

SUPPLEMENTARY DATA

**Supplementary Table 1.** Baseline characteristics for sub-cohort and cardiovascular cases.

	Sub-cohort	cases
Participants (n)	218	134
Female (%)	81.7	79.3
Age (years)	57.9 ± 6.7	58.6 ± 6.9
Diabetes duration (years)	5.3 (2.3-10.2)	6.2 (2.6-12.6)
HbA1c (%)	8.0 ± 1.6	8.2 ± 1.7
HbA1c (mol/mmol)	64.0 ± 17.5	66.0 ± 18.6
Glucose-lowering treatment (%)	89.0	80.7
SBP (mm Hg)	141.7 ± 20.8	145.6 ± 23.2
DBP (mm Hg)	82.1 ± 10.2	81.6 ± 11.0
Use of blood pressure-lowering drugs (%)	38.5	48.9
Prior cardiovascular events (%)	13.8	29.6
Current smokers (%)	22.5	31.9
BMI (kg/m <sup>2</sup> )	29.4 ± 4.9	30.3 ± 4.9
Waist (cm)	97.2 ± 12.3	99.9 ± 12.7
Serum creatinine (umol/l)	61.5 ± 18.7	64.2 ± 24.3
eGFR (ml/min/1.73m <sup>2</sup> )	95.3 ± 16.0	93.3 ± 17.8
Total cholesterol (mmol/l)	5.2 ± 1.2	5.4 ± 1.1
HDL cholesterol (mmol/l)	1.0 ± 0.3	1.0 ± 0.3
Triglycerides (mmol/l)	2.0 (1.4-3.1)	2.5 (1.6-3.2)
Use of lipid-lowering drugs (%)	4.1	5.2
<i>Protein-bound plasma AGEs</i>		
CML (nmol/mmol lysine)	65.8 (54.2-76.8)	65.2 (53.8-77.4)
CEL (nmol/mmol lysine)	28.5 (23.7-32.2)	28.7 (24.6-34.6)
Pentosidine (mmol/mmol lysine)	0.7 (0.5-0.9)	0.7 (0.5-0.9)

Data are presented as frequencies (%), means ± SD, or medians (interquartile range). HbA1c: glycated hemoglobin, SBP: systolic blood pressure, DBP: diastolic blood pressure, BMI: body mass index, eGFR, estimated glomerular filtration rate, AGEs: advanced glycation endproducts. CML: N<sup>ε</sup>-(carboxymethyl)lysine, CEL: N<sup>ε</sup>-(carboxyethyl)lysine.

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**Supplementary Table 2.** Multivariable adjusted hazard ratios and 95% confidence intervals for the associations between plasma AGEs and specific incident cardiovascular events.

	M	Fatal events	Total CHD	Total Stroke	Total PAD	Total CHF
AGE score	1	1.10 (0.85-1.42)	1.13 (0.89-1.45)	1.47 (0.98-2.19)	0.84 (0.57-1.26)	1.03 (0.65-1.61)
	2	1.22 (0.90-1.65)	<b>1.35 (1.01-1.80)</b>	<b>1.95 (1.13-3.38)</b>	0.77 (0.45-1.31)	1.55 (0.78-3.10)
	3	1.16 (0.85-1.62)	1.32 (0.96-1.80)	<b>2.06 (1.13-3.75)</b>	0.76 (0.43-1.34)	1.73 (0.77-3.91)
CML	1	1.02 (0.68-1.53)	0.94 (0.73-1.21)	<b>1.70 (1.09-2.67)</b>	0.79 (0.54-1.17)	0.92 (0.57-1.46)
	2	1.32 (0.77-2.27)	1.17 (0.85-1.61)	<b>2.87 (1.44-5.75)</b>	0.86 (0.50-1.47)	1.50 (0.72-3.11)
	3	1.26 (0.71-2.25)	1.09 (0.77-1.53)	<b>2.73 (1.31-5.70)</b>	0.88 (0.49-1.56)	1.59 (0.64-3.90)
CEL	1	<b>1.75 (1.19-2.58)</b>	1.26 (0.98-1.63)	1.37 (0.83-2.25)	1.05 (0.72-1.53)	1.36 (0.68-2.14)
	2	<b>2.03 (1.34-3.08)</b>	<b>1.35 (1.02-1.79)</b>	1.59 (0.89-2.83)	1.05 (0.66-1.67)	1.77 (0.93-3.36)
	3	<b>2.20 (1.39-3.46)</b>	<b>1.37 (1.03-1.82)</b>	1.81 (0.97-3.40)	1.02 (0.63-1.64)	2.07 (0.99-4.31)
Pentosidine	1	1.18 (0.80-1.74)	1.14 (0.88-1.48)	1.20 (0.77-1.87)	0.81 (0.53-1.23)	0.84 (0.51-1.38)
	2	1.29 (0.84-1.98)	1.20 (0.89-1.62)	1.28 (0.74-2.22)	0.66 (0.39-1.11)	0.88 (0.43-1.77)
	3	1.27 (0.81-1.99)	1.14 (0.82-1.57)	1.18 (0.63-2.22)	0.67 (0.40-1.13)	0.81 (0.33-1.97)

Data were analyzed using Cox regression analyses. Hazard ratio (HR) is expressed per standard deviation increase of  $\log_e$ -transformed AGE

Model (M) 1: adjusted for age, sex and cohort

Model 2: model 1 + adjustment for diabetes duration, total cholesterol to HDL-cholesterol ratio, smoking and systolic blood pressure, prior cardiovascular events, triglycerides, BMI, glucose-, lipid- and blood pressure-lowering treatment.

Model 3: model 2 + eGFR and HbA1c.