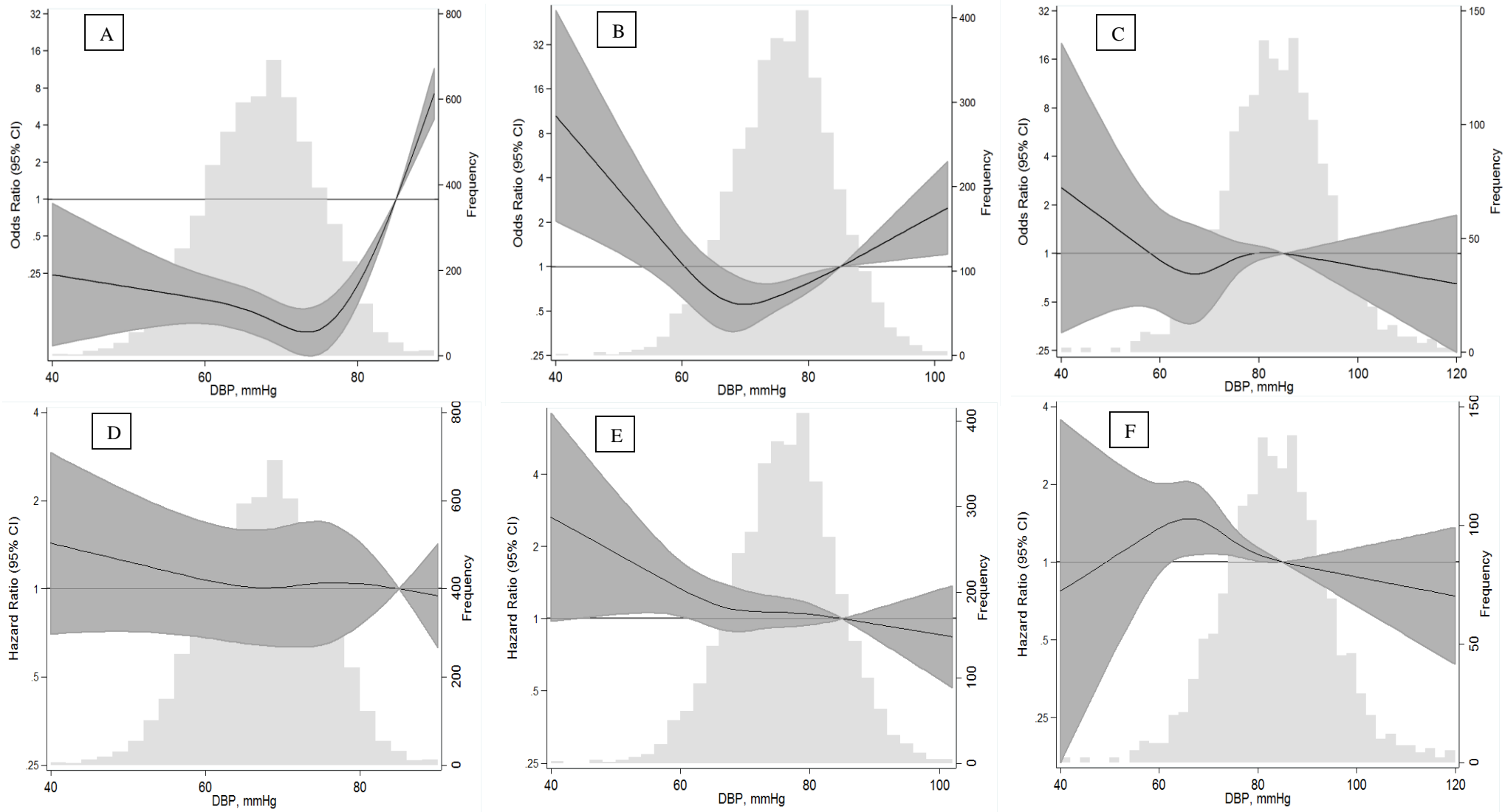
eFigure 3-Adjusted* Odds Ratio (95% confidence interval) for Prevalent Elevated hs-cTnT (≥ 14 ng/L) and Hazard Ratio (95% confidence interval) for incident CHD, according to Pulse Pressure (SBP minus DBP)



- A- OR of hs-cTnT ≥ 14 ng/L according to baseline Pulse Pressure, adjusted for base model
- B- HR of incident CHD according to baseline Pulse Pressure, adjusted for base model

*Base model adjusted for: age (years), race-center, gender, body mass index in kg/m^2 , smoking (current; former; never), alcohol intake (current; former; never), hypertension medication use (yes, no), diagnosed diabetes (yes, no), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), current use of cholesterol-lowering medication (yes or no), and estimated glomerular filtration rate in $\text{mL}/\text{min}/1.73\text{m}^2$. **Restricted Cubic Spline with background distributional histogram of baseline Pulse Pressure. Note that the "frequency" axis label identifies the number ARIC participants at each point on this background histogram. The shaded area around the regression line represents the 95% confidence interval**

eFigure 4-Adjusted* Odds Ratio (95% confidence interval) for Prevalent Elevated hs-cTnT (≥ 14 ng/L) and Hazard Ratio (95% confidence interval) for incident CHD, according to baseline Diastolic Blood Pressure (DBP); stratified by SBP category (<120, 120-139, ≥ 140 mmHg)



- A- OR of hs-cTnT ≥ 14 ng/L according to baseline DBP, among persons with SBP <120 mmHg
- B- OR of hs-cTnT ≥ 14 ng/L according to baseline DBP, among persons with SBP 120-139 mmHg
- C- OR of hs-cTnT ≥ 14 ng/L according to baseline DBP, among persons with SBP ≥ 140 mmHg
- D- HR of incident CHD according to baseline DBP, among persons with SBP <120 mmHg
- E- HR of incident CHD according to baseline DBP, among persons with SBP 120-139 mmHg
- F- HR of incident CHD according to baseline DBP, among persons with SBP ≥ 140 mmHg

*Model adjusted for: age (years), race-center, gender, body mass index in kg/m^2 , smoking (current; former; never), alcohol intake (current; former; never), hypertension medication use (yes, no), diagnosed diabetes (yes, no), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), current use of cholesterol-lowering medication (yes or no), and estimated glomerular filtration rate in $\text{mL}/\text{min}/1.73\text{m}^2$. **Restricted Cubic Spline with background distributional histogram of baseline Diastolic Blood Pressure. Note that the "frequency" axis label identifies the number ARIC participants at each point on this background histogram. The shaded area around the regression line represents the 95% confidence interval**

References

1. Rosamond WD, Chang PP, Baggett C, et al. Classification of heart failure in the atherosclerosis risk in communities (ARIC) study: a comparison of diagnostic criteria. *Circulation. Heart failure*. Mar 1 2012;5(2):152-159.