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

| Demographics | Women (N=113) | Men (N=150) | Women (N=567) | Men (N=611) | p-value<sup>a</sup> | p-value<sup>a</sup> |
|--------------|---------------|-------------|---------------|-------------|-----------------|-----------------|
| Age, years   | 29.8 (6.3)    | 30.0 (6.4)  | 25.5 (7.3)    | 26.6 (6.8)  | 0.69            | 0.005           |
| Age at diabetes onset, years | 22.9 (8.1)    | 23.7 (8.0)  | 19.7 (8.3)    | 21.1 (7.6)  | 0.43            | 0.002           |
| Intensive treatment, % | 49.6          | 46.7        | 51.0          | 48.4        | 0.64            | 0.39            |
| Primary prevention, % | 41.6          | 39.3        | 53.1          | 52.2        | 0.71            | 0.76            |
| Duration of diabetes, years | 6.9 (4.5)     | 6.3 (4.2)   | 5.8 (4.2)     | 5.6 (4.0)   | 0.29            | 0.48            |
| Current cigarette smoker, % | 30.1          | 26.7        | 14.6          | 18.0        | 0.54            | 0.12            |

**Physical**

| BMI, kg/m² | 23.9 (3.0) | 24.4 (2.8) | 23.0 (2.8) | 23.5 (2.6) | 0.15            | 0.001           |

**Blood Pressure**

| Systolic, mmHg | 112.6 (11.4) | 118.7 (10.7) | 109.7 (10.9) | 117.3 (11.1) | <0.001          | <0.001           |
| Diastolic, mmHg | 72.2 (7.9)   | 74.7 (8.9)   | 70.1 (8.7)   | 74.3 (8.6)   | 0.01            | <0.001           |
| Pulse pressure, mmHg | 40.3 (9.8)  | 44.0 (9.7)   | 39.5 (9.5)   | 43.0 (9.4)   | 0.003           | <0.001           |
| Pulse rate, bpm | 73.0 (11.3)  | 65.9 (10.8)  | 70.7 (10.5)  | 65.4 (10.9)  | <0.001          | <0.001           |

**Lipids**

| Total cholesterol, mg/dl | 186.5 (32.4) | 181.5 (35.7) | 178.8 (31.4) | 171.1 (33.6) | 0.10            | <0.001           |
| HDL cholesterol, mg/dl   | 53.4 (12.6)  | 45.4 (11.1)  | 54.8 (12.5)  | 47.4 (10.9)  | <0.001          | <0.001           |
| LDL cholesterol, mg/dl   | 117.4 (26.7) | 117.3 (31.7) | 108.8 (27.6) | 107.3 (29.6) | 0.79            | 0.28             |
| Triglycerides, mg/dl     | 78.8 (37.6)  | 98.1 (74.2)  | 76.1 (36.2)  | 82.5 (49.1)  | 0.007           | 0.04             |

**Kidney Disease**

| Sustained AER ≥30 mg/24 h, % | 7.1          | 5.3          | 3.9          | 4.9          | 0.56            | 0.39             |

**Glycemic Control**

| HbA1c, % | 9.2 (1.7) | 9.0 (1.6) | 9.0 (1.7) | 8.7 (1.5) | 0.60            | <0.001           |
| HbA1c, mmol/mol | 76.7 (18.0) | 75.1 (17.1) | 75.4 (18.0) | 71.2 (16.4) | 0.60            | <0.001           |

To convert 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.
<sup>a</sup> P-value for differences by sex by the Wilcoxon rank-sum test for continuous variables or chi-square test for categorical variables.

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**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<sup>a</sup> |
|----------------------|---------------|-------------|--------------------------------------|
| **Physical**         |               |             |                                      |
| BMI, kg/m<sup>2</sup>| 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<sup>b</sup> | 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.

<sup>a</sup> 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.

<sup>b</sup> Triglyceride values were log transformed.

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

| Time-dependent Covariates    | Any CVD Covariate | Women vs. Men Adjusted for Covariate | MACE Covariate | Women vs. Men Adjusted for Covariate |
|-----------------------------|-------------------|--------------------------------------|----------------|--------------------------------------|
|                             | Hazard Ratio (95% CI) |                                     | Hazard Ratio (95% CI) |                                     |
| Physical                    | -----              | 0.87 (0.68, 1.12)                    | -----          | 0.79 (0.56, 1.10)                    |
| BMI, per 5 kg/m²            | 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.

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

| Risk Factor Targets         | Women      | Men      | Any CVD     | MACE       |
|-----------------------------|------------|----------|-------------|------------|
|                             |            |          | Hazard Ratio (95% CI) | Hazard Ratio (95% CI) |
| 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)   |

*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.*
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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