Supplemental Online Content

Frimodt-Møller EK, Vittinghoff E, Kaur G, Biering-Sørensen T, Soliman EZ, Marcus GM. Association between intensive vs standard blood pressure control and incident left ventricular conduction disease: a post hoc analysis of the SPRINT randomized clinical trial. *JAMA Cardiol*. Published online May 3, 2023. doi:10.1001/jamacardio.2023.0845

This supplemental material has been provided by the authors to give readers additional information about their work.

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Supplemental Methods

Definition of comorbidities

Clinical or subclinical cardiovascular disease included one or more of the following: (a) previous myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, carotid endarterectomy, carotid stenting, (b) peripheral artery disease with revascularization, (c) acute coronary syndrome with or without resting ECG changes, ECG changes on a graded exercise test, or positive cardiac imaging study, (d) at least a 50% diameter stenosis of a coronary, carotid, or lower extremity artery, (e) abdominal aortic aneurysm $\geq$ 5 cm with or without repair, (f) coronary artery calcium score $\geq$ 400 Agatston units within the past 2 years, (g) ankle branchial index $\leq$ 0.9 within the past 2 years, or (h) left ventricular hypertrophy by ECG, echocardiogram report, or other cardiac imaging procedure report within the past 2 years. Atrial fibrillation was defined by its presence on baseline ECG or self-reported. History of congestive heart failure was self-reported.

Adjudication of incident myocardial infarction and heart failure (referred in the context as congestive heart failure, or CHF) for time-updated sensitivity analyses:

Myocardial infarction (MI), defined as the death of part of the myocardium due to an occlusion of a coronary artery from any cause, including spasm, embolus, thrombus or rupture of a plaque. SPRINT used standard case definitions for both fatal and nonfatal MI based on the combination of symptoms, elevation in biomarkers, and/or ECG findings. The algorithm for classifying MI includes elements of the clinical presentation (signs and symptoms), results of cardiac biomarker determinations, and ECG readings. The definition includes MI that occurred during surgery/procedure and MI aborted by thrombolytic therapy or procedure. SPRINT adjudicators were guided by specific, pre-specified

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definitions and operational rules. MI was ascertained both from adjudication of hospital records for clinical events and also from the finding of new significant Q waves from the standardized interpretation of the study visit-obtained ECG (silent or unrecognized MI).

Heart Failure (HF) was defined as hospitalization, or emergency department visit requiring treatment with infusion therapy for a clinical syndrome that presents with multiple signs and symptoms consistent with cardiac decompensation/inadequate cardiac pump function. Adjudication will use the ARIC study adjudication system (Rosamond and others, 2009). The SPRINT HF outcome included definite or possible acute decompensation,

The identification and classification of HF cases relied on multiple pieces of key clinical data as well as adjudicators' clinical judgment, guided by specific, pre-specified definitions and operational rules. For participants with advanced CKD with or without chronic dialysis, the ascertainment of HF can be particularly difficult, since the fluid overload can be purely the consequence of fluid retention by the kidney or absence of kidneys. Under these circumstances, the adjudicators used their best judgment, utilizing all available information.

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eTable 1. Electrocardiographic Findings by Minnesota codes

Electrocardiographic finding	Minnesota code
Left anterior fascicular block	7-7
Left bundle branch block	7-1-1, 7-1-2
Intraventricular conduction delay	7-4
Right bundle branch block	7-2-1, 7-2-2
Ventricular pacemaker	6-8
Ventricular pre-excitation	6-4-1, 6-4-2
Left posterior fascicular block*	QRS axis between 90° and 180° and a QRS duration of less than 0.12 seconds in the absence of right ventricular hypertrophy, lateral myocardial infarction, ventricular pre-excitation, left bundle branch block, and pacemaker on the ECG.

*As left posterior fascicular block (LPFB) was not part of the Minnesota classification, the presence of LPFB was defined in accordance with previous literature.

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eTable 2. Type of Incident Left-Ventricular Conduction Disease First Detected According to Randomization Assignment Group

Type of first incident left ventricular conduction disease	Standard treatment N=3,918	Intensive treatment N=3,956
Left anterior fascicular block	34	30
Left posterior fascicular block	1	0
Left bundle branch block	32	25
Intraventricular conduction delay	49	32

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eTable 3. Risk of Left-Ventricular Conduction Disease or Incident Ventricular Pacing in the Intensive Treatment Group Compared with the Standard Treatment Group

Outcome	Number of events	Model	Hazard ratio (95% CI)	P value
Left-ventricular conduction disease or new ventricular pacing	275	Unadjusted	0.79 (0.62-0.99)	0.047
		Adjusted	0.77 (0.60-0.98)	0.031

Adjusted models included age, sex, race, clinical or subclinical cardiovascular disease, congestive heart failure, and chronic kidney disease.

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eTable 4. Risk of Left-Ventricular Conduction Disease in the Intensive Treatment Group Compared with Standard Treatment Group when Adjusting for Time-Updated Myocardial Infarction and Congestive Heart Failure

Time-updated variable (n of events post-intervention)	Adjusted Hazard Ratio (95% CI)	P value
Myocardial infarction (33)*	0.74 (0.56-0.98)	0.04
Congestive heart failure (53)*	0.74 (0.56-0.98)	0.04

*None of these events occurred before a left-ventricular conduction disease diagnosis.

Models were adjusted for age, sex, race, clinical or subclinical cardiovascular disease, prevalent congestive heart failure, and chronic kidney disease.

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eTable 5. Competing Risk Regression with All-Cause Death as a Competing Risk

Outcome	Number of events	Model	Subdistribution hazard ratio (95% CI)	P value
Left-ventricular conduction disease	203	Unadjusted	0.76 (0.57-0.99)	0.048
		Adjusted	0.75 (0.56-0.99)	0.042
Right bundle branch block	184	Unadjusted	0.96 (0.72-1.29)	0.80
		Adjusted	0.96 (0.72-1.28)	0.79

Risk of incident left-ventricular conduction disease and right bundle branch block when considering all-cause death as a competing risk.

Number of all-cause deaths, n = 211.

Adjusted models included age, sex, race, clinical or subclinical cardiovascular disease, congestive heart failure, and chronic kidney disease.

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eTable 6. Baseline Characteristics Associated with Incident Left Ventricular Conduction Disease in Unadjusted Models.

Characteristic	Hazard ratio (95% CI)	P-value
Intensive BP control	0.75 (0.57-0.99)	0.046
Age[a]	1.47 (1.26-1.70)	<0.001
Male sex	2.33 (1.65-3.29)	<0.001
Race		
White	Reference	
Non-white	0.63 (0.46-0.86)	0.004
Ethnicity		
Hispanic	Reference	
Non-Hispanic	0.93 (0.61-1.42)	0.73
Body mass index[b]	1.18 (0.88-1.59)	0.27
Smoking		
Never	Reference	
Ever smoked	1.25 (0.96-1.63)	0.10
Vigorous activity		
None	Reference	
1-3 times/month	0.72 (0.45-1.13)	0.16
1 time/month	0.68 (0.39-1.17)	0.16
2-4 times/week	1.10 (0.73-1.45)	0.86
>5 times/week	0.80 (0.50-1.29)	0.36
Aspirin use	1.16 (0.88-1.53)	0.29
Clinical or subclinical cardiovascular disease	1.81 (1.33-2.46)	<0.001
Atrial fibrillation	2.12 (0.87-5.16)	0.10
Congestive heart failure	2.03 (1.13-3.64)	0.017
Chronic kidney failure	1.38 (1.03-1.85)	0.029

[a] Interpreted as a hazard for every 10-year increase
[b] Interpreted as a hazard for every 10 kg/m^2 increase

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Figure legends:

eFigure 1. CONSORT Flow Diagram

Inclusions and exclusions of the participants in the present study.

ECG: electrocardiogram, **SPRINT:** Systolic Blood Pressure Intervention Trial.

eFigure 2. Interaction Analyses

Interactions between randomization assignment, listed covariates, and the risk of incident left-ventricular conduction disease. The models were adjusted for age, sex, race, clinical or subclinical cardiovascular disease, congestive heart failure, and chronic kidney disease.

[a] Age is stratified by the mean age in study cohort.

Circles represent hazard ratios and error bars denote 95% confidence intervals.

CVD: Cardiovascular disease (see text for criteria)

eFigure 3. Blood Pressure Control Group and Baseline Characteristics Associated with Incident Left-Ventricular Conduction Disease After Multivariable Adjustment

Baseline characteristics associated with incident left-ventricular conduction disease. Multivariable adjustment included treatment group, age, sex, race, clinical or subclinical cardiovascular disease, congestive heart failure, and chronic kidney disease.

[a] Interpreted as a hazard for every 10-year increase

[b] Interpreted as a hazard for every 10 kg/m^2-increase

Blue circles represent hazard ratios and error bars denote 95% confidence intervals.

CVD: Cardiovascular disease

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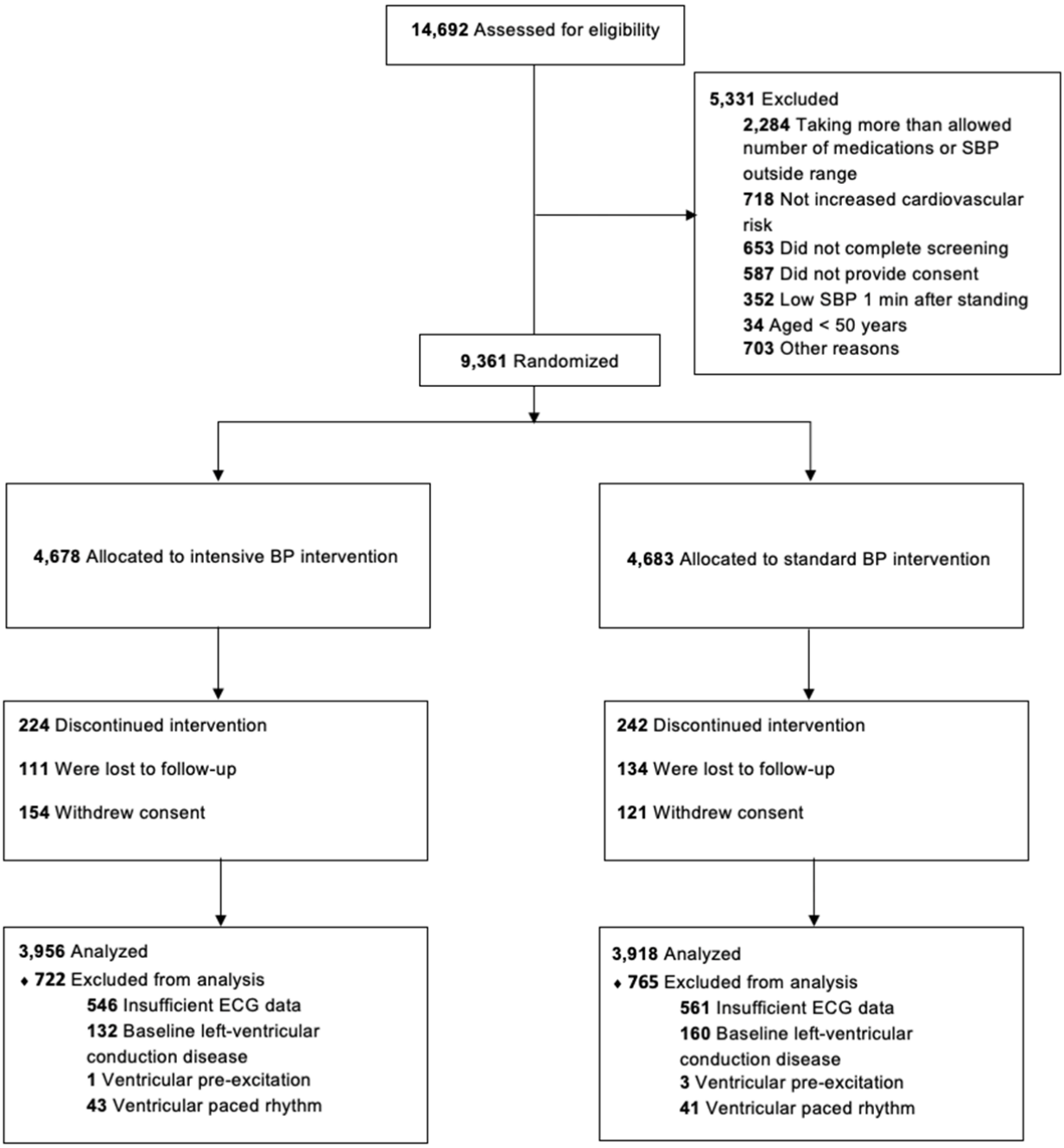
eFigure 1. CONSORT Flow Diagram



Inclusions and exclusions of the participants in the present study.

BP: blood pressure, **ECG:** electrocardiogram

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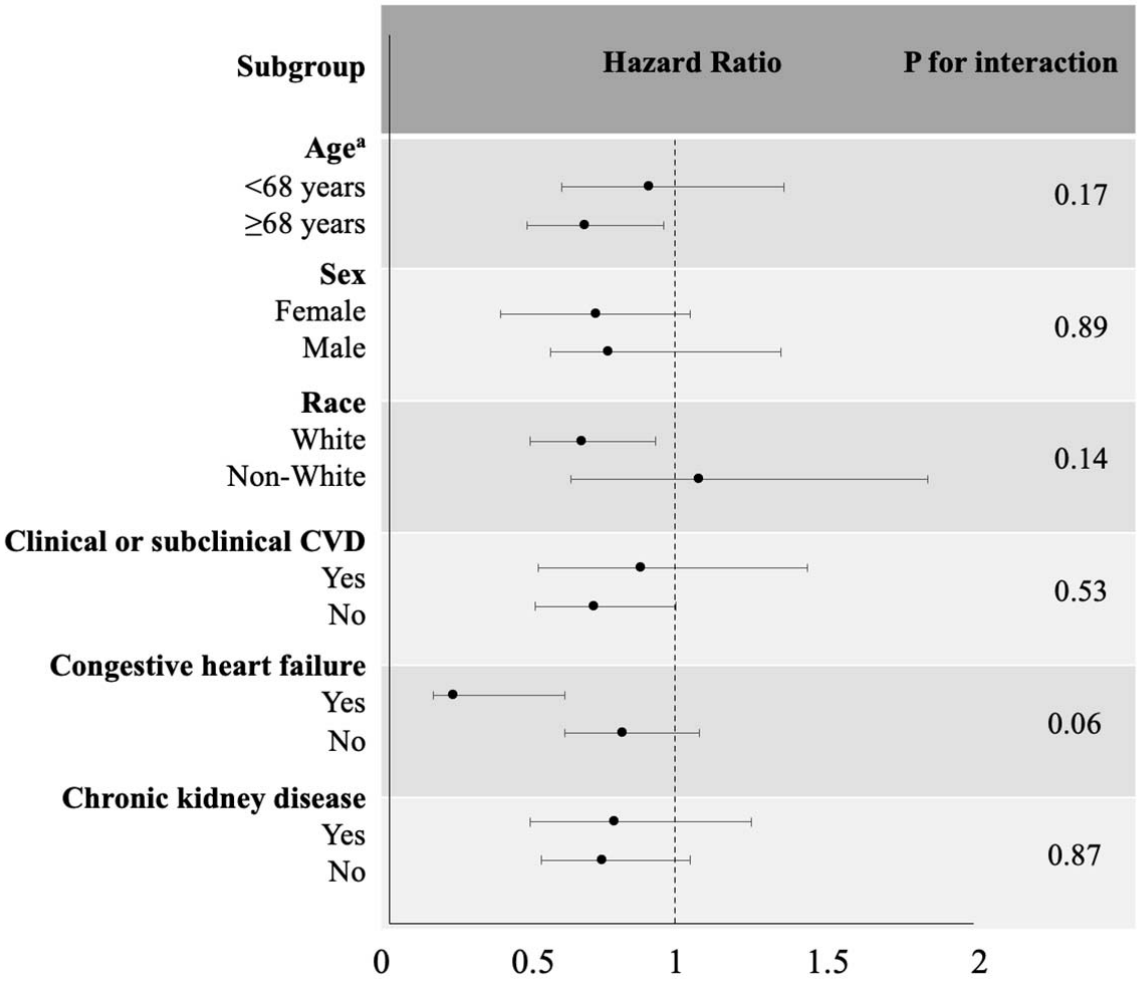
eFigure 2. Interaction Analyses



Interactions between randomization assignment, listed covariates, and the risk of incident left-ventricular conduction disease. The models were adjusted for age, sex, race, clinical or subclinical cardiovascular disease, congestive heart failure, and chronic kidney disease.

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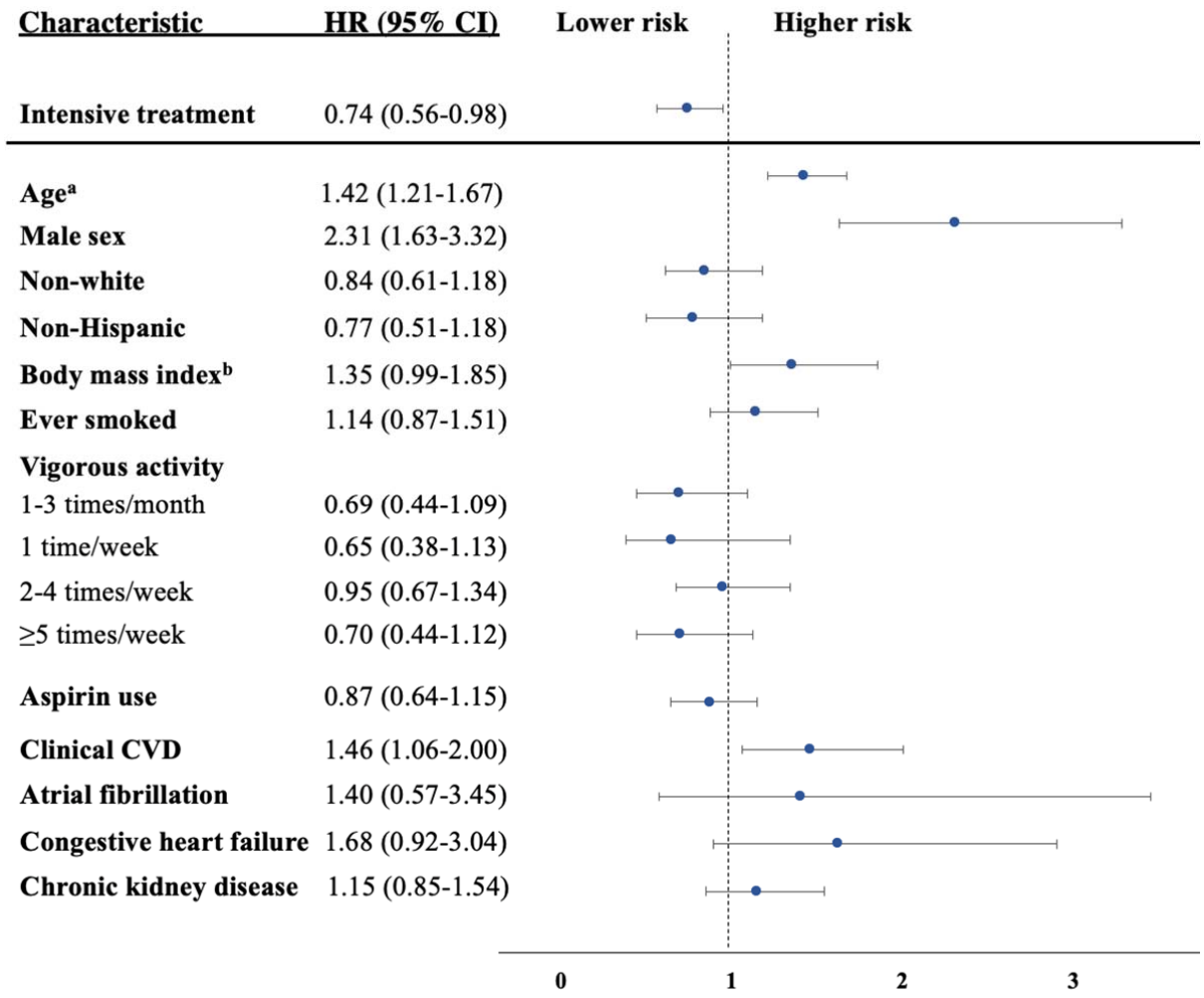

Baseline characteristics associated with incident left-ventricular conduction disease. Multivariable adjustment included treatment group, age, sex, race, clinical or subclinical cardiovascular disease, congestive heart failure, and chronic kidney disease.

[a] Interpreted as a hazard for every 10-year increase

[b] Interpreted as a hazard for every 10 kg/m^2-increase

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