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Table S1. Characteristics of Participants by Quartiles of SD of Fasting Plasma Glucose in The Look AHEAD Study

	Entire Sample N=3560	Quartiles of SD of Fasting Plasma Glucose, mg/Dl				*P* Value
		Q1 (< 10.15) N=892	Q2 (10.15-17.53) N=888	Q3 (17.53-29.80) N=890	Q4 (> 29.80) N=890	
At Baseline						
Age, years	58.4 (6.7)	59.2 (6.7)	59.1 (6.7)	58.2 (6.5)	57.1 (6.6)	<0.001
Women, %	62.1	63.5	59.6	62.4	62.9	0.336
Randomization arm, %						0.336
Diabetes support and education	48.9	49.1	47.6	47.5	51.4	
Intensive lifestyle intervention	51.1	50.9	52.4	52.5	48.6	
Race/ethnicity, %						0.019
White	67.0	66.6	69.5	67.5	64.4	
Non-Hispanic Black	17.1	16.6	16.6	17.8	17.3	
Hispanic	12.6	12.4	10.6	11.2	16.0	
Body mass index, kg/m^2	36.0 (5.9)	35.3 (5.9)	35.7 (5.8)	36.2 (5.8)	36.9 (6.0)	<0.001
Current smoking, %	3.7	2.9	3.6	3.2	4.9	0.100
Alcohol drinking, %	33.4	34.5	33.5	34.3	31.2	0.442
Use of antihypertensive medication, %	70.9	72.3	69.8	71.2	70.3	0.672
Duration of diabetes, years	5.0 (2.0-9.0)	3.0 (1.0-6.0)	4.0 (2.0-8.0)	5.0 (3.0-10.0)	7.0 (3.0-11.0)	<0.001
eGFR, mL/min/1.73m^2	90.9 (15.7)	89.8 (15.4)	89.7 (15.6)	91.2 (15.7)	93.0 (16.1)	<0.001
During Follow-up						
Average systolic blood pressure, mm Hg	125.6 (13.9)	123.1 (13.2)	125.9 (13.5)	126.6 (14.0)	126.7 (14.6)	<0.001
Average diastolic blood pressure, mm Hg	68.4 (8.0)	67.7 (8.0)	68.8 (7.9)	68.6 (7.9)	68.7 (8.1)	0.0121
Average total-to-HDL cholesterol ratio	4.2 (1.2)	4.1 (1.1)	4.1 (1.0)	4.3 (1.3)	4.5 (1.2)	<0.001
Fasting plasma glucose, mg/dL						
Baseline fasting plasma glucose, mg/dL	151.4 (44.5)	123.9 (21.4)	137.8 (24.2)	154.4 (33.9)	189.6 (57.6)	<0.001
12-month fasting plasma glucose, mg/dL	136.4 (41.7)	119.7 (22.9)	127.3 (26.4)	137.9 (35.1)	160.6 (59.5)	<0.001
24-month fasting plasma glucose, mg/dL	140.0 (45.0)	120.5 (22.3)	129.5 (26.4)	140.4 (35.7)	169.7 (65.4)	<0.001
36-month fasting plasma glucose, mg/dL	142.3 (45.6)	122.3 (22.3)	132.1 (26.1)	143.9 (35.7)	170.8 (67.4)	<0.001
Average fasting plasma glucose, mg/dL	142.5 (33.9)	121.6 (21.2)	131.7 (22.1)	144.1 (27.2)	172.7 (38.1)	<0.001
Hemoglobin A$_{1C}$, %						
Baseline hemoglobin A$_{1C}$, %	7.2 (1.1)	6.5 (0.7)	6.9 (0.8)	7.3 (0.9)	8.1 (1.3)	<0.001
12-month hemoglobin A$_{1C}$, %	6.8 (1.1)	6.3 (0.7)	6.5 (0.8)	6.8 (1.0)	7.6 (1.4)	<0.001
24-month hemoglobin A$_{1C}$, %	6.9 (1.3)	6.3 (0.7)	6.6 (0.9)	7.0 (1.0)	7.9 (1.6)	<0.001
36-month hemoglobin A$_{1C}$, %	7.0 (1.3)	6.3 (0.8)	6.6 (0.8)	7.0 (1.1)	8.0 (1.7)	<0.001
Average hemoglobin A$_{1C}$, %	7.0 (1.0)	6.4 (0.7)	6.7 (0.7)	7.0 (0.8)	7.9 (1.1)	<0.001

Data are mean (SD), median (interquartile range), or number (proportion) as appropriate.

eGFR indicates estimated glomerular filtration rate; HDL, high-density lipoprotein; SD, standard deviation.

1

Table S2. Hazard Ratios for Clinical Outcomes by Variation Independent of the Mean of HbA$_{1C}$ in the Look AHEAD Study

Outcome	Quartiles of Variation Independent of the Mean of HbA$_{1C}$, %				P_{trend}	Per SD
	Q1 (< 0.091)	Q2 (0.091-0.139)	Q3 (0.139-0.203)	Q4 (> 0.203)		
All-Cause Mortality						
Model 1	Reference	0.92 (0.58-1.48)	1.24 (0.80-1.94)	**1.68 (1.10-2.58)***	0.007	**1.32 (1.16-1.51)‡**
Model 2	Reference	0.94 (0.58-1.50)	1.16 (0.73-1.83)	**1.59 (1.02-2.46)***	0.023	**1.31 (1.14-1.50)‡**
Cardiovascular Mortality						
Model 1	Reference	4.47 (0.97-20.74)	**5.55 (1.22-25.16)***	**5.83 (1.28-26.59)***	0.021	**1.33 (1.01-1.76)***
Model 2	Reference	4.17 (0.89-19.52)	4.45 (0.97-20.52)	4.54 (0.97-21.29)	0.076	1.30 (0.94-1.81)
CVD Composite ^{A}						
Model 1	Reference	1.14 (0.85-1.53)	1.02 (0.75-1.39)	1.02 (0.74-1.39)	0.897	1.00 (0.90-1.12)
Model 2	Reference	1.09 (0.80-1.47)	0.93 (0.68-1.28)	0.90 (0.66-1.25)	0.374	0.98 (0.87-1.10)
Heart Failure Event						
Model 1	Reference	1.72 (0.84-3.52)	2.02 (1.00- 4.07)	1.55 (0.74-3.28)	0.226	1.08 (0.86-1.35)
Model 2	Reference	1.56 (0.76-3.23)	1.60 (0.78-3.28)	1.30 (0.61-2.75)	0.562	1.01 (0.80-1.29)

Data are hazard ratios (95% confidence intervals) unless otherwise indicated.

^{A} CVD Composite was as composite of myocardial infarction, hospitalization for angina, stroke and death for cardiovascular causes.

Model 1 adjusted for age, sex, race/ethnicity, and randomization arm. Model 2 includes variables in model 1 with further adjustment for body mass index, current smoking , alcohol drinking, use of antihypertensive medications, average ratio of total to high-density lipoprotein cholesterol, estimated glomerular filtration rate, duration of diabetes and average systolic blood pressure.

AHEAD indicates Action for Health in Diabetes; CVD, cardiovascular disease; HbA$_{1C}$, hemoglobin A$_{1C}$; Q, quartile; SD, standard deviation.

P<0.05, † P<0.01, ‡ P<0.001

2

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Table S3. Hazard Ratios for Clinical Outcomes by Coefficient of Variation of HbA$_{1C}$ in the Look AHEAD Study

Outcome	Quartiles of Coefficient of Variation of HbA$_{1C}$, %				P_{trend}	Per SD
	Q1 (< 0.039)	Q2 (0.039-0.062)	Q3 (0.062-0.096)	Q4 (> 0.096)		
All-Cause Mortality						
Model 1	Reference	1.01 (0.62-1.62)	1.41 (0.89-2.23)	**2.18 (1.41-3.37)‡**	<0.001	**1.38 (1.22-1.57)‡**
Model 2	Reference	0.99 (0.61-1.62)	1.31 (0.82-2.09)	**1.92 (1.22-3.02)†**	0.002	**1.35 (1.18-1.54)‡**
Model 3	Reference	0.98 (0.60-1.59)	1.26 (0.79-2.02)	**1.76 (1.09-2.84)***	0.012	**1.32 (1.14-1.53)‡**
Cardiovascular Mortality						
Model 1	Reference	1.49 (0.42-5.29)	1.87 (0.54-6.41)	**4.91 (1.62-14.94)†**	0.001	**1.52 (1.18-1.96)†**
Model 2	Reference	1.35 (0.37-4.89)	1.69 (0.49-5.85)	**3.46 (1.09-10.99)***	0.020	**1.47 (1.09-1.99)***
Model 3	Reference	1.31 (0.36-4.77)	1.61 (0.46-5.63)	3.09 (0.92-10.42)	0.048	**1.41 (1.01-1.97)***
CVD Composite ^{Δ}						
Model 1	Reference	1.04 (0.76-1.42)	1.14 (0.83-1.55)	1.36 (1.00-1.84)	0.041	1.11 (1.00-1.23)
Model 2	Reference	0.99 (0.72-1.35)	1.03 (0.75-1.41)	1.13 (0.82-1.55)	0.420	1.04 (0.93-1.16)
Model 3	Reference	0.94 (0.69-1.30)	0.95 (0.69-1.31)	0.94 (0.67-1.32)	0.733	0.97 (0.86-1.09)
Heart Failure Event						
Model 1	Reference	1.85 (0.85-4.00)	**2.47 (1.17-5.22)***	**2.49 (1.16-5.34)***	0.013	**1.28 (1.05-1.55)***
Model 2	Reference	1.74 (0.80-3.79)	1.86 (0.86-3.99)	1.76 (0.81-3.83)	0.196	1.17 (0.95-1.44)
Model 3	Reference	1.62 (0.74-3.52)	1.60 (0.74-3.47)	1.25 (0.55-2.83)	0.760	1.03 (0.81-1.30)

Data are hazard ratios (95% confidence intervals) unless otherwise indicated.

^{Δ} CVD Composite was as composite of myocardial infarction, hospitalization for angina, stroke, and death for cardiovascular causes.

Model 1 adjusted for age, sex, race/ethnicity, and randomization arm. Model 2 includes variables in model 1 with further adjustment for body mass index, current smoking , alcohol drinking, use of antihypertensive medications, average ratio of total to high-density lipoprotein cholesterol, estimated glomerular filtration rate, duration of diabetes and average systolic blood pressure; Model 3 includes model 2 plus further adjustment for average HbA$_{1C}$.

AHEAD indicates Action for Health in Diabetes; CVD, cardiovascular disease; HbA$_{1C}$, hemoglobin A$_{1C}$; Q, quartile; SD, standard deviation.

* P<0.05, † P<0.01, ‡ P<0.001

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Table S4. Hazard Ratios for Clinical Outcomes by Average Successive Variability of HbA$_{1C}$ in the Look AHEAD Study

Outcome	Quartiles of Average Successive Variability of HbA$_{1C}$, %				P_{trend}	Per SD
	Q1 (< -0.267)	Q2 (-0.267,-0.067)	Q3 (-0.067, 0.133)	Q4 (> 0.133)		
All-Cause Mortality						
Model 1	Reference	0.98 (0.64-1.50)	0.80 (0.51-1.27)	1.31 (0.86-2.00)	0.387	1.06 (0.89-1.26)
Model 2	Reference	1.03 (0.67-1.59)	0.86 (0.54-1.37)	1.34 (0.87-2.06)	0.328	1.07 (0.90-1.27)
Model 3	Reference	1.09 (0.70-1.69)	0.89 (0.56-1.43)	1.27 (0.82-1.97)	0.454	1.04 (0.88-1.22)
Cardiovascular Mortality						
Model 1	Reference	0.91 (0.37-2.25)	0.33 (0.09-1.22)	1.45 (0.60-3.47)	0.749	1.17 (0.81-1.69)
Model 2	Reference	1.07 (0.40-2.85)	0.43 (0.11-1.65)	1.49 (0.58-3.86)	0.670	1.21 (0.83-1.76)
Model 3	Reference	1.14 (0.43-3.06)	0.46 (0.12-1.74)	1.38 (0.53-3.61)	0.802	1.14 (0.79-1.62)
CVD Composite [*]						
Model 1	Reference	1.09 (0.81-1.47)	0.90 (0.66-1.23)	1.18 (0.87-1.59)	0.534	1.10 (0.98-1.23)
Model 2	Reference	1.14 (0.84-1.54)	0.93 (0.68-1.28)	1.06 (0.78-1.44)	0.987	1.06 (0.95-1.19)
Model 3	Reference	1.21 (0.90-1.65)	0.99 (0.72-1.37)	1.00 (0.74-1.37)	0.748	1.03 (0.93-1.14)
Heart Failure Event						
Model 1	Reference	0.98 (0.51-1.88)	0.84 (0.42-1.65)	1.25 (0.66-2.36)	0.622	1.22 (0.97-1.55)
Model 2	Reference	1.14 (0.59-2.20)	0.89 (0.44-1.79)	1.08 (0.56-2.09)	0.980	1.17 (0.93-1.47)
Model 3	Reference	1.28 (0.66-2.48)	0.98 (0.49-1.97)	0.93 (0.48-1.81)	0.706	1.08 (0.87-1.33)

Data are hazard ratios (95% confidence intervals) unless otherwise indicated.

[*] CVD Composite was as composite of myocardial infarction, hospitalization for angina, stroke, and death for cardiovascular causes.

Model 1 adjusted for age, sex, race/ethnicity, and randomization arm. Model 2 includes variables in model 1 with further adjustment for body mass index, current smoking , alcohol drinking, use of antihypertensive medications, average ratio of total to high-density lipoprotein cholesterol, estimated glomerular filtration rate, duration of diabetes and average systolic blood pressure; Model 3 includes model 2 plus further adjustment for average HbA$_{1C}$.

AHEAD indicates Action for Health in Diabetes; CVD, cardiovascular disease; HbA$_{1C}$, hemoglobin A$_{1C}$; Q, quartile; SD, standard deviation.

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Table S5. Hazard Ratios for Clinical Outcomes by Variability Independent of the Mean of Fasting Plasma Glucose in the Look AHEAD Study

| Outcome | Quartiles of Variability Independent of the Mean of FPG, mg/dL | | | | P_{trend} | Per SD |
	Q1 (< 0.05)	Q2 (0.05-0.08)	Q3 (0.08-0.12)	Q4 (> 0.12)		
All-Cause Mortality						
Model 1	Reference	1.16 (0.72-1.90)	**1.77 (1.13-2.78)***	**1.79 (1.14-2.82)***	0.003	**1.16 (1.03-1.31)***
Model 2	Reference	1.14 (0.70-1.85)	1.58 (1.00-2.50)	1.53 (0.96-2.43)	0.035	1.13 (0.99-1.29)
Cardiovascular Mortality						
Model 1	Reference	0.41 (0.13-1.30)	0.52 (0.18-1.54)	1.49 (0.66-3.39)	0.257	**1.26 (1.03-1.55)***
Model 2	Reference	0.41 (0.13-1.33)	0.30 (0.08-1.11)	1.25 (0.52-2.99)	0.612	1.28 (0.99-1.66)
CVD Composite [A]						
Model 1	Reference	0.83 (0.61-1.13)	0.98 (0.72-1.32)	1.09 (0.81-1.46)	0.391	1.02 (0.92-1.13)
Model 2	Reference	0.84 (0.61-1.15)	0.89 (0.65-1.21)	1.02 (0.75-1.39)	0.824	1.00 (0.89-1.11)
Heart Failure Event						
Model 1	Reference	1.18 (0.56-2.47)	1.50 (0.74-3.04)	**2.01 (1.03-3.96)***	0.027	1.14 (0.94-1.38)
Model 2	Reference	1.04 (0.49-2.21)	1.17 (0.56-2.42)	1.61 (0.81-3.23)	0.144	1.10 (0.89-1.37)

Data are hazard ratios (95% confidence intervals) unless otherwise indicated.

[A] CVD Composite was as composite of myocardial infarction, hospitalization for angina, stroke and death for cardiovascular causes.

Model 1 adjusted for age, sex, race/ethnicity, and randomization arm. Model 2 includes variables in model 1 with further adjustment for body mass index, current smoking , alcohol drinking, use of antihypertensive medications, average ratio of total to high-density lipoprotein cholesterol, estimated glomerular filtration rate, duration of diabetes and average systolic blood pressure.

AHEAD indicates Action for Health in Diabetes; CVD, cardiovascular disease; FPG, fasting plasma glucose; Q, quartile; SD, standard deviation.

* $P<0.05$

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Table S6. Hazard Ratios for Clinical Outcomes by Coefficient of Variation of Fasting Plasma Glucose in the Look AHEAD Study

| Outcome | Quartiles of Coefficient of Variation of Fasting Plasma Glucose, mg/dL | | | | P_{trend} | Per SD |
	Q1 (< 0.08)	Q2 (0.08-0.13)	Q3 (0.13-0.20)	Q4 (> 0.20)		
All-Cause Mortality						
Model 1	Reference	1.40 (0.86-2.28)	**1.82 (1.14-2.91)***	**2.10 (1.33-3.32)†**	0.001	**1.30 (1.13-1.49)‡**
Model 2	Reference	1.33 (0.81-2.16)	**1.64 (1.02-2.64)***	**1.75 (1.08-2.81)***	0.015	**1.23 (1.06-1.43)†**
Model 3	Reference	1.30 (0.80-2.12)	1.58 (0.98-2.55)	1.60 (0.98-2.63)	0.046	**1.20 (1.03-1.40)***
Cardiovascular Mortality						
Model 1	Reference	1.55 (0.55-4.35)	0.55 (0.14-2.21)	**2.82 (1.09-7.32)***	0.060	**1.44 (1.09-1.90)***
Model 2	Reference	1.55 (0.54-4.48)	0.35 (0.07-1.78)	2.15 (0.76-6.06)	0.289	1.34 (0.98-1.84)
Model 3	Reference	1.51 (0.52-4.37)	0.33 (0.06-1.70)	1.92 (0.65-5.69)	0.441	1.30 (0.93-1.81)
CVD Composite [Δ]						
Model 1	Reference	0.92 (0.68-1.26)	1.02 (0.75-1.39)	1.28 (0.95-1.72)	0.075	**1.12 (1.01-1.24)***
Model 2	Reference	0.89 (0.65-1.23)	0.92 (0.67-1.26)	1.09 (0.80-1.49)	0.552	1.06 (0.95-1.19)
Model 3	Reference	0.86 (0.63-1.18)	0.86 (0.63-1.19)	0.97 (0.70-1.34)	0.864	1.02 (0.91-1.15)
Heart Failure Event						
Model 1	Reference	0.94 (0.43-2.07)	1.64 (0.81-3.30)	**2.28 (1.17-4.43)***	0.004	**1.33 (1.10-1.62)†**
Model 2	Reference	0.80 (0.36-1.80)	1.28 (0.62-2.62)	1.68 (0.84-3.36)	0.061	1.23 (0.99-1.52)
Model 3	Reference	0.77 (0.34-1.73)	1.18 (0.57-2.43)	1.41 (0.68-2.90)	0.193	1.16 (0.92-1.45)

Data are hazard ratios (95% confidence interval) unless otherwise indicated.

[Δ] CVD Composite was as composite of myocardial infarction, hospitalization for angina, stroke, and death for cardiovascular causes.

Model 1 adjusted for age, sex, race/ethnicity, and randomization arm. Model 2 includes variables in model 1 with further adjustment for body mass index, current smoking, alcohol drinking, use of antihypertensive medications, average ratio of total to high-density lipoprotein cholesterol, estimated glomerular filtration rate, duration of diabetes and average systolic blood pressure; Model 3 includes model 2 plus further adjustment for average fasting plasma glucose.

AHEAD indicates Action for Health in Diabetes; CVD, cardiovascular disease; Q, quartile; SD, standard deviation.

* P<0.05, † P<0.01, ‡ P<0.001

6

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Table S7. Hazard Ratios for Clinical Outcomes by Average Successive Variability of Fasting Plasma Glucose in the Look AHEAD Study

Outcome	Quartiles of Average Successive Variability of Fasting Plasma Glucose, mg/dL				P_{trend}	Per SD
	Q1 (< -10.67)	Q2 (-10.33, -2.67)	Q3 (-2.33, 4.67)	Q4 (> 5.00)		
All-Cause Mortality						
Model 1	Reference	0.98 (0.65-1.49)	0.67 (0.42-1.08)	1.24 (0.82-1.88)	0.628	1.06 (0.89-1.24)
Model 2	Reference	1.11 (0.72-1.72)	0.80 (0.49-1.31)	1.31 (0.86-2.01)	0.422	1.07 (0.91-1.25)
Model 3	Reference	1.19 (0.77-1.86)	0.87 (0.53-1.43)	1.31 (0.86-2.01)	0.413	1.06 (0.91-1.23)
Cardiovascular Mortality						
Model 1	Reference	1.85 (0.69-4.94)	0.70 (0.20-2.48)	2.10 (0.77-5.72)	0.369	1.19 (0.83-1.71)
Model 2	Reference	2.16 (0.73-6.39)	0.94 (0.25-3.55)	2.18 (0.74-6.41)	0.351	1.17 (0.82-1.68)
Model 3	Reference	2.44 (0.81-7.37)	1.08 (0.28-4.20)	2.17 (0.74-6.39)	0.356	1.15 (0.82-1.60)
CVD Composite [Δ]						
Model 1	Reference	0.87 (0.65-1.17)	0.88 (0.66-1.19)	0.83 (0.61-1.12)	0.254	0.92 (0.83-1.03)
Model 2	Reference	0.94 (0.70-1.28)	0.97 (0.72-1.31)	0.78 (0.57-1.06)	0.153	0.91 (0.82-1.01)
Model 3	Reference	1.03 (0.76-1.39)	1.08 (0.79-1.47)	0.77 (0.57-1.06)	0.162	0.91 (0.83-1.01)
Heart Failure Event						
Model 1	Reference	0.58 (0.30-1.12)	0.57 (0.29-1.14)	1.05 (0.58-1.89)	0.930	1.14 (0.90-1.45)
Model 2	Reference	0.75 (0.38-1.51)	0.75 (0.37-1.52)	1.07 (0.58-1.98)	0.831	1.13 (0.90-1.42)
Model 3	Reference	0.85 (0.42-1.72)	0.86 (0.42-1.77)	1.06 (0.57-1.95)	0.867	1.09 (0.89-1.35)

Data are hazard ratios (95% confidence intervals) unless otherwise indicated.

[Δ] CVD Composite was as composite of myocardial infarction, hospitalization for angina, stroke and death for cardiovascular causes.

Model 1 adjusted for age, sex, race/ethnicity, and randomization arm. Model 2 includes variables in model 1 with further adjustment for body mass index, current smoking ,

alcohol drinking, use of antihypertensive medications, average ratio of total to high-density lipoprotein cholesterol, estimated glomerular filtration rate, duration of diabetes and

average systolic blood pressure; Model 3 includes model 2 plus further adjustment for average fasting plasma glucose.

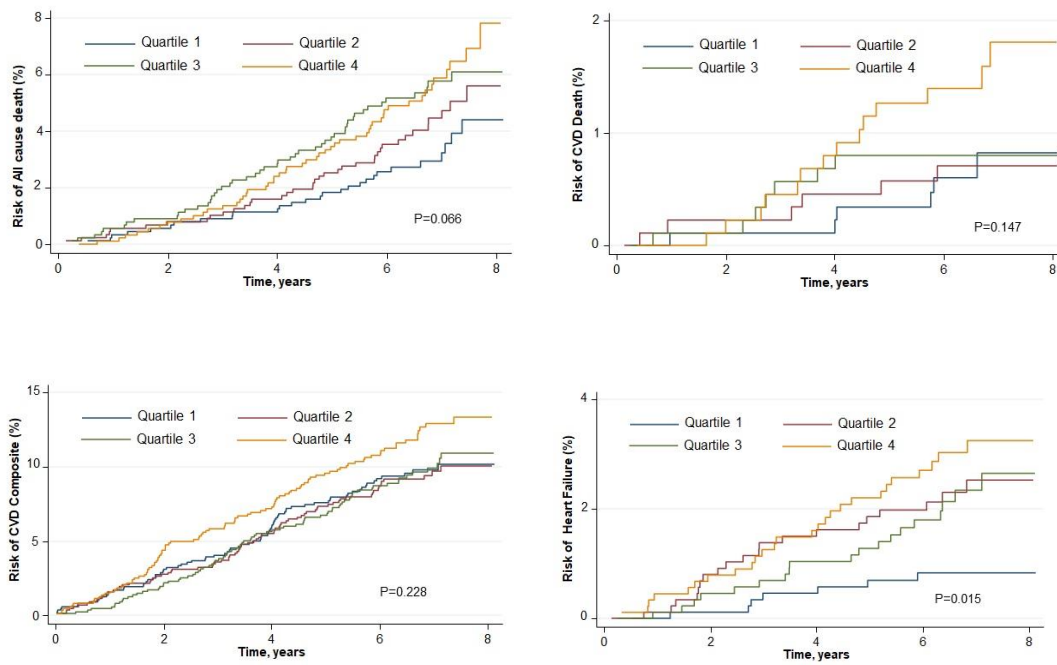AHEAD indicates Action for Health in Diabetes; CVD, cardiovascular disease; Q, quartile; SD, standard deviation.

Figure S1. Risk of Clinical Outcomes by Quartile of SD of Fasting Plasma Glucose.

CVD Composite was as composite of myocardial infarction, stroke, hospitalization for angina and death for cardiovascular causes. CVD indicates cardiovascular disease and SD, standard deviation.