**ONLINE RESOURCES**

**Vitamin E homologues α - and γ-tocopherol are not associated with bone turnover markers or bone mineral density in perimenopausal and postmenopausal women**

TC Yang • GG Duthie • LS Aucott • HM Macdonald

**Corresponding Author:** Tiffany C Yang, PhD, MPH, RD

Natural Products Group

Rowett Institute of Nutrition and Health, University of Aberdeen

Aberdeen AB21 9SB, United Kingdom

Telephone: +44 (0) 1224 438402

Email: tcyang@abdn.ac.uk

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Online Resource 1. Factor loadings for the three retained factors from PCA on inflammatory markers. Only factor loadings >0.3 are shown.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Factor1 | Factor2 | Factor3 |
| SAA | 0.91842 | . | . |
| hs-CRP | 0.68856 | 0.41807 | . |
| IL-6 | . | 0.94916 | . |
| E-selectin | . | . | 0.98959 |

hs-CRP= high sensitivity C-reactive protein; IL-6= interleukin-6; SAA=serum amyloid A

Online Resource 2. Main sources of dietary α- and γ-tocopherol from visits 2 and 3 as a percentage of total α- and γ-tocopherol intake.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | % Total Intake | | | |
|  | Visit 2 | | Visit 3 | |
|  | α-tocopherol | γ-tocopherol | α-tocopherol | γ-tocopherol |
| Fats and Oils | 30 | 26 | 20 | 19 |
| Biscuits, Cakes, Puddings, Sweets | 12 | 29 | 11 | 29 |
| Cereals | 5 | 7 | 21 | 14 |
| Sauces and Condiments | 1 | 10 | 1 | 9 |
| Savoury Snacks | 7 | 5 | 6 | 6 |
| Vegetables | 12 | 2 | 11 | 2 |
| Fruits | 6 | 1 | 6 | 2 |
| Bread | 4 | 6 | 3 | 6 |

Online Resource 3. Spearman correlations between dietary intake at Visit 3 with serum tocopherol concentrations and Visit 2 dietary intake.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | Visit 3 dietary intake | | | |
|  |  | α-tocopherol (mg/day)1 | | γ-tocopherol (mg/day)1 | |
|  | N | Total | Vitamin E supplement non-users3 | Total | Vitamin E supplement non-users3 |
| Visit 2 dietary intake |  |  |  |  |  |
| α-tocopherol (mg/day)1 | 1547 | 0.461 | - | 0.408 | - |
| *p-*value |  | <.0001 | - | <.0001 | - |
| γ-tocopherol (mg/day)1 | 1547 | 0.402 | - | 0.471 | - |
| *p-*value |  | <.0001 | - | <.0001 | - |
| Visit 3 serum |  |  |  |  |  |
| α-tocopherol (µmol/L) |  |  |  |  |  |
| Unadjusted | 1604 | 0.001 | 0.007 | 0.003 | 0.009 |
| *p-*value |  | 0.98 | 0.77 | 0.90 | 0.73 |
| Adjusted2 |  | 0.025 | 0.033 | 0.016 | 0.022 |
| *p-*value |  | 0.31 | 0.19 | 0.52 | 0.37 |
| γ-tocopherol (µmol/L) |  |  |  |  |  |
| Unadjusted | 1604 | -0.040 | -0.047 | -0.028 | -0.034 |
| *p-*value |  | 0.11 | 0.06 | 0.25 | 0.17 |
| Adjusted2 |  | -0.034 | -0.041 | -0.025 | -0.031 |
| *p-*value |  | 0.18 | 0.10 | 0.32 | 0.22 |
| α:γ tocopherol ratio (µmol/L) |  |  |  |  |  |
| Unadjusted | 1604 | 0.027 | 0.035 | 0.026 | 0.032 |
| *p-*value |  | 0.29 | 0.16 | 0.30 | 0.20 |
| Adjusted2 |  | 0.035 | 0.043 | 0.031 | 0.038 |
| *p-*value |  | 0.17 | 0.09 | 0.22 | 0.14 |
| 1tocopherol residual |  |  |  |  |  |
| 2adjusted for cholesterol |  |  |  |  |  |
| 3N= 1591 tocopherol residual with unadjusted serum tocopherols, N=1581 tocopherol residual with adjustment for serum cholesterol | | | | | |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Online Resource 4. Covariates and outcomes in relation to quartiles of serum α- and γ-tocopherol. | | | | | | | | | | | | | | | | | | | | |
|  | α-tocopherol | | | | | | | |  | |  | γ-tocopherol | | | | | | | |  |
| Range (µmol/L): | Quartile 1 ≤ 10.29 | | Quartile 2 10.29 to 12.41 | | Quartile 3 12.41 to 15.09 | | Quartile 4 > 15.09 | |  |  | | Quartile 1 ≤ 0.51 | | Quartile 2 0.51 to 0.67 | | Quartile 3 0.67 to 0.87 | | Quartile 4 > 0.87 | |  |
|  | N | Mean(SD) | N | Mean(SD) | N | Mean(SD) | N | Mean(SD) | *P-*trend | |  | N | Mean(SD) | N | Mean(SD) | N | Mean(SD) | N | Mean(SD) | *P-*trend |
| Age (years) | 507 | 65.8 (2.3) | 507 | 66.0 (2.1) | 508 | 66.2 (2.2) | 507 | 66.2 (2.0) | 0.002 | |  | 507 | 65.9 (2.2) | 507 | 65.9 (2.1) | 508 | 66.3 (2.2) | 507 | 65.9 (2.1) | 0.52 |
| BMI (kg/m2) | 505 | 28.6 (5.5) | 505 | 28.1 (4.8) | 505 | 27.6 (4.8) | 507 | 27.2 (4.2) | <0.0001 | |  | 506 | 26.7 (4.6) | 502 | 27.7 (5.0) | 507 | 27.8 (4.9) | 507 | 29.2 (4.7) | <0.0001 |
| Energy intake (kcal/day) | 399 | 2459 (307) | 399 | 2472 (301) | 404 | 2463 (308) | 402 | 2497 (300) | 0.1 | |  | 416 | 2477 (315) | 404 | 2456 (298) | 401 | 2483 (296) | 383 | 2474 (307) | 0.75 |
| Physical activity level | 399 | 1.7 (0.2) | 399 | 1.7 (0.2) | 404 | 1.7 (0.2) | 402 | 1.7 (0.2) | 0.1 | |  | 416 | 1.7 (0.2) | 404 | 1.7 (0.2) | 401 | 1.7 (0.2) | 383 | 1.7 (0.2) | 0.76 |
| Plasma cholesterol total (mmol/L) | 399 | 1.4 (3.3) | 399 | 1.4 (3.0) | 404 | 1.8 (3.9) | 402 | 1.6 (3.5) | <0.0001 | |  | 416 | 1.4 (3.0) | 404 | 1.4 (3.1) | 401 | 1.7 (4.1) | 383 | 1.8 (3.5) | <0.0001 |
| Alcohol consumption (g/day) | 505 | 4.9 (0.9) | 500 | 5.5 (0.9) | 501 | 5.8 (0.9) | 504 | 6.4 (1.0) | 0.12 | |  | 503 | 5.3 (1.0) | 503 | 5.6 (1.1) | 502 | 5.7 (1.1) | 502 | 6.0 (1.1) | 0.52 |
| Serum α-tocopherol (µmol/L) |  |  |  |  |  |  |  |  |  | |  | 507 | 11.5 (4.4) | 507 | 12.2 (3.1) | 508 | 13.1 (3.2) | 507 | 14.6 (3.7) | <0.0001 |
| Serum γ-tocopherol (µmol/L) | 507 | 0.6 (0.2) | 507 | 0.7 (0.2) | 508 | 0.8 (0.2) | 507 | 0.9 (0.3) | <0.0001 | |  | - | - | - | - | - | - | - |  |  |
|  | N | Median (IQR) | N | Median (IQR) | N | Median (IQR) | N | Median (IQR) | *P-*trend | |  | N | Median (IQR) | N | Median (IQR) | N | Median (IQR) | N | Median (IQR) | *P-*trend |
| L1-L4 LS BMD (g/cm2) | 495 | 1.1 (0.2) | 502 | 1.1 (0.1) | 500 | 1.1 (0.2) | 502 | 1.1 (0.1) | 0.92 | |  | 496 | 1.1 (0.1) | 497 | 1.1 (0.2) | 505 | 1.1 (0.2) | 501 | 1.1 (0.2) | 0.11 |
| FN BMD (g/cm2) | 479 | 0.9 (0.1) | 475 | 0.9 (0.1) | 484 | 0.9 (0.1) | 489 | 0.9 (0.1) | 0.07 | |  | 480 | 0.9 (0.1) | 485 | 0.9 (0.1) | 478 | 0.9 (0.1) | 484 | 0.9 (0.1) | <0.0001 |
| hs-CRP (mg/L) | 505 | 4.3 (11.2) | 500 | 3.1 (4.5) | 501 | 3.1 (4.9) | 504 | 2.9 (5.5) | 0.005 | |  | 503 | 3.1 (9.4) | 503 | 3.5 (8.4) | 502 | 3.3 (5.1) | 502 | 3.4 (4.0) | <0.0001 |
| IL-6 (ng/mL) | 507 | 2.3 (1.7) | 507 | 2.0 (1.6) | 508 | 1.9 (1.9) | 507 | 1.7 (1.7) | <0.0001 | |  | 507 | 1.9 (1.7) | 507 | 2.0 (1.6) | 508 | 2.0 (1.8) | 507 | 2.1 (1.9) | 0.09 |
| SAA (mg/L) | 507 | 50.7 (38.2) | 507 | 47.5 (35.7) | 508 | 44.6 (36.3) | 507 | 47.3 (33.3) | 0.12 | |  | 507 | 43.0 (34.6) | 507 | 46.6 (36.3) | 508 | 47.9 (35.7) | 507 | 52.5 (36.5) | <0.0001 |
| E-selectin (ng/mL) | 504 | 40.2 (15.6) | 503 | 38.5 (14.4) | 502 | 38.4 (15.0) | 504 | 39.2 (14.3) | 0.43 | |  | 505 | 36.3 (14.3) | 503 | 38.7 (14.1) | 505 | 38.8 (14.6) | 500 | 42.5 (15.9) | <0.0001 |
|  | N | Mean (SD)/% | N | Mean (SD)/% | N | Mean (SD)/% | N | Mean (SD)/% | *P-*value | |  | N | Mean (SD)/% | N | Mean (SD)/% | N | Mean (SD)/% | N | Mean (SD)/% | *P-*value |
| Vitamin E supplementation\* |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| Yes | 1 | 12.7 (2.2) | 0 | 16.2 (0.3) | 2 | 23.2 (3.6) | 10 | 28.1 (1.1) | <0.0001 | |  | 10 | 0.1 (0.02) | 1 | 0.2 (0.02) | 0 | 0.3 (0.02) | 2 | 0.8 (0.2) | <0.0001 |
| No | 506 | 8.5 (1.6) | 507 | 11.4 (0.6) | 506 | 13.6 (0.7) | 497 | 17.8 (2.7) |  | |  | 497 | 0.4 (0.1) | 506 | 0.6 (0.05) | 508 | 0.8 (0.1) | 505 | 1.1 (0.2) |  |
| Smoking status |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| Current | 64 | 12.7 | 46 | 9.2 | 39 | 7.7 | 3 | 6.7 | 0.0065 | |  | 56 | 11.1 | 41 | 8.1 | 50 | 9.9 | 36 | 7.1 | 0.12 |
| Non-smoker | 438 | 87.3 | 456 | 90.8 | 468 | 92.3 | 472 | 93.3 |  | |  | 448 | 88.9 | 463 | 91.9 | 455 | 90.1 | 468 | 92.9 |  |
| National Deprivation Category |  |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |
| 1 | 126 | 24.9 | 124 | 24.6 | 136 | 27 | 154 | 30.5 | 0.1 | |  | 140 | 27.7 | 120 | 23.8 | 135 | 26.8 | 145 | 28.7 | 0.62 |
| 2 | 206 | 40.7 | 220 | 43.7 | 228 | 45.3 | 208 | 41.1 |  | |  | 208 | 41.2 | 227 | 45 | 219 | 43.4 | 208 | 41.2 |  |
| 3 | 43 | 8.5 | 40 | 7.9 | 41 | 8.2 | 37 | 7.3 |  | |  | 37 | 7.3 | 42 | 8.3 | 39 | 7.7 | 43 | 8.5 |  |
| 4 | 79 | 15.6 | 66 | 13.1 | 62 | 12.3 | 69 | 13.6 |  | |  | 69 | 13.7 | 67 | 13.2 | 75 | 14.9 | 65 | 12.9 |  |
| 5 | 34 | 6.7 | 47 | 9.3 | 27 | 5.4 | 29 | 5.7 |  | |  | 34 | 6.7 | 41 | 8.1 | 28 | 5.6 | 34 | 6.7 |  |
| 6 | 18 | 3.6 | 7 | 1.4 | 9 | 1.8 | 9 | 1.8 |  | |  | 17 | 3.4 | 8 | 1.6 | 8 | 1.6 | 10 | 2 |  |
| BMD=bone mineral density; LS=lumbar spine; FN=femoral neckhs-CRP=high sensitivity C-reactive protein; IL-6=interleukin-6; SAA=serum amyloid A; fDPD/Cr=free deoxypyridoline expressed relative to creatinine; fPYD/Cr=free pyridinoline expressed relative to creatinine; P1NP=N-terminal propeptide of type 1 collagen; National Deprivation Category 1 indicates most affluent/least deprived. | | | | | | | | | | | | | | | | | | | | |
| \*N denotes number of individuals taking/not taking vitamin supplements in each quartile of serum tocopherol concentrations amongst all participants. Corresponding mean(SD) values indicate the serum tocopherol concentration in individuals who take/don't take vitamin E supplements. | | | | | | | | | | | | | | | | | | | | |
| *P*-trend using orthogonal contrasts with log-transformed variables. | | | | | | | | | | | | | | | | | | | |  |
| *P*-values from Chi-squared or Fisher's exact tests. | | | | | |  |  |  |  | |  |  |  |  |  |  |  |  |  |  |