Supplement Table 1: Baseline characteristics of analyzed and all participants in the ACCORD and VADT trials.

	ACCORD *Analyzed*	**ACCORD** *All*	**VADT** *Analyzed*	**VADT** *All*
n	1,150	10,251	447	1,791
Age (yrs)	62 ± 6	63 ± 7	59 ± 8	60 ± 9
Sex (% males)	54%	61%	97%	97%
Race (% white)	64%	62%	63%	62%
BMI (kg/m^2)	32 ± 5	32 ± 5	31 ± 4	31 ± 4
History of CVD (%)	33%	35%	33%	40%
Statin use (%)	63%	64%	61%	58%
Systolic BP (mmHg)	136 ± 17	136 ± 17	131 ± 16	132 ± 17
Diastolic BP (mmHg)	75 ± 11	75 ± 11	77 ± 10	76 ± 10
Diabetes duration (years)	10 (5, 15)	10 (5, 15)	10 (5, 15)	10 (6,16)
HbA_{1c} (%)	8.4 ± 1.0	8.3 ± 1.1	9.4 ± 1.5	9.4 ± 1.5
HbA_{1c} (mmol/mol)	69 ± 12	67 ± 12	80 ± 16	80 ± 17
Total chol. (mg/dl)	184 ± 41	183 ± 42	181 ± 43	183 ± 47
LDL chol. (mg/dl)	105 ± 34	105 ± 34	106 ± 30	108 ± 32
HDL chol. (mg/dl)	42 ± 11	42 ± 12	37 ± 10	36 ± 10
Triglycerides (mg/dl)	152 (106, 224)	155 (106, 229)	147 (107, 204)	151 (109, 210)
uACR (mg/g)	13 (7, 43)	14 (7, 47)	16 (5, 51)	19 (6, 70)
eGFR (ml/min·1.73 m^2)	85 ± 17	84 ± 18	85 ± 17	84 ± 18

Data are %, means ± SD or Medians (25th, 75th percentile). BMI, body-mass index; BP, blood pressure; HbA_{1c}, hemoglobin A_{1c}; uACR, urine albumin-creatinine ratio; eGFR, estimated glomerular filtration rate.

Supplement Table 2: Association of ACCORD AGE-score (univariate and multivariable) and individual AGEs (univariate) with baseline clinical and demographic characteristics.

	AGE-score		**G-H1**	**MG-H1**	**3DG-H1**	**CML**	**CEL**
	Univariate	*Multivariable*	10 ± 4	330 ± 172	344 ± 212	122 ± 61	89 ± 37
Age	0.14 (0.02)*	-0.03 (0.02)	0.24 (0.03)*	0.14 (0.03)*	0.09 (0.03)*	0.11 (0.03)*	0.11 (0.03)*
Male sex	0.04 (0.05)	0.03 (0.04)	-0.11 (0.06)	-0.01 (0.06)	0.15 (0.06)*	0.10 (0.06)	0.09 (0.06)
Non-Hispanic white	0.19 (0.05)*	0.12 (0.05)*	0.05 (0.06)	0.11 (0.06)	0.23 (0.06)*	0.25 (0.06)*	0.24 (0.06)*
CVD history	0.22 (0.05)*	0.14 (0.05)*	0.24 (0.06)*	0.22 (0.06)*	0.27 (0.06)*	0.22 (0.06)*	0.13 (0.06)*
Systolic BP (1 SD)	0.03 (0.03)	0.01 (0.03)	-0.02 (0.03)	0.02 (0.03)	0.02 (0.03)	0.02 (0.03)	-0.01 (0.03)
Diastolic BP (1SD)	-0.10 (0.02)*	-0.02 (0.03)	-0.13 (0.03)*	-0.11 (0.03)*	-0.07 (0.03)*	-0.07 (0.03)*	-0.10 (0.03)*
Diabetes duration (1SD)	0.13 (0.03)*	0.06 (0.02)*	0.15 (0.03)*	0.15 (0.03)*	0.04 (0.03)	0.14 (0.03)*	0.13 (0.03)*
Hemoglobin A_{1c} (1 SD)	-0.03 (0.03)	-0.02 (0.02)	-0.01 (0.03)	0.01 (0.03)	-0.02 (0.03)	-0.07 (0.03)*	-0.06 (0.03)
eGFR (1SD)	-0.42 (0.02)*	-0.41 (0.02)*	-0.52 (0.03)*	-0.38 (0.03)*	-0.35 (0.03)*	-0.42 (0.03)*	-0.43 (0.03)*
uACR 30-300	0.20 (0.06)*	0.09 (0.05)	0.21 (0.07)*	0.18 (0.07)*	0.16 (0.07)*	0.21 (0.07)*	0.19 (0.07)*
uACR > 300	0.38 (0.11)*	0.19 (0.10)	0.43 (0.14)*	0.39 (0.13)*	0.37 (0.14)*	0.42 (0.13)*	0.28 (0.13)*

Data are β-estimates (SE). Multivariable model for AGE-score includes all listed variables. β-estimates for individual AGEs are standardized to 1 SD of natural log-transformed values. Values in the second row for individual AGEs describe means ± SD of concentrations in ng/ml. *p<0·05.

Supplement Table 3: Association of baseline AGE-score with secondary renal outcomes by **selected subgroups in ACCORD defined by categories or medians (age, systolic blood pressure, type 2 diabetes [T2D] duration and hemoglobin A1c).**

	Subgroup	40% RFL	Macroalbuminuria	High-risk CKD
Glucose arm	Intensive	1.38 (0.98-1.93)	1.84 (1.08-3.11)	1.88 (1.13-3.13)
	Standard	1.44 (1.08-1.91)	1.42 (0.94-2.13)	1.80 (1.18-2.75)
Blood pressure arm	Intensive	1.28 (0.84-1.96)	1.47 (0.50-4.33)	2.27 (0.86-5.98)
	Standard	1.44 (1.11-1.86)	1.55 (1.12-2.14)	1.91 (1.35-2.71)
Lipid arm	Intensive	1.05 (0.70-1.57)	2.44 (1.32-4.52)	1.50 (0.87-2.57)
	Standard	1.58 (1.22-2.05)	1.24 (0.86-1.77)	2.09 (1.41-3.11)
Age	< 61.6 years	1.48 (1.03-2.12)	1.64 (1.11-2.41)	1.34 (0.83-2.14)
	≥ 61.6 years	1.42 (1.07-1.89)	1.58 (0.94-2.66)	2.98 (1.82-4.87)
Sex	Male	1.32 (0.96-1.81)	1.23 (0.80-1.90)	1.53 (1.06-2.23)
	Female	1.49 (1.10-2.01)	2.02 (1.23-3.34)*	3.24 (1.73-6.10)*
Race/ethnicity	White	1.44 (1.10-1.89)	2.09 (1.15-3.79)	2.31 (1.23-4.32)
	Non-white	1.45 (0.99-2.12)	1.34 (0.94-1.92)	1.91 (1.28-2.86)
Systolic BP	< 136 mmHg	1.39 (0.98-1.97)	1.57 (0.99-2.49)	2.08 (1.25-3.44)
	≥ 136 mmHg	1.49 (1.11-2.00)	1.31 (0.87-1.97)	2.20 (1.37-3.53)
T2D duration	< 10.9 years	1.10 (0.80-1.52)	1.58 (0.96-2.60)	2.26 (1.29-3.96)
	≥ 10.9 years	1.82 (1.33-2.49)	1.37 (0.88-2.12)	1.94 (1.27-2.98)
Hemoglobin A_{1c}	< 8.4% (68 mmol/mol)	1.89 (1.34-2.67)*	1.61 (0.95-2.74)	2.66 (1.58-4.50)
	≥ 8.4% (68 mmol/mol)	1.16 (0.86-1.56)	1.39 (0.94-2.04)	1.68 (1.09-2.57)
eGFR	≥ 90 ml/min·1.73m^2	1.32 (0.95-1.85)	1.32 (0.72-2.41)	1.84 (0.83-4.11)
	< 90 ml/min·1.73m^2	1.44 (1.07-1.94)	1.65 (1.14-2.37)	1.83 (1.28-2.61)
uACR	< 30 mg/g	1.45 (1.08-1.95)	1.94 (1.05-3.48)	2.69 (1.32-5.47)
	≥ 30 mg/g	1.37 (0.97-1.93)	1.22 (0.84-1.77)	1.66 (1.07-2.58)

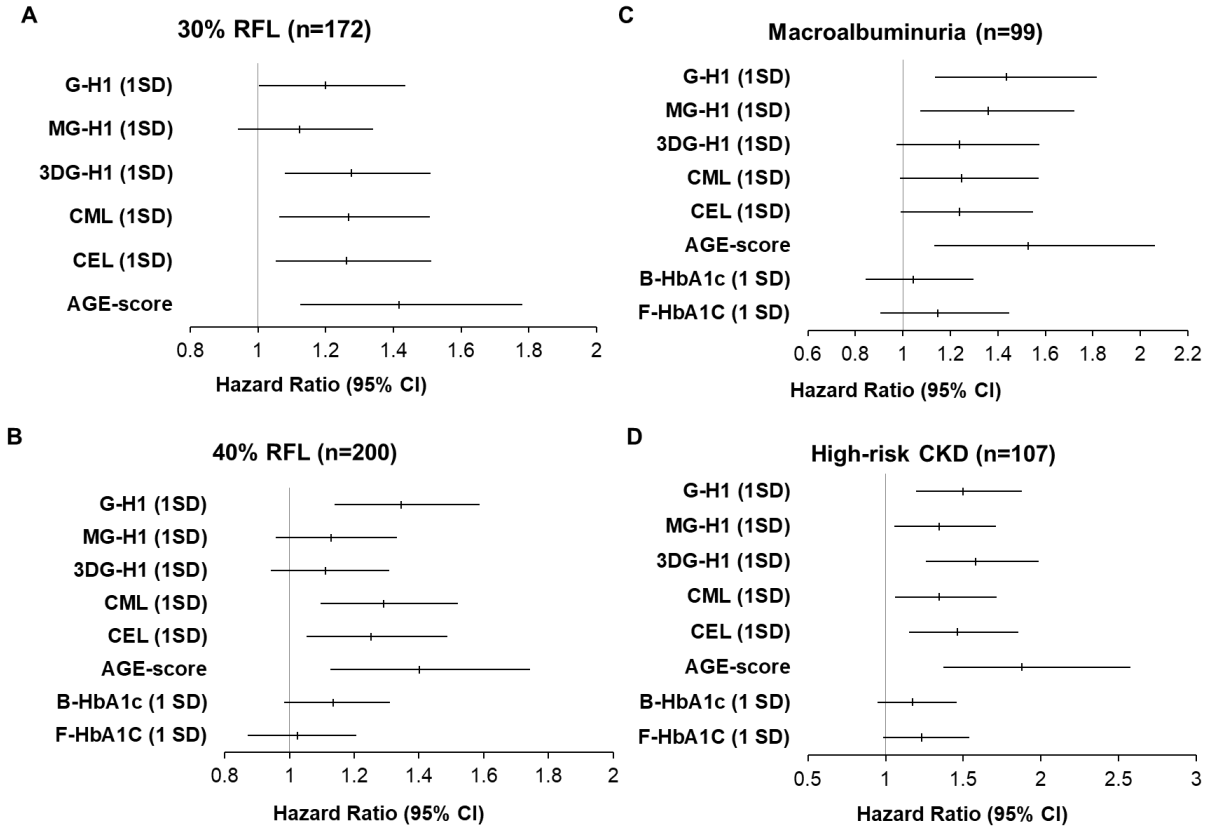
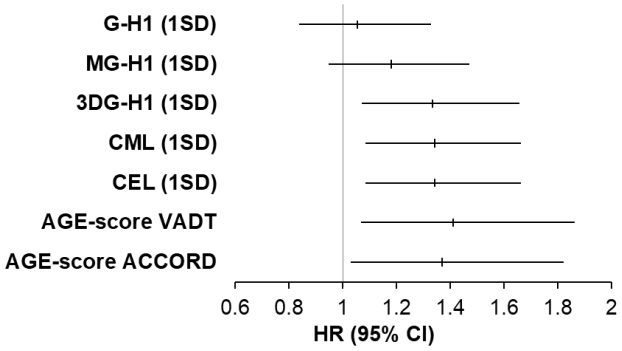
Data are hazard ratios (95% CI), *p<0·05 for interaction

Supplement Table 4: Baseline characteristics of analyzed VADT participants with and without incident primary renal outcome (30% Renal Function Loss).

	Cases	*Non-cases*	*p-value*
n	101	345	
Age (yrs)	59 ± 8	59 ± 8	0.6
Sex (% males)	99 %	96%	0.2
Race (% white)	65%	62%	0.6
BMI (kg/m^2)	31 ± 4	31 ± 5	0.3
History of CVD (%)	42%	31%	0.06
Statin use (%)	69%	59%	0.08
History of hypertension (%)	70%	68%	0.8
Systolic BP (mmHg)	133 ± 19	130 ± 16	0.16
Diastolic BP (mmHg)	77 ± 11	77 ± 10	0.7
Diabetes duration (years)	11 (6-15)	9 (5-15)	0.06
HbA_{1c} (%)	9.6 ± 1.4	9.4 ± 1.4	0.11
HbA_{1c} (mmol/mol)			
uACR (mg/g)	39 (9-111)	12 (5-37)	<0.0001
eGFR (ml/min·1.73 m^2)	85 ± 17	85 ± 17	0.9

Data are %, means ± SD or Medians (25th, 75th percentile), *p<0·05 vs. non-cases, chi-square, Student t-test or Mann-Whitney non-parametric test. RFL, renal function loss; CKD, chronic kidney disease; BMI, body-mass index; BP, blood pressure; HbA_{1c}, hemoglobin A_{1c}; uACR, urine albumin-creatinine ratio; eGFR, estimated glomerular filtration rate.

Supplement Figure 1: Association of renal outcomes with individual AGEs and AGE-score in ACCORD. **Panel A:** 30% renal function loss (RFL) – primary outcome. **Panel B:** 40% renal function loss (RFL). **Panel C:** Incident macroalbuminuria by quartiles of AGE-score. **Panels D:** High-risk CKD by quartiles of AGE-score. All models were adjusted for study arm and baseline age, gender, race/ethnicity, type 2 diabetes duration, systolic blood pressure, baseline hemoglobin A_{1c}, eGFR and uACR. **Panels B-D** show association of secondary renal outcomes with baseline hemoglobin A_{1c} (B-HbA1c) and follow-up hemoglobin A1c (F-HbA1c) tested in the same model with AGE-score. F-HbA1c was included as time-varying variable from all visits until the time of the event.



Supplement Figure 2: Association of 30% RFL with individual AGEs and AGE-score in VADT. AGE-score VADT was calculated as average of z-scores of individual AGEs. AGE-score ACCORD was calculated using ACCORD-derived regression coefficients for individual AGEs and tested in the VADT. All models were adjusted for study arm and baseline age, gender, race/ethnicity, type 2 diabetes duration, systolic blood pressure, hemoglobin A_{1c}, eGFR and uACR.