Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. eTable 1. Characteristics of Women and Men at DCCT Baseline, by Presence or Absence of Any CVD

	Any CVD					
	Yes			No		
	Women (N=113)	Men (N=150)		Women (N=567)	Men (N=611)	
Demographics	Mean (SD) or %		p-value[a]			p-value[a]
Age, years	29.8 (6.3)	30.0 (6.4)	0.69	25.5 (7.3)	26.6 (6.8)	0.005
Age at diabetes onset, years	22.9 (8.1)	23.7 (8.0)	0.43	19.7 (8.3)	21.1 (7.6)	0.002
Intensive treatment, %	49.6	46.7	0.64	51.0	48.4	0.39
Primary prevention, %	41.6	39.3	0.71	53.1	52.2	0.76
Duration of diabetes, years	6.9 (4.5)	6.3 (4.2)	0.29	5.8 (4.2)	5.6 (4.0)	0.48
Current cigarette smoker, %	30.1	26.7	0.54	14.6	18.0	0.12
Physical						
BMI, kg/m^2	23.9 (3.0)	24.4 (2.8)	0.15	23.0 (2.8)	23.5 (2.6)	0.001
Blood Pressure						
Systolic, mmHg	112.6 (11.4)	118.7 (10.7)	<0.001	109.7 (10.9)	117.3 (11.1)	<0.001
Diastolic, mmHg	72.2 (7.9)	74.7 (8.9)	0.01	70.1 (8.7)	74.3 (8.6)	<0.001
Pulse pressure, mmHg	40.3 (9.8)	44.0 (9.7)	0.003	39.5 (9.5)	43.0 (9.4)	<0.001
Pulse rate, bpm	73.0 (11.3)	65.9 (10.8)	<0.001	70.7 (10.5)	65.4 (10.9)	<0.001
Lipids						
Total cholesterol, mg/dl	186.5 (32.4)	181.5 (35.7)	0.10	178.8 (31.4)	171.1 (33.6)	<0.001
HDL cholesterol, mg/dl	53.4 (12.6)	45.4 (11.1)	<0.001	54.8 (12.5)	47.4 (10.9)	<0.001
LDL cholesterol, mg/dl	117.4 (26.7)	117.3 (31.7)	0.79	108.8 (27.6)	107.3 (29.6)	0.28
Triglycerides, mg/dl	78.8 (37.6)	98.1 (74.2)	0.007	76.1 (36.2)	82.5 (49.1)	0.04
Kidney Disease						
Sustained AER ≥30 mg/24 h, %	7.1	5.3	0.56	3.9	4.9	0.39
Glycemic Control						
HbA1c, %	9.2 (1.7)	9.0 (1.6)	0.60	9.0 (1.7)	8.7 (1.5)	<0.001
HbA1c, mmol/mol	76.7 (18.0)	75.1 (17.1)	0.60	75.4 (18.0)	71.2 (16.4)	<0.001

To covert cholesterol to mmol/L, multiply values by 0.0259.
AER=albumin excretion rate, BMI=body mass index, HDL=high-density lipoprotein, LDL=low-density lipoprotein.
[a] P-value for differences by sex by the Wilcoxon rank-sum test for continuous variables or chi-square test for categorical variables.

eTable 2. Rate of Change of Cardiometabolic Risk Factors and HbA1c During DCCT/EDIC for Women and Men

	Women (N=680)	**Men (N=761)**	**Women vs. Men Comparison[a]**		
	Mean Slope during EDIC Beta (SE)		Difference in Slopes Beta (SE)	t-value	p-value
Physical					
BMI, kg/m^2	0.105 (0.007)	0.108 (0.006)	-0.003 (0.009)	-0.36	0.72
Waist circumference, cm	0.266 (0.018)	0.294 (0.017)	-0.028 (0.025)	-1.15	0.25
Blood Pressure					
Systolic, mmHg	0.233 (0.015)	0.172 (0.014)	0.061 (0.020)	3.01	0.003
Diastolic, mmHg	0.025 (0.009)	0.045 (0.009)	-0.020 (0.013)	-1.51	0.13
Pulse pressure, mmHg	0.208 (0.011)	0.127 (0.010)	0.081 (0.015)	5.45	<0.001
Pulse rate, bpm	-0.056 (0.013)	0.015 (0.013)	-0.071 (0.018)	-3.92	<0.001
Lipids					
Total cholesterol, mg/dl	0.129 (0.051)	0.108 (0.049)	0.021 (0.071)	0.30	0.76
HDL cholesterol, mg/dl	0.241 (0.022)	0.139 (0.021)	0.103 (0.031)	3.31	0.001
LDL cholesterol, mg/dl	-0.145 (0.045)	-0.112 (0.043)	-0.033 (0.062)	-0.53	0.60
Triglycerides, mg/dl[b]	0.003 (0.001)	0.005 (0.001)	-0.003 (0.001)	-2.36	0.02
Glycemic Control					
HbA1c, %	-0.006 (0.002)	-0.005 (0.002)	-0.001 (0.003)	-0.24	0.81

ACE=angiotensin-converting enzyme, ARB=angiotensin II receptor blocker, BMI=body mass index, HDL=high-density lipoprotein, LDL=low-density lipoprotein.

[a] Separate LMM models assessing the differences between sexes (women vs. men) in the mean slope of each quantitative risk factor over repeated time points. DCCT/EDIC study year was included in each model as a quantitative random effect. An interaction between sex and study year was included to test the hypothesis of equality of mean slopes. Separate nested models were used to estimate the mean slopes within each sex. Each model was adjusted for DCCT baseline age and treatment group. The mean slope over the duration of the study, difference in slopes (women – men), t-values, and p-values are presented from each model. The signed t-value corresponds to the magnitude and directionality of the association.

[b] Triglyceride values were log transformed.

eTable 3. Risk of Cardiovascular Disease in Women vs Men After Individual Adjustment for Cardiometabolic Risk Factors

Time-dependent Covariates	Any CVD		MACE	
	Covariate	Women vs. Men Adjusted for Covariate	Covariate	Women vs. Men Adjusted for Covariate
	Hazard Ratio (95% CI)[a]		Hazard Ratio (95% CI)[a]	
-----	-----	0.87 (0.68, 1.12)	-----	0.79 (0.56, 1.10)
Physical				
BMI, per 5 kg/m^2	1.24 (1.06,1.46)	0.90 (0.70,1.15)	1.04 (0.83,1.30)	0.79 (0.56,1.11)
Waist circumference, per 10 cm	1.23 (1.10,1.38)	1.15 (0.86,1.53)	1.07 (0.90,1.26)	0.90 (0.60,1.34)
Blood Pressure				
Systolic, per 5 mmHg	1.27 (1.18,1.36)	1.09 (0.85,1.41)	1.25 (1.13,1.38)	0.96 (0.67,1.36)
Diastolic, per 5 mmHg	1.27 (1.13,1.43)	1.04 (0.80,1.35)	1.14 (0.97,1.35)	0.87 (0.61,1.25)
Pulse pressure, per 5 mmHg	1.30 (1.18,1.43)	0.92 (0.72,1.18)	1.33 (1.18,1.51)	0.82 (0.59,1.16)
Pulse rate, per 5 bpm	1.34 (1.22,1.46)	0.75 (0.59,0.97)	1.43 (1.26,1.61)	0.66 (0.47,0.94)
Lipids				
Total, per 10 mg/dl	1.12 (1.07,1.18)	0.82 (0.64,1.06)	1.12 (1.05,1.20)	0.74 (0.53,1.04)
HDL, per 10 mg/dl	0.82 (0.73,0.92)	1.09 (0.83,1.42)	0.80 (0.68,0.94)	1.01 (0.69,1.47)
LDL, per 10 mg/dl	1.15 (1.09,1.21)	0.92 (0.72,1.17)	1.14 (1.06,1.23)	0.82 (0.58,1.15)
Triglycerides, per 10%	1.09 (1.06,1.12)	1.00 (0.78,1.28)	1.10 (1.07,1.14)	0.91 (0.65,1.29)
Medications				
ACE inhibitor or ARB, yes vs. no	1.07 (0.81,1.40)	0.91 (0.70,1.17)	0.88 (0.61,1.28)	0.82 (0.57,1.16)
β-blockers, yes vs. no	2.02 (1.36,3.00)	0.90 (0.69,1.15)	2.50 (1.59,3.93)	0.81 (0.57,1.15)
Calcium channel blockers, y vs. n)	1.65 (1.13,2.41)	0.91 (0.70,1.17)	2.00 (1.25,3.19)	0.83 (0.59,1.18)
Lipid-lowering, yes vs. no	0.98 (0.73,1.30)	0.90 (0.70,1.16)	0.77 (0.52,1.13)	0.80 (0.56,1.14)
Glycemic Control				
HbA1c, per 1%	1.57 (1.40,1.76)	0.82 (0.64,1.05)	1.80 (1.55,2.10)	0.71 (0.50,1.00)

ACE=angiotensin-converting enzyme, ARB=angiotensin II receptor blocker, BMI=body mass index, HDL=high-density lipoprotein, LDL=low-density lipoprotein.

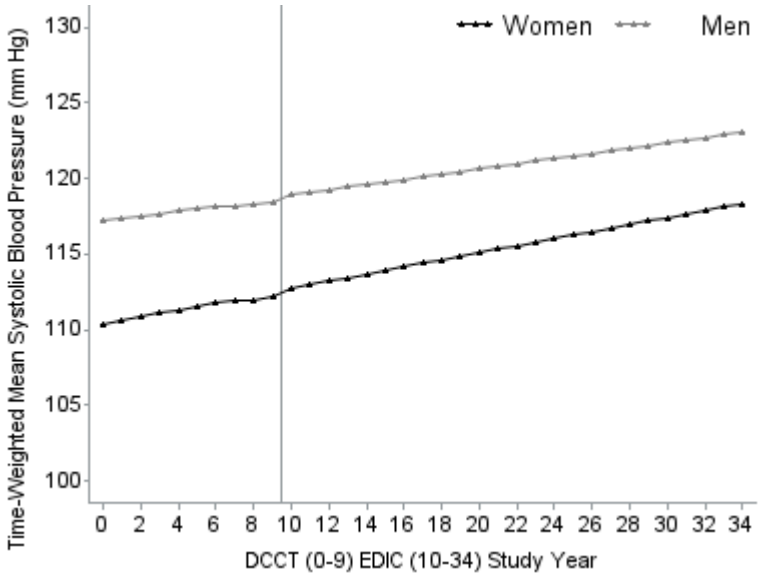
[a] Separate Cox proportional hazard regression models assessing the difference between sexes (women vs. men) on the risk of cardiovascular disease, after separate adjustments for each cardiometabolic risk factor as a time-dependent covariate. Each model was further adjusted for DCCT baseline age and treatment group. The hazard ratios (95% CI) for the time-dependent covariate and for the sex effect are presented from each model.

eTable 4. Associations Between Risk Factor Levels or Targets and Cardiovascular Disease Risk During DCCT/EDIC in Women and Men

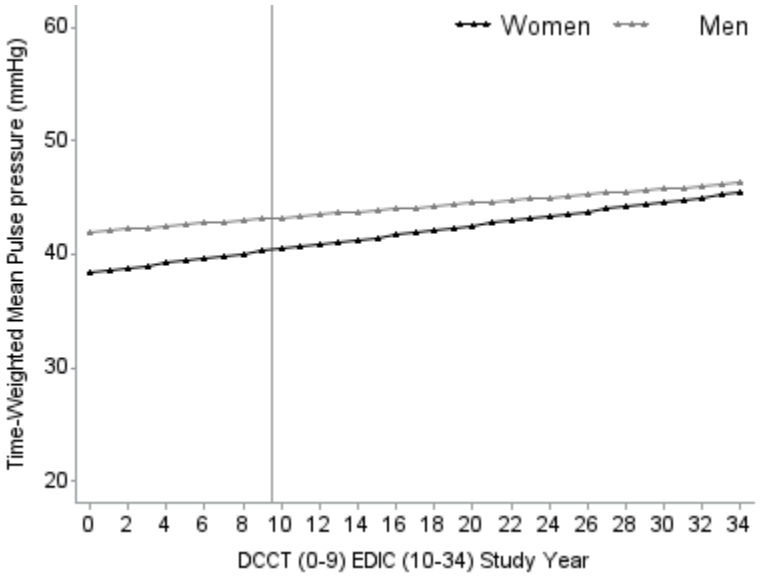
			Any CVD		MACE	
	Women	**Men**	**Women**	**Men**	**Women**	**Men**
	Mean (SD) or %		Hazard Ratio (95% CI)[a]		Hazard Ratio (95% CI)[a]	
Risk Factor Targets						
HDL ≥50 mg/dl women, ≥40 mg/dl men	74.3	86.6	0.76 (0.49,1.17)	0.60 (0.40,0.88)	0.54 (0.30,0.96)	0.50 (0.30,0.83)

[a] Separate stratified Cox proportional hazard regression models adjusted for DCCT baseline age and treatment group. The hazard ratios (95% CI) for the time-dependent covariate are presented from each model. An interaction between sex and risk factor was evaluated in each model.

eFigure. Mean Slope During EDIC for Women vs Men



A.



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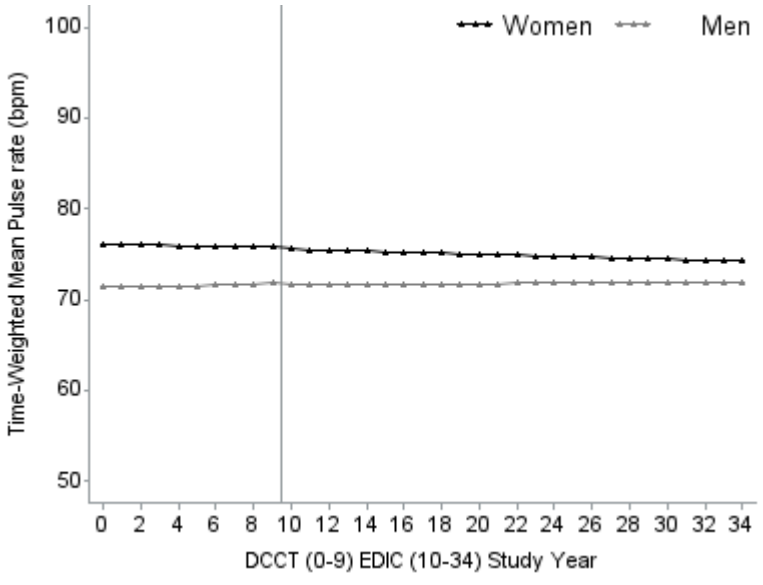

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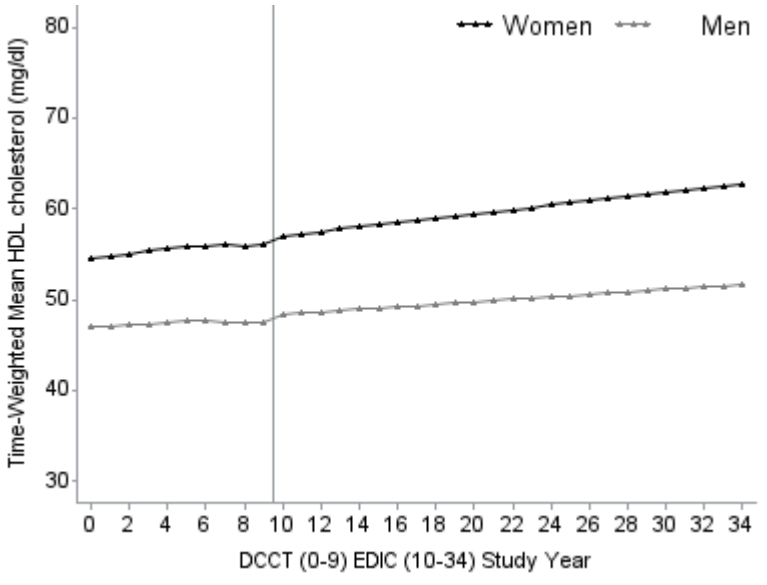

D.

Data are from LMM models assessing the differences between women and men in the mean slope of each quantitative risk factor over repeated time points. Each model was adjusted for DCCT baseline age and treatment group.

eAppendix. DCCT/EDIC Research Group

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