

SUPPLEMENTARY DATA

Supplementary Table S1. Time-updated Cumulative BPs (mmHg-Years) and CAD in individuals with childhood-onset type 1 diabetes

	Model for SBP		Model for DBP		Model for MAP	
Variables *	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
Cumulative BP (per 500 mmHg-years)	1.3 (1.04, 1.7)	0.025	1.5 (1.02, 2.2)	0.042	1.4 (1.03, 2.0)	0.031
Age	1.4 (1.01, 1.9)	0.041	1.4 (1.04, 1.9)	0.028	1.4 (1.03, 1.9)	0.033
Diabetes duration	1.7 (1.3, 2.3)	<0.001	1.7 (1.3, 2.3)	<0.001	1.7 (1.3, 2.3)	<0.001
Female	1.4 (0.9, 1.9)	0.069	1.4 (0.9, 2.0)	0.055	1.4 (0.9, 1.9)	0.059
Ever smoking	1.1 (0.7, 1.3)	0.915	1.1 (0.7, 1.4)	0.971	1.1 (0.7, 1.3)	0.952
BMI	0.9 (0.7, 1.02)	0.083	0.9 (0.7, 1.02)	0.080	0.9 (0.7, 1.02)	0.080
HbA1c	1.3 (1.04, 1.5)	0.016	1.3 (1.04, 1.5)	0.018	1.3 (1.04, 1.5)	0.017
non-HDL cholesterol	1.6 (1.4, 1.9)	<0.001	1.6 (1.4, 2.0)	<0.001	1.6 (1.4, 2.0)	<0.001
HDL cholesterol	0.8 (0.7, 0.94)	0.010	0.8 (0.7, 0.95)	0.012	0.8 (0.7, 0.95)	0.011
Raised albuminuria	2.5 (1.8, 3.6)	<0.001	2.6 (1.8, 3.6)	<0.001	2.5 (1.8, 3.6)	<0.001
Current antihypertensive use	0.4 (0.3, 0.6)	<0.001	0.4 (0.3, 0.6)	<0.001	0.4 (0.3, 0.6)	<0.001

Per SD increase if a continuous variable, unless specified

* BMI, HbA1c, and lipids (non-HDLC, HDLC and triglycerides) were updated means (time- invariant) in the models

BP: blood pressure, CAD: coronary artery disease, DBP: diastolic blood pressure, HR: hazard ratio, MAP: mean arterial pressure, SBP: systolic blood pressure, SD: standard deviation

SUPPLEMENTARY DATA

Supplementary Table S2. Sensitivity, Specificity and AUC by Different Cut-offs of Time-weighted BPs

BP (mmHg)	Sensitivity	Specificity	AUC	p value for AUC comparison
SBP				
≥110	0.7534 (0.6895, 0.8082)	0.4378 (0.3886, 0.4870)	0.5956 (0.5578, 0.6335)	0.336
≥120	0.4795 (0.4110, 0.5479)	0.7487 (0.7047, 0.7902)	0.6141 (0.5745, 0.6537)	ref
≥130	0.2557 (0.2008, 0.3151)	0.9119 (0.8834, 0.9379)	0.5838 (0.5516, 0.6160)	0.075
≥140	0.1142 (0.0776, 0.1598)	0.9637 (0.9430, 0.9819)	0.5389 (0.5159, 0.5620)	<0.001
Optimal cutoff by Youden Index criteria :116.1 mmHg	0.5753 (0.5069, 0.6417)	0.6891 (0.6403, 0.7350)	0.648 (0.601, 0.695)	/
DBP				
≥60	0.9315 (0.8995, 0.9635)	0.0777 (0.0518, 0.1036)	0.5036 (0.4817, 0.5256)	<0.001
≥70	0.6530 (0.5890, 0.7169)	0.4896 (0.4404, 0.5415)	0.5683 (0.5278, 0.6088)	0.068
≥80	0.3288 (0.2690, 0.3882)	0.8808 (0.8472, 0.9119)	0.6048 (0.5697, 0.6399)	ref
≥90	0.0868 (0.0500, 0.1233)	0.9741 (0.9585, 0.9896)	0.5304 (0.5101, 0.5507)	<0.001
Optimal cutoff by Youden Index criteria :78.6 mmHg	0.3699 (0.3058, 0.4375)	0.8523 (0.8129, 0.8862)	0.611 (0.563, 0.660)	/
MAP				
≥80	0.8128 (0.7580, 0.8630)	0.2694 (0.2254, 0.3135)	0.5411 (0.5070, 0.5752)	<0.001
≥90	0.4749 (0.4064, 0.5388)	0.7668 (0.7254, 0.8083)	0.6209 (0.5816, 0.6602)	ref
≥100	0.1872 (0.1370, 0.2374)	0.9482 (0.9249, 0.9689)	0.5677 (0.5395, 0.5959)	0.003
≥110	0.0594 (0.0274, 0.0913)	0.9948 (0.9870, 1.0000)	0.5271 (0.5110, 0.5432)	<0.001
Optimal cutoff by Youden Index criteria :91.4 mmHg	0.4384 (0.3712, 0.5068)	0.8187 (0.7765, 0.8558)	0.633 (0.585, 0.681)	/

AUC: area under receiver operating curve, BP: blood pressure, CAD: coronary artery disease, DBP: diastolic blood pressure, MAP: mean arterial pressure, SBP: systolic blood pressure

SUPPLEMENTARY DATA

Supplementary Table S3. Stratified Analysis of Time-weighted BPs and CAD by Antihypertensive Use

	Subgroup of never treated with antihypertensives (n=223, events=89)		Subgroup of ever treated with antihypertensives (n=382, events=130)	
	HR (95% CI)	p value	HR (95% CI)	p value
BP \geq 120/80 vs. <120/80	2.3 (1.3, 4.1)	0.007	2.7 (1.7, 4.1)	<0.001
MAP \geq 90 vs. <90	2.6 (1.5, 4.7)	0.001	4.0 (2.5, 6.3)	<0.001

Adjusted for age, sex, diabetes duration, ever smoking, time-weighted HbA1c, and updated mean BMI, HDL and non-HDL cholesterol, and raised albuminuria

BMI: body mass index, BP: blood pressure, CAD: coronary artery disease, CI: confidence interval, HbA1c: hemoglobin A1c, HDL: high density lipoprotein, HR: hazard ratio, MAP: mean arterial pressure

SUPPLEMENTARY DATA

Supplementary Table S4. Dose-gradient Association of Time-weighted HbA1c and CAD

	Model 1		Model 2	
HbA1c, %	HR (95% CI)	p value	HR (95% CI)	p value
<7	ref		Ref	
7-<8	1.3 (0.6, 2.8)	0.441	1.6 (0.7, 3.3)	0.251
8-<9	2.1 (1.06, 4.4)	0.033	2.1 (1.0, 4.3)	0.0497
9-<10	2.8 (1.4, 5.7)	0.005	1.9 (0.9, 3.9)	0.094
10+	3.9 (1.9, 8.0)	<0.001	2.2 (1.04, 4.7)	0.041

Model 1: Adjusted for diabetes duration, sex

Model 2: Model 1+ time-weighted SBP, ever smoking, updated means BMI, HDL and non-HDL cholesterol, and raised albuminuria

BMI: body mass index, CAD: coronary artery disease, CI: confidence interval, HbA1c: hemoglobin A1c, HDL: high density lipoprotein, HR: hazard ratio, SBP: systolic blood pressure

SUPPLEMENTARY DATA

Supplementary Table S5. Dose-Gradient Associations of Time-weighted BPs and MACE

	Model 1		Model 2	
N=642; MACE events=162	HR (95% CI)	p value	HR (95% CI)	p value
SBP, mmHg				
<110	1.05 (0.6, 1.7)	0.858	1.3 (0.8, 2.3)	0.284
110 to <120	ref		ref	
120 to <130	1.9 (1.2, 3.2)	0.011	2.1 (1.2, 3.4)	0.006
130 to <140	2.8 (1.5, 5.0)	<0.001	2.3 (1.2, 4.3)	0.009
140+	5.4 (3.0, 9.7)	<0.001	5.1 (2.7, 9.3)	<0.001
DBP, mmHg				
<60	1.4 (0.7, 2.7)	0.350	1.2 (0.6, 2.6)	0.566
60 to <70	ref		ref	
70 to <80	1.6 (1.001, 2.6)	0.049	1.6 (0.96, 2.7)	0.069
80 to <90	6.8 (4.1, 11.2)	<0.001	5.4 (3.2, 9.2)	<0.001
90+	13.9 (7.5, 25.6)	<0.001	7.8 (4.0, 15.2)	<0.001
MAP, mmHg				
<80	1.54 (0.9, 2.6)	0.098	1.7 (0.9, 2.9)	0.052
80 to <90	ref		ref	
90 to <100	3.9 (2.4, 6.3)	<0.001	3.6 (2.2, 5.9)	<0.001
100 to <110	8.6 (5.0, 14.6)	<0.001	6.2 (3.4, 11.3)	<0.001
110+	21.4. (10.0, 45.6)	<0.001	13.9 (6.3, 30.8)	<0.001

Model 1: Adjusted for age, sex, diabetes duration, and current use of antihypertensive medications

Model 2: Model 1+ time-weighted HbA1c, ever smoking, updated mean BMI, HDL and non-HDL cholesterol, and raised albuminuria

BMI: body mass index, BP: blood pressure, MACE: major atherosclerosis cardiovascular disease, CI: confidence interval, DBP: diastolic blood pressure, HbA1c: hemoglobin A1c, HDL: high density lipoprotein, HR: hazard ratio, MAP: mean arterial pressure.

SUPPLEMENTARY DATA

Supplementary Table S6. Risk Stratification by Time-weighted BPs and Time-weighted HbA1c for MACE Risk Prediction

	Model 1		Model 2	
N=642; MACE events=162	HR (95% CI)	p value	HR (95% CI)	p value
SBP/DBP				
BP≥120/80 vs. <120/80	3.1 (2.1, 4.5)	<0.001	2.1 (1.4, 3.1)	<0.001
BP<120/80, and HbA1c<8	ref		ref	
BP≥120/80, and HbA1c<8	3.2 (1.5, 7.0)	0.004	2.5 (1.05, 6.0)	0.038
BP<120/80, and HbA1c≥8	2.2 (1.1, 4.5)	0.022	1.4 (0.6, 3.1)	0.390
BP≥120/80, and HbA1c≥8	7.2 (3.6, 14.5)	<0.001	3.5 (1.6, 8.0)	0.002
MAP				
MAP≥90 vs. <90	4.5 (3.1, 6.5)	<0.001	3.3 (2.2, 4.9)	<0.001
MAP<90, and HbA1c<8	ref		ref	
MAP≥90, and HbA1c<8	7.4 (3.4, 16.1)	<0.001	4.9 (2.1, 11.6)	<0.001
MAP<90, and HbA1c≥8	3.0 (1.5, 5.9)	0.002	1.9 (0.9, 4.1)	0.099
MAP≥90, and HbA1c≥8	12.0 (6.0, 24.3)	<0.001	6.1 (2.7, 13.7)	<0.001

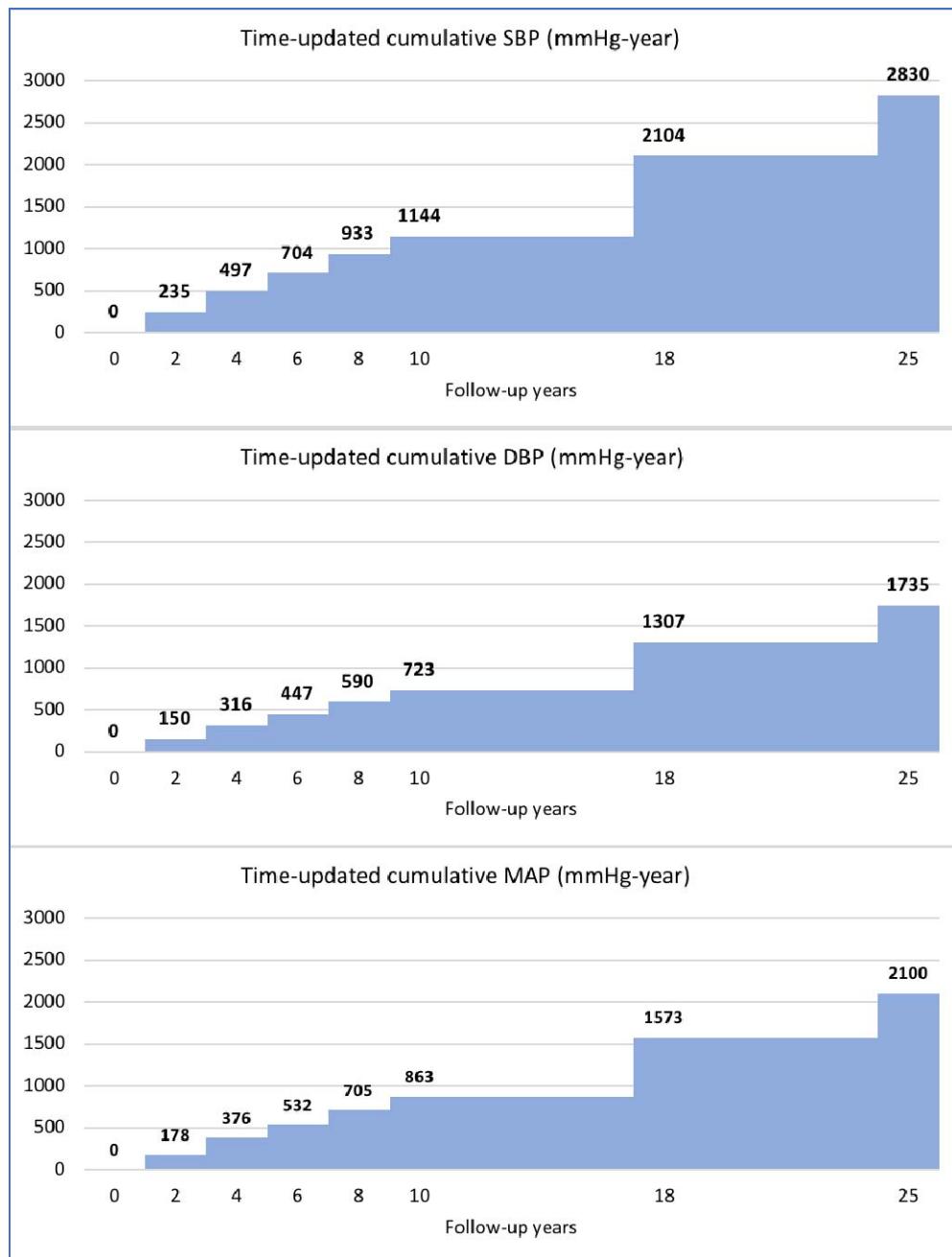
Model 1: Adjusted for age, sex, diabetes duration, and current use of antihypertensive medications

Model 2: Model 1+ ever smoking, updated mean BMI, HDL and non-HDL cholesterol, and raised albuminuria

BMI: body mass index, BP: blood pressure, MACE: major atherosclerosis cardiovascular disease, CI: confidence interval, HbA1c: hemoglobin A1c, HDL: high density lipoprotein, HR: hazard ratio, MAP: mean arterial pressure

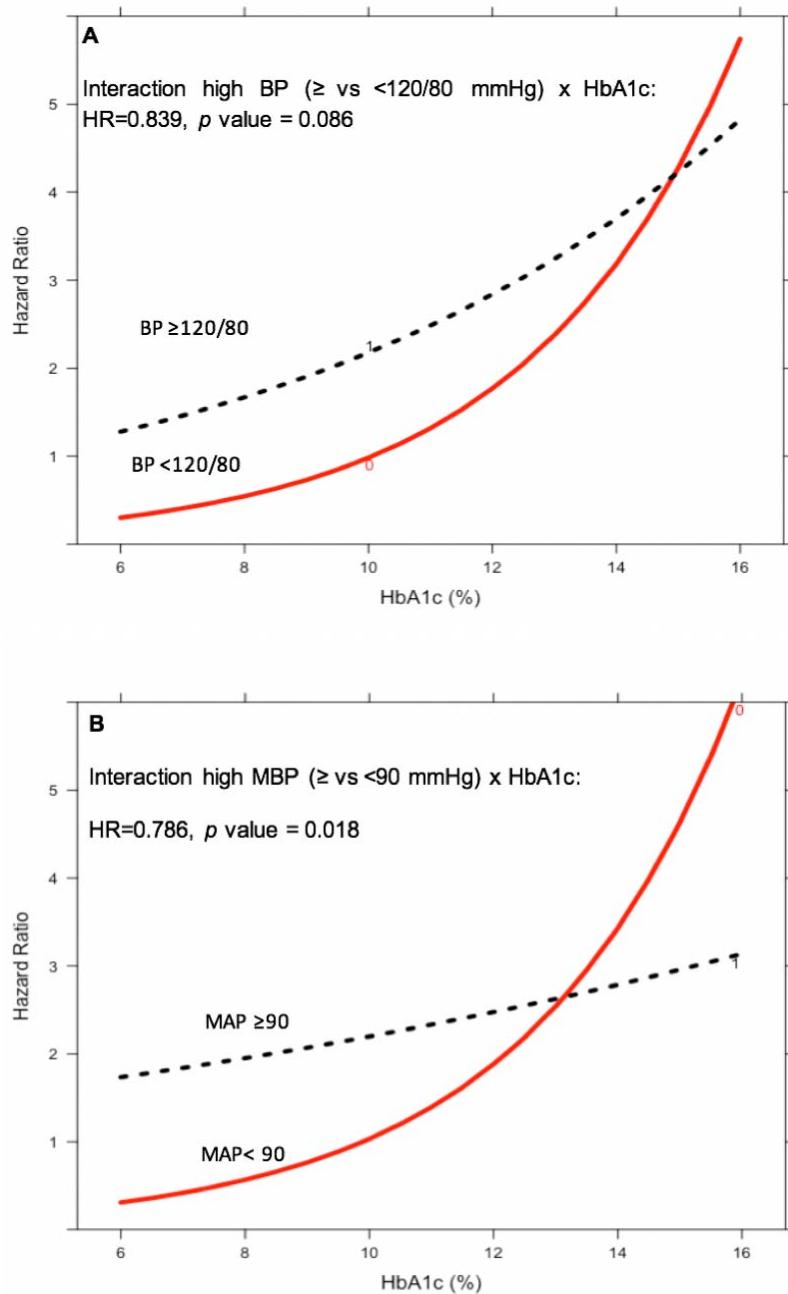
SUPPLEMENTARY DATA

Supplementary Figure S1. Time-updated Cumulative BPs (mmHg-Years) over the Follow-up



SUPPLEMENTARY DATA

Supplementary Figure S2. Model-based Interaction Plot between Time-weighted BP and HbA1c



BP: blood pressure; CAD: coronary artery disease, MAP: mean arterial pressure

SUPPLEMENTARY DATA

Supplementary Figure S3. Population Attributable Risk Fraction (PARF) Estimation

