

SUPPLEMENTAL MATERIALS

Table of Contents

1. **Table S1.** DKD outcomes among the TODAY participants who developed incident (A) microalbuminuria (UACR ≥ 30 mg/g), (B) macroalbuminuria (UACR ≥ 300 mg/g), (C) hyperfiltration, and (D) rapid eGFR decline during the study, overall, and by sex and race-ethnicity
2. **Figure S1.** Cumulative incidence of rapid eGFR decline by sex and race-ethnicity
3. **Table S2.** Univariable Cox proportional hazard models predicting microalbuminuria (UACR ≥ 30 mg/g) and macroalbuminuria (UACR ≥ 300 mg/g)
4. **Table S3.** Univariable Cox proportional hazard models predicting hyperfiltration and rapid eGFR decline
5. **Figure S2.** Longitudinal association of UACR (mg/g) and eGFR (mL/min/1.73m²) with HbA1c and other characteristics, in models adjusted for age, sex, and race-ethnicity
6. **Figure S3.** Chronic Kidney Disease risk by KDIGO classification at year 14 in study
7. **Listing of the TODAY Study Group**

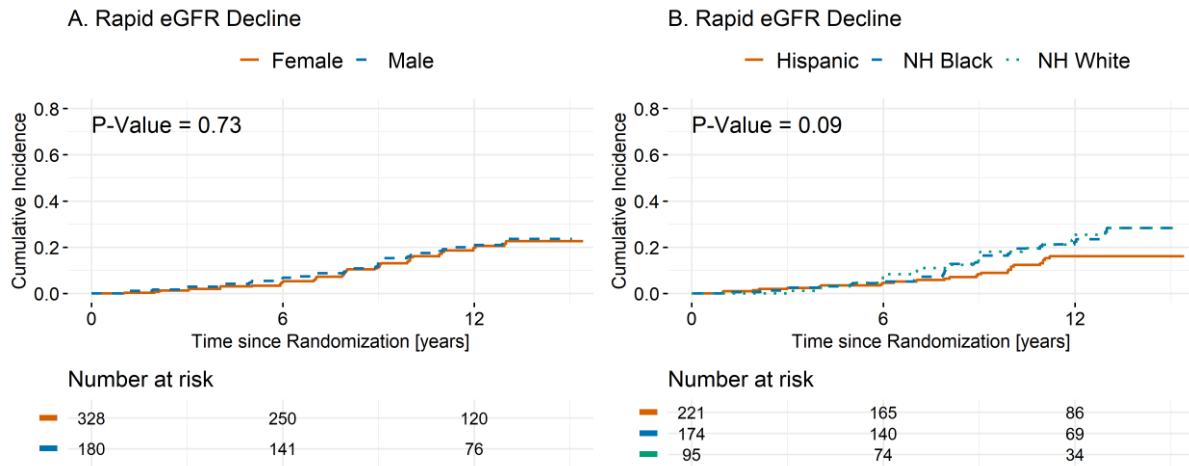
Table S1. DKD outcomes among the TODAY participants who developed incident (A) microalbuminuria (UACR \geq 30 mg/g), (B) macroalbuminuria (UACR \geq 300 mg/g), (C) hyperfiltration, and (D) rapid eGFR decline during the study, by sex and race-ethnicity

DKD Outcomes	N of Cases at Baseline	Prevalence at Baseline (%)	N at Risk	N of Cases	Incidence Rate (per 100 Person-Yrs)	Cumulative Incidence (%)*
A. UACR \geq30 mg/g						
Overall	54	8.0%	623	216	4.3	47.3%
Sex						
Female	36	8.2%	404	134	4.0	45.1%
Male	18	7.6%	219	82	4.7	49.1%
Race-ethnicity						
Non-Hispanic Black	16	7.1%	208	81	4.5	51.7%
Hispanic	24	8.9%	246	88	4.7	48.4%
Non-Hispanic White	11	8.3%	121	31	3.0	33.0%
B. UACR \geq300 mg/g						
Overall	10	1.5%	667	63	1.0	15.5%
Sex						
Female	7	1.6%	433	38	0.9	13.1%
Male	3	1.3%	234	25	1.1	18.6%
Race-ethnicity						
Non-Hispanic Black	2	0.9%	222	20	0.9	17.2%
Hispanic	5	1.8%	265	27	1.1	15.1%
Non-Hispanic White	3	2.3%	129	6	0.5	6.0%
C. Hyperfiltration						
Overall	63	12.3%	447	185	5.3	49.2%
Sex						

DKD Outcomes	N of Cases at Baseline	Prevalence at Baseline (%)	N at Risk	N of Cases	Incidence Rate (per 100 Person-Yrs)	Cumulative Incidence (%)*
Female	50	15.2%	278	123	5.8	52.2%
Male	13	7.1%	169	62	4.3	42.5%
Race-ethnicity						
Non-Hispanic Black	19	10.9%	156	52	3.7	38.3%
Hispanic	34	15.3%	188	97	7.5	63.0%
Non-Hispanic White	10	10.5%	85	28	3.8	36.5%
D. Rapid eGFR Decline						
Overall	2	0.4%	508	83	1.7	22.9%
Sex						
Female	0	0.0%	328	51	1.6	21.6%
Male	2	1.1%	180	32	1.8	23.4%
Race-ethnicity						
Non-Hispanic Black	1	0.6%	174	35	2.0	27.7%
Hispanic	1	0.5%	221	26	1.2	15.5%
Non-Hispanic White	0	0.0%	95	19	2.0	27.2%

* Cumulative incidence provided at year 14 of follow-up.

Figure S1. Cumulative incidence of rapid eGFR decline by sex and race-ethnicity



* Kaplan-Meier cumulative incidence curves for rapid eGFR decline, with number of participants at risk at 0, 6, and 12 years. The number at risk beyond year 12 declines as a function of staggered entry into the cohort from 2004 to 2008. P-value for difference by sex and race-ethnicity based on log-rank test. Female and Hispanic: solid red lines; Male and Non-Hispanic (NH) Black: dashed blue lines; NH White: dotted green lines; Data from the ‘other’ race-ethnicity group are not included due to small numbers.

Table S2. Univariable Cox proportional hazard models predicting microalbuminuria (UACR ≥ 30 mg/g) and macroalbuminuria (UACR ≥ 300 mg/g)*

Characteristics (reference group or unit change)*	UACR ≥ 30 mg/g			UACR ≥ 300 mg/g		
	Hazard Ratio	95% CI	P-value	Hazard Ratio	95% CI	P-value
Age (per year)	1.00	0.93, 1.07	0.99	0.92	0.82, 1.05	0.21
Type 2 diabetes duration (per month)	1.01	0.99, 1.04	0.17	1.02	0.98, 1.06	0.25
Maternal diabetes (yes vs. no)	1.23	0.90, 1.68	0.19	2.24	1.22, 4.12	0.009
Birthweight (vs. normal 2500-4000 g)						
Small (<2500 g)	1.21	0.72, 2.05	0.47	2.47	1.17, 5.22	0.02
Large (>4000 g)	0.82	0.53, 1.27	0.37	1.29	0.61, 2.74	0.50
BMI (per 5 kg/m ²)	1.09	1.02, 1.17	0.02	0.92	0.79, 1.08	0.32
Baseline HbA1c (per %)	1.35	1.13, 1.61	0.0007	2.37	1.75, 3.20	<.0001
Loss of glycemic control during TODAY (yes vs. no)	2.30	1.75, 3.03	<.0001	4.75	2.59, 8.71	<.0001
HbA1c (per %)	1.23	1.17, 1.29	<.0001	1.24	1.14, 1.35	<.0001
Anti-hypertensive medication use (yes vs. no)	2.52	1.89, 3.36	<.0001	4.07	2.43, 6.82	<.0001
SBP (per 10 mm Hg)	1.32	1.18, 1.47	<.0001	1.28	1.05, 1.55	0.01
DBP (per 10 mm Hg)	1.44	1.25, 1.64	<.0001	1.35	1.06, 1.72	0.02
Hypertension (yes vs. no)	1.82	1.39, 2.40	<.0001	4.36	2.29, 8.28	<.0001
eGFR (per 10 mL/min/1.73m ²)	1.11	1.04, 1.18	0.001	1.09	0.98, 1.21	0.11
Hyperfiltration (yes vs. no)	1.63	1.21, 2.18	0.001	1.84	1.08, 3.12	0.02
Baseline serum uric acid (per mg/dL)	1.14	1.03, 1.26	0.01	1.12	0.92, 1.36	0.24

Characteristics (<i>reference group or unit change</i>) [*]	UACR \geq 30 mg/g			UACR \geq 300 mg/g		
	Hazard Ratio	95% CI	P-value	Hazard Ratio	95% CI	P-value
Lipid-lowering medication use (<i>yes vs. no</i>)	1.57	1.03, 2.39	0.03	1.73	0.87, 3.41	0.12
HDL cholesterol (<i>per mg/dL</i>)	0.98	0.97, 0.99	0.003	0.98	0.96, 1.01	0.20
LDL cholesterol (<i>per mg/dL</i>)	1.00	0.99, 1.01	0.42	1.00	0.99, 1.01	0.28
LDL dyslipidemia (<i>yes vs. no</i>)	1.21	0.83, 1.75	0.32	1.58	0.88, 2.85	0.12
Log triglycerides (<i>per SD</i>)	1.49	1.29, 1.71	<.0001	1.76	1.43, 2.17	<.0001
Triglyceride dyslipidemia (<i>yes vs. no</i>)	1.51	1.15, 1.99	0.003	2.27	1.37, 3.77	0.001
Log insulin sensitivity (<i>per SD</i>)	0.73	0.64, 0.82	<.0001	0.75	0.60, 0.92	0.007
Log C-peptide index (<i>per SD</i>)	0.73	0.65, 0.81	<.0001	0.69	0.56, 0.85	0.0005
Log cODI (<i>per SD</i>)	0.66	0.60, 0.74	<.0001	0.65	0.53, 0.80	<.0001

* Hazard ratios (95% confidence intervals and p-values) per reference group or unit change (as indicated) in separate Cox proportional hazards model predicting the risk of UACR \geq 30 mg/g or UACR \geq 300 mg/g during the study. Factors are entered as fixed or as time-dependent covariates in the models.

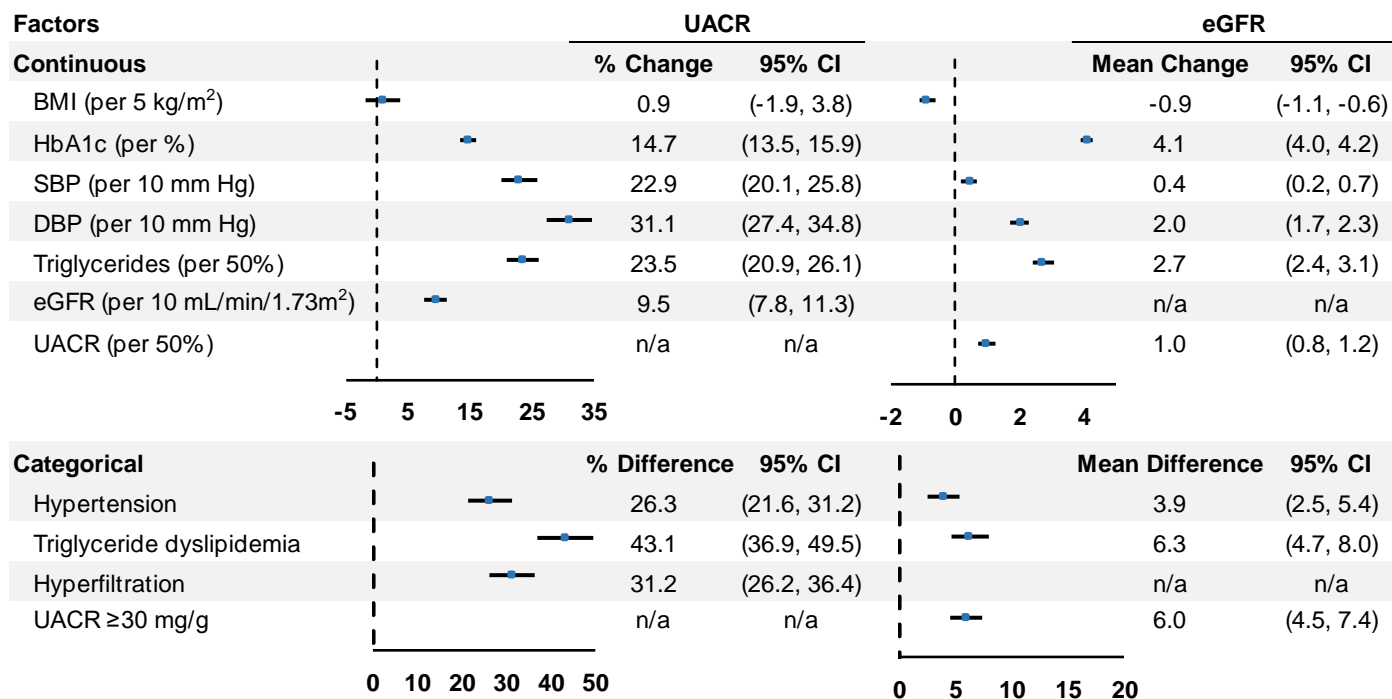
Table S3. Univariable Cox proportional hazard models predicting hyperfiltration and rapid eGFR decline *

Characteristics (reference group or unit change)*	Hyperfiltration			Rapid eGFR Decline		
	Hazard Ratio	95% CI	P-value	Hazard Ratio	95% CI	P-value
Age (<i>per year</i>)	0.97	0.90, 1.04	0.34	1.09	0.98, 1.22	0.11
Type 2 diabetes duration (<i>per month</i>)	1.00	0.98, 1.02	0.99	1.01	0.98, 1.04	0.58
Maternal diabetes (<i>yes vs. no</i>)	1.76	1.28, 2.43	0.0005	1.45	0.95, 2.22	0.10
Birthweight (<i>vs. normal 2500-4000 g</i>)						
Small (<2500 g)	1.57	0.92, 2.68	0.10	1.89	0.95, 3.76	0.07
Large (>4000 g)	1.86	1.23, 2.80	0.003	0.94	0.47, 1.87	0.86
BMI (<i>per 5 kg/m²</i>)	0.93	0.85, 1.01	0.09	0.95	0.82, 1.08	0.40
Baseline HbA1c (<i>per %</i>)	1.10	0.91, 1.33	0.32	1.56	1.21, 2.01	0.0007
Loss of glycemic control during TODAY (<i>yes vs. no</i>)	1.12	0.81, 1.54	0.48	1.79	1.17, 2.75	0.007
HbA1c (<i>per %</i>)	1.09	1.03, 1.15	0.001	1.13	1.06, 1.22	0.0006
Anti-hypertensive medication use (<i>yes vs. no</i>)	0.85	0.60, 1.21	0.37	2.00	1.31, 3.07	0.001
SBP (<i>per 10 mm Hg</i>)	0.93	0.82, 1.04	0.21	1.24	1.05, 1.47	0.01
DBP (<i>per 10 mm Hg</i>)	1.02	0.88, 1.18	0.82	1.41	1.14, 1.73	0.001
Hypertension (<i>yes vs. no</i>)	0.84	0.62, 1.13	0.25	1.60	1.05, 2.46	0.03
Log UACR (<i>per SD</i>)	1.09	0.93, 1.28	0.28	1.42	1.16, 1.74	0.02
Microalbuminuria (<i>yes vs. no</i>)	1.41	0.83, 2.38	0.20	1.69	1.10, 2.59	0.02
Lipid-lowering medication use (<i>yes vs. no</i>)	0.74	0.41, 1.33	0.32	1.19	0.63, 2.25	0.59
HDL cholesterol (<i>per mg/dL</i>)	0.98	0.97, 0.99	0.11	0.99	0.98, 1.01	0.70

Characteristics (<i>reference group or unit change</i>) [*]	Hyperfiltration			Rapid eGFR Decline		
	Hazard Ratio	95% CI	P-value	Hazard Ratio	95% CI	P-value
LDL cholesterol (<i>per mg/dL</i>)	0.97	0.99, 1.00	0.12	1.00	0.97, 1.01	0.43
LDL dyslipidemia (<i>yes vs. no</i>)	0.71	0.44, 1.14	0.15	1.13	0.66, 1.94	0.65
Log triglycerides (<i>per SD</i>)	1.27	1.09, 1.47	0.002	1.10	0.89, 1.37	0.36
Triglyceride dyslipidemia (<i>yes vs. no</i>)	1.17	0.87, 1.58	0.30	1.16	0.75, 1.78	0.50
Log insulin sensitivity (<i>per SD</i>)	0.99	0.86, 1.13	0.84	0.99	0.82, 1.21	0.96
Log C-peptide index (<i>per SD</i>)	0.73	0.64, 0.82	<.0001	0.87	0.75, 1.00	0.05
Log cODI (<i>per SD</i>)	0.76	0.67, 0.86	<.0001	0.86	0.70, 1.04	0.12

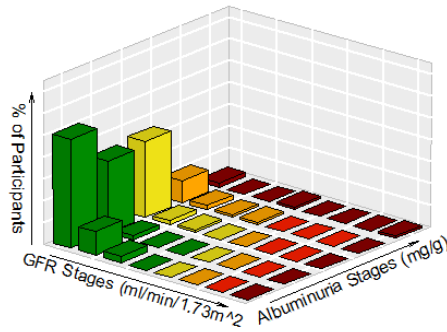
* Hazard ratios (95% confidence intervals and p-values) per reference group or unit change (as indicated) in separate Cox proportional hazards model predicting the risk of hyperfiltration or rapid eGFR decline during the study. Factors are entered as fixed or as time-dependent covariates in the models.

Figure S2. Longitudinal association of UACR (mg/g) and eGFR (mL/min/1.73m²) with HbA1c and other clinical characteristics, in models adjusted for age, sex, and race-ethnicity*



* Data from multivariable linear mixed models regressing the log of UACR or eGFR on each characteristic separately, adjusting for age, sex and race-ethnicity. The characteristics (continuous or binary) were measured repeatedly over time during the study and entered in the models as time-dependent covariates. For continuous covariates, the estimate represents the percent change in UACR or the mean change in eGFR per unit increase in the predictor or as specified. For categorical covariates, the estimate represents the percent difference in mean UACR or the difference in mean eGFR between groups (yes vs. no). The percent change or percent difference is calculated as $[100(e^{\beta}-1)]$, where β is the beta estimate coefficient from the linear mixed model, and 95% confidence intervals (CI) are given.

Figure S3. Chronic Kidney Disease risk by KDIGO classification at year 14 in study



Composite ranking for relative risks by GFR and albuminuria (KDIGO 2009)				Albuminuria stages, description and range (mg/g)					Total
				A1		A2	A3		
				Optimal and high-normal		High	Very high and nephrotic		
				<10	10-29	30-299	300-1999	≥2000	
GFR stages, description and range (ml/min Per 1.73 min ²)	G1	High and optimal	>105	50 32%	33 21%	35 23%	11 7%	2 1%	130 84%
			90-104	11 7%	2 1%	2 1%	2 1%	0 0%	17 11%
	G2	Mild	75-89	3 2%	0 0%	1 <1%	1 <1%	0 0%	5 3%
			60-74	0 0%	0 0%	0 0%	1 <1%	1 <1%	2 1%
	G3a	Mild-moderate	45-59	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%
	G3b	Moderate-severe	30-44	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%
	G4	Severe	15-29	0 0%	0 0%	0 0%	0 0%	1 <1%	1 <1%
G5	Kidney failure	<15	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	
Total				64 41%	35 23%	38 24%	15 9%	4 3%	156 100%

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