**SUPPLEMENTAL MATERIALS:**

**Supplemental Material Table 1. Assessment of Potential Selection Bias in KEEPS Continuation Study**

| **KEEPS Measure** | **N** | **Non-participants (n=37)** | **Participants (n=76)** | **P-value** |
| --- | --- | --- | --- | --- |
| *Randomized treatment group* | 113 |  |  | 0.019 |
| . Placebo |  | 7 (18.9%) | 33 (43.4%) |  |
| . Transdermal E2 |  | 12 (32.4%) | 23 (30.3%) |  |
| . Oral CEE |  | 18 (48.6%) | 20 (26.3%) |  |
| *Baseline (year 0) measurements* |  |  |  |  |
| Age (years)^ | 113 | 53.1 (51.9, 54.6) | 53.3 (51.8, 54.7) | 0.907 |
| Menopausal age (months, at randomization)^ | 113 | 18.0 (9.6, 25.0) | 18.8 (12.0, 27.6) | 0.720 |
| BMI (kg/m2)^ | 113 | 26.9 (25.1, 30.7) | 25.9 (24.3, 30.8) | 0.607 |
| Waist Circumference (cm)^ | 110 | 85.0 (77.0, 91.0) | 83.0 (75.0, 92.0) | 0.502 |
| Average systolic blood pressure (mm Hg)^ | 113 | 126.0 (116.0, 139.0) | 120.0 (110.3, 128.0) | 0.018 |
| Average diastolic blood pressure (mm Hg)^ | 113 | 78.5 (72.5, 83.0) | 74.8 (70.0, 80.0) | 0.151 |
| Total cholesterol (mg/dL)^ | 111 | 218.0 (209.0, 246.0) | 217.5 (194.5, 237.5) | 0.244 |
| HDL cholesterol (mg/dL)^ | 111 | 59.0 (47.0, 73.0) | 61.0 (51.0, 69.5) | 0.509 |
| LDL cholesterol (mg/dL)^ | 111 | 141.0 (123.8, 157.0) | 136.4 (116.6, 154.6) | 0.272 |
| Triglycerides (mg/dL)^ | 111 | 89.0 (74.0, 148.0) | 83.0 (61.5, 113.5) | 0.179 |
| Fasting blood glucose (mg/dL)^ | 111 | 92.0 (87.0, 97.0) | 92.0 (87.0, 98.0) | 0.638 |
| Coronary artery calcification (Agatston Units)\* | 113 | 1.9 [0.0, 31.6] | 0.9 [0.0, 30.2] | 0.070 |
| CIMT (mm)^ | 113 | 0.67 (0.62, 0.73) | 0.65 (0.62, 0.73) | 0.474 |
| *End-of-trial (year 4) measurements* |  |  |  |  |
| BMI (kg/m2)^ | 102 | 27.8 (24.0, 29.9) | 27.0 (24.2, 31.7) | 0.851 |
| Waist Circumference (cm)^ | 96 | 89.5 (78.8, 96.5) | 87.8 (81.3, 96.0) | 0.892 |
| Average systolic blood pressure (mm Hg)^ | 102 | 123.0 (117.0, 133.0) | 116.5 (109.0, 125.0) | 0.042 |
| Average diastolic blood pressure (mm Hg)^ | 102 | 78.5 (69.0, 85.0) | 74.5 (68.0, 80.5) | 0.128 |
| Total cholesterol (mg/dL)^ | 100 | 205.0 (187.0, 235.0) | 213.0 (196.0, 232.0) | 0.406 |
| HDL cholesterol (mg/dL)^ | 100 | 48.0 (39.0, 56.0) | 57.0 (48.0, 64.0) | 0.020 |
| LDL cholesterol (mg/dL)^ | 100 | 133.6 (110.2, 159.2) | 136.4 (117.6, 154.0) | 0.809 |
| Triglycerides (mg/dL)^ | 100 | 102.0 (78.0, 148.0) | 100.0 (72.0, 118.0) | 0.576 |
| Coronary artery calcification (Agatston Units)\* | 107 | 3.9 [0.0, 39.3] | 3.3 [0.0, 67.6] | 0.335 |
| CIMT (mm)^ | 109 | 0.69 (0.63, 0.76) | 0.69 (0.64, 0.75) | 0.678 |

\* Median [minimum, maximum]; *P* from Wilcoxon rank sum test

^ Median (25th, 75th percentiles); *P* from Wilcoxon rank sum test

Abbreviations: HDL, high density lipoprotein; LDL, low density lipoprotein

**Supplemental Table 2. Changes in CIMT values by group with inclusion of 37 non-participants (N=113 for BL to 4y Trends)**

| **Measurement** | **Overall** | **Placebo** | **Transdermal E2** | **Oral CEE** | ***P*** + |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |
| **CIMT from Basline to 4 yr** | *N=113* | *N=40* | *N=35* | *N=38* | *0.416* |
| . Baseline value (mean±SD), mm | 0.677±0.080 | 0.679±0.072 | 0.684±0.084 | 0.668±0.084 |  |
| . Follow-up value (mean±SD), mm | 0.701±0.094 | 0.705±0.095 | 0.715±0.104 | 0.685±0.088 |  |
| *. Absolute change (95% CI), mm* | 0.024 (0.016, 0.032)\* | 0.025 (0.012, 0.039)\* | *0.030 (0.016, 0.045)\** | *0.017 (0.003, 0.031)\** |  |
| ***. Annual change (95% CI), mm*** | ***0.006 (0.004, 0.008)\**** | ***0.006 (0.003, 0.010)\**** | ***0.008 (0.004, 0.011)\**** | ***0.004 (0.001, 0.008)\**** |  |
|  |  |  |  |  |  |
| **CIMT from 4 to 7 yr** | *N=74* | *N=31* | *N=23* | *N=20* | *0.524* |
| . Year 4 value (mean±SD), mm | 0.699±0.093 | 0.705±0.095 | 0.706±0.097 | 0.680±0.087 |  |
| . Follow-up value (mean±SD) , mm | 0.736±0.095 | 0.748±0.096 | 0.739±0.099 | 0.715±0.093 |  |
| *. Absolute change (95% CI), mm* | *0.038 (0.029, 0.046)\** | *0.043 (0.030, 0.057)\** | *0.033 (0.018, 0.048)\** | *0.034 (0.017, 0.050)\** |  |
| ***. Annual change (95% CI), mm*** | ***0.013 (0.010, 0.015)\* ^*** | ***0.014 (0.010, 0.019)\**** | ***0.011 (0.006, 0.016)\**** | ***0.012 (0.006, 0.017)\* ^*** |  |
|  |  |  |  |  |  |
| **CIMT from Baseline to 7 yr** | *N=76* | *N=33* | *N=23* | *N=20* | *0.085* |
| . Baseline value, mm | 0.672±0.075 | 0.671±0.073 | 0.672±0.077 | 0.672±0.078 |  |
| . Follow-up value, mm | 0.733±0.099 | 0.744±0.100 | 0.738±0.102 | 0.708±0.093 |  |
| *. Absolute change (95% CI), mm* | *0.061 (0.048, 0.075)\** | *0.073 (0.053, 0.093)\** | *0.066 (0.042, 0.090)\** | *0.036 (0.011, 0.062)\** |  |
| ***. Annual change (95% CI), mm*** | ***0.009 (0.007, 0.011)\**** | ***0.010 (0.008, 0.013)\**** | ***0.009 (0.006, 0.013)\**** | ***0.005 (0.002, 0.009)\**** |  |
|  |  |  |  |  |  |

+ *P*-value from ANCOVA model to assess change in CIMT across treatments after adjustment for baseline CIMT; for this two-stage derived variable analysis was performed using a slope from fitting each participant’s data with a linear regression model.

\* Within-person change from baseline to 4 or 7 years, and from 4 to 7 years, were all significant, except for the change at 4 years in the Oral CEE group.

^ Wilcoxon signed-rank test demonstrated that annual change during the 4 to 7-year interval was significantly greater than that during baseline to 4 years.

Abbreviations: BL, baseline prior to randomization.

**Trends in CIMT with Inclusion of 37 Non-Participants (N=113 for BL to 4y Trends)**

