

SUPPLEMENTARY MATERIALS FOR
Early trajectory of estimated glomerular filtration rate and long-term advanced kidney and
cardiovascular complications in type 1 diabetes

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Supplementary Table S1. Distribution of eGFR Annual Decline in DCCT (n=1435).

DCCT eGFR Annual Decline (%)	Overall	Adolescents	Adults	P-value
	N=1435	N=195	N=1240	
≥3	149 (10.4%)	30 (15.4%)	119 (9.6%)	<0.0001
2 to 2.99	178 (12.4%)	47 (26.4%)	131 (10.6%)	
1 to 1.99	331 (23.1%)	45 (23.1%)	286 (23.1%)	
<1	777 (54.2%)	73 (37.4%)	704 (56.8%)	

Supplementary Table S2. Association between Annual DCCT eGFR Annual Decline ($\geq 2\%$ vs. $< 2\%$, and as a quantitative variable) and EDIC Outcomes, using Cox Proportional Hazards Models Stratified by Number of DCCT eGFR Measurements.

	Unadjusted		Adjusted*		Further Adjusted* for Adult/Adolescent		Further Adjusted* for DCCT closeout eGFR	
Outcome	HR (95% CI)	P-Value	HR (95% CI)	P-Value	HR (95% CI)	P-Value	HR (95% CI)	P-Value
eGFR Decline $\geq 2\%$ vs. $< 2\%$								
CVD	0.81 (0.58, 1.13)	0.2114	0.90 (0.64, 1.27)	0.5484	0.91 (0.64, 1.28)	0.5857	0.86 (0.57, 1.31)	0.4878
MACE	0.77 (0.47, 1.25)	0.2923	0.89 (0.54, 1.46)	0.6316	0.90 (0.55, 1.48)	0.6816	0.75 (0.42, 1.33)	0.3174
eGFR<60 ml/min/1.73 m ²	1.56 (1.14, 2.15)	0.0061	1.77 (1.28, 2.44)	0.0006	1.74 (1.25, 2.42)	0.0011	1.09 (0.70, 1.69)	0.7084
Quantitative Annual Decline								
CVD	1.03 (0.97, 1.10)	0.3054	1.04 (0.99, 1.11)	0.1455	1.05 (0.99, 1.11)	0.1320	1.07 (0.99, 1.15)	0.1126
MACE	1.01 (0.92, 1.11)	0.8074	1.03 (0.95, 1.13)	0.4325	1.04 (0.95, 1.13)	0.3982	1.01 (0.90, 1.12)	0.8845
eGFR<60 ml/min/1.73 m ²	1.09 (1.00, 1.19)	0.0567	1.11 (1.02, 1.22)	0.0190	1.11 (1.01, 1.22)	0.0236	0.98 (0.89, 1.07)	0.5953

*Adjusted for current age, current BMI, current duration, sex, mean updated HbA1c, group, and cohort.

Numbers are shown as the Hazard Ratio (95% confidence interval)

DCCT=Diabetes Control and Complications Trial; HR=hazard ratio; CVD=Cardiovascular Disease; MACE=Major Adverse Cardiovascular Events.

Supplementary Table S3. Association between Annual eGFR Decline ($\geq 3\%$ vs. $< 3\%$, $\geq 2\%$ vs. $< 2\%$, and as a quantitative variable) and EDIC Outcomes in Cox Proportional Hazards Models **Excluding Adolescents** (n=1240)

	Unadjusted		Adjusted*		Further Adjusted* for DCCT closeout eGFR	
Outcome	HR (95% CI)	P-Value	HR (95% CI)	P-Value	HR (95% CI)	P-Value
eGFR Annual Decline $\geq 3\%$ ("Early Rapid eGFR Loss")						
CVD	0.98 (0.61, 1.58)	0.9496	0.89 (0.55, 1.44)	0.6473	0.86 (0.52, 1.45)	0.5806
MACE	1.59 (0.86, 2.92)	0.1377	1.46 (0.80, 2.69)	0.2193	1.34 (0.68, 2.64)	0.3905
eGFR<60 ml/min/1.73 m ²	2.11 (1.34, 3.34)	0.0014	1.84 (1.17, 2.91)	0.0089	0.82 (0.46, 1.48)	0.5186
eGFR Annual Decline $\geq 2\%$						
CVD	0.93 (0.65, 1.33)	0.7062	0.91 (0.64, 1.30)	0.5982	0.88 (0.56, 1.37)	0.5703
MACE	0.90 (0.53, 1.51)	0.6812	0.88 (0.52, 1.49)	0.6447	0.74 (0.40, 1.36)	0.3302
eGFR<60 ml/min/1.73 m ²	1.79 (1.25, 2.56)	0.0013	1.81 (1.26, 2.59)	0.0012	0.95 (0.58, 1.55)	0.8286
Quantitative Annual Decline						
CVD	1.05 (0.99, 1.11)	0.0960	1.05 (0.99, 1.11)	0.1287	1.07 (0.99, 1.16)	0.0896
MACE	1.03 (0.94, 1.13)	0.5470	1.03 (0.94, 1.13)	0.5001	1.00 (0.90, 1.12)	0.9669
eGFR<60 ml/min/1.73 m ²	1.12 (1.01, 1.24)	0.0255	1.13 (1.03, 1.25)	0.0126	0.96 (0.88, 1.06)	0.4196

*Adjusted for current age, current BMI, current duration, sex, mean updated HbA1c, group, and cohort. HR=hazard ratio

Supplementary Table S4. Association between Annual eGFR Decline ($\geq 3\%$ vs. $< 3\%$, $\geq 2\%$ vs. $< 2\%$, and as a quantitative variable) and EDIC Outcomes using Cox Proportional Hazards Models **Excluding Participants with DCCT Closeout T1D Duration <10 years** (n=812)

	Unadjusted		Adjusted*		Further Adjusted* for Adult/Adolescent		Further Adjusted* for DCCT closeout eGFR	
Outcome	HR (95% CI)	P-Value	HR (95% CI)	P-Value	HR (95% CI)	P-Value	HR (95% CI)	P-Value
eGFR Annual Decline $\geq 3\%$ ("Early Rapid eGFR Loss")								
CVD	1.50 (0.85, 2.66)	0.1589	1.35 (0.75, 2.44)	0.3180	1.36 (0.76, 2.44)	0.3037	1.20 (0.63, 2.28)	0.5815
MACE	2.70 (1.41, 5.15)	0.0026	2.60 (1.31, 5.15)	0.0063	2.62 (1.32, 5.19)	0.0058	2.42 (1.08, 5.43)	0.0323
eGFR<60 ml/min/1.73 m ²	2.81 (1.66, 4.75)	0.0001	2.37 (1.30, 4.34)	0.0049	2.35 (1.28, 4.31)	0.0058	1.26 (0.57, 2.79)	0.5697
eGFR Annual Decline $\geq 2\%$								
CVD	0.91 (0.60, 1.40)	0.6746	0.96 (0.62, 1.49)	0.8708	0.98 (0.63, 1.52)	0.9241	0.83 (0.49, 1.42)	0.5032
MACE	0.94 (0.52, 1.67)	0.8214	1.00 (0.56, 1.81)	0.9881	1.03 (0.57, 1.87)	0.9233	0.81 (0.41, 1.62)	0.5563
eGFR<60 ml/min/1.73 m ²	1.90 (1.28, 2.83)	0.0014	2.03 (1.34, 3.08)	0.0008	1.99 (1.30, 3.04)	0.0016	1.34 (0.77, 2.34)	0.2953
Quantitative Annual Decline								
CVD	1.05 (0.98, 1.13)	0.1485	1.06 (0.98, 1.14)	0.1688	1.06 (0.98, 1.14)	0.1532	1.04 (0.93, 1.15)	0.5127
MACE	1.04 (0.97, 1.11)	0.3084	1.04 (0.96, 1.12)	0.3681	1.04 (0.96, 1.12)	0.3265	0.97 (0.86, 1.09)	0.6096
eGFR<60 ml/min/1.73 m ²	1.31 (1.14, 1.51)	0.0002	1.29 (1.13, 1.49)	0.0003	1.29 (1.12, 1.48)	0.0004	1.14 (0.95, 1.37)	0.1594

*Adjusted for current age, current BMI, current duration, sex, mean updated HbA1c, group, and cohort. HR=hazard ratio

Supplementary Table S5. Association between Annual DCCT Early-Stage Rapid eGFR Loss and EDIC Outcomes **Excluding Participants with Baseline eGFR ≥ 140 ml/min/1.73 m²**, using Cox Proportional Hazards Models Stratified by Number of DCCT eGFR Measurements.

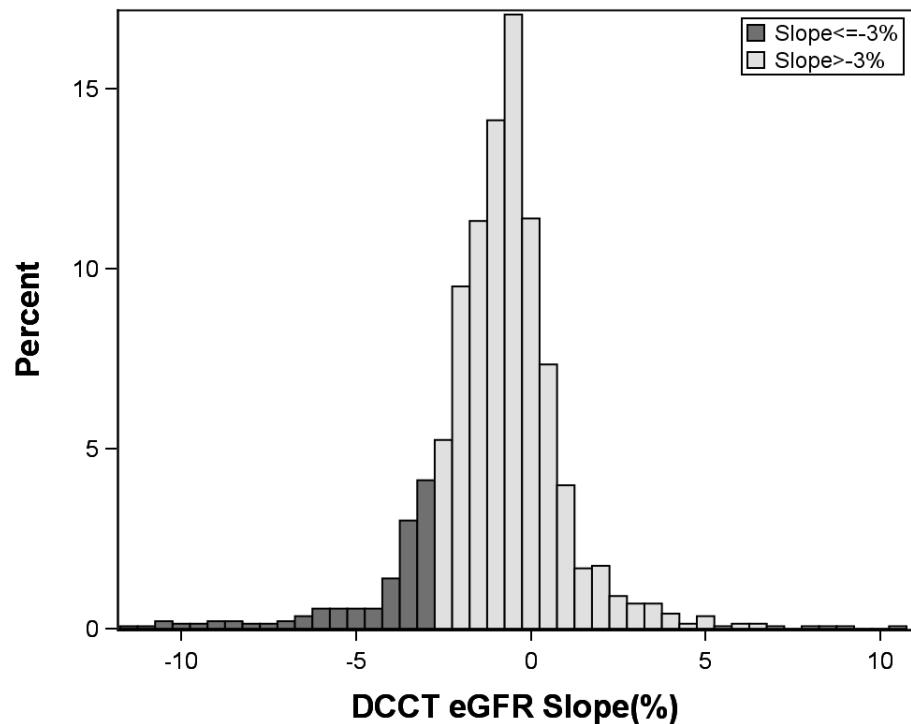
Outcome	Unadjusted		Adjusted*		Further Adjusted* for Adult/Adolescent		Further Adjusted* for DCCT closeout eGFR	
	HR (95% CI)	P-Value	HR (95% CI)	P-Value	HR (95% CI)	P-Value	HR (95% CI)	P-Value
Early-Stage Rapid eGFR Loss								
CVD	1.15 (0.73, 1.81)	0.5432	1.11 (0.69, 1.76)	0.6733	1.11 (0.70, 1.76)	0.6574	1.09 (0.65, 1.82)	0.7507
MACE	1.86 (1.04, 3.31)	0.0367	1.80 (0.98, 3.28)	0.0561	1.81 (0.99, 3.28)	0.0520	1.61 (0.81, 3.20)	0.1703
eGFR<60 ml/min/1.73 m ²	1.99 (1.27, 3.12)	0.0027	1.81 (1.14, 2.87)	0.0112	1.77 (1.12, 2.81)	0.0150	0.81 (0.45, 1.47)	0.4971
DCCT Closeout eGFR								
CVD	0.98 (0.97, 0.99)	0.0028	1.00 (0.98, 1.01)	0.7638	1.00 (0.98, 1.01)	0.7560	1.00 (0.98, 1.02)	0.8973
MACE	0.98 (0.96, 0.99)	0.0015	0.99 (0.97, 1.00)	0.1378	0.99 (0.97, 1.00)	0.1340	0.99 (0.97, 1.01)	0.5052
eGFR<60 ml/min/1.73 m ²	0.96 (0.95, 0.97)	<0.0001	0.95 (0.94, 0.97)	<0.0001	0.95 (0.94, 0.97)	<0.0001	0.95 (0.94, 0.97)	<0.0001

*Adjusted for current age, current BMI, current duration, sex, mean updated HbA1c, group, and cohort.

Numbers are shown as the Hazard Ratio (95% confidence interval)

DCCT=Diabetes Control and Complications Trial; HR=Hazard Ratio; CVD=Cardiovascular Disease; MACE=Major Adverse Cardiovascular Events.

Supplementary Figure S1. Distribution of DCCT eGFR Slope (Expressed as %).



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