**Supplemental Table 1.** Serum metabolites significantly altered at the Bonferroni correction threshold in response to alpha-tocopheryl acetate (ATA) supplementation in VEAPS and ATBC following multivariable adjustment

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Metabolite** | **VEAPS (n=154)**  **(ATA, 400 IU/day)** | | | **ATBC (n=100)**  **(ATA, 50 IU/day)** | | |
| Effect size (β) a | Standard error | P value | Effect size (β) a | Standard error | P value |
| Alpha-CEHC sulfate | 1.60 | 0.10 | 1.7 × 10-33 | 1.50 | 0.15 | 4.2 × 10-16 |
| Beta-tocopherol and gamma-tocopherol | -1.34 | 0.13 | 5.4 × 10-20 | -1.02 | 0.18 | 4.0 × 10-7 |
| Alpha-tocopherol | 1.06 | 0.15 | 1.9 × 10-11 | 0.96 | 0.19 | 1.8 × 10-6 |
| C22 lactone sulfate | -0.74 | 0.16 | 5.6 × 10-6 | -0.19 | 0.23 | 0.4 |

Abbreviations: ATA = alpha-tocopheryl acetate; ATBC = Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study; IU = International Units; VEAPS = Vitamin E Atherosclerosis Prevention Study

aThe effect size indicates the change in log-metabolite concentration for the ATA arm versus no ATA arm. Linear regression models were used to estimate the effect size and P value, adjusted for age, height, weight, smoking status, smoking years, serum high-density- and total- lipoprotein cholesterol, and alcohol consumption.

**Supplemental Table 2.** Serum metabolites significantly altered at the Bonferroni correction threshold in response to alpha-tocopheryl acetate (ATA) supplementation for ATBC participants having on-study serum collected within the first 1000 days of supplementation

|  |  |  |  |
| --- | --- | --- | --- |
| **Metabolite** | **ATBC (n=62)**  **(ATA, 50 IU/day)** | | |
| Effect size (β) a | Standard error | P value |
| Alpha-CEHC sulfate | 1.46 | 0.19 | 1.1 × 10-10 |
| Beta-tocopherol and gamma-tocopherol | -0.72 | 0.16 | 2.1 × 10-5 |
| Alpha-tocopherol | 0.89 | 0.20 | 4.0 × 10-5 |
| C22 lactone sulfate | -0.11 | 0.23 | 0.63 |

Abbreviations: ATA = alpha-tocopheryl acetate; ATBC = Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study; IU = International Units; VEAPS = Vitamin E Atherosclerosis Prevention Study

aThe effect size indicates the change in log-metabolite concentration for the ATA arm versus no ATA arm. Linear regression models were used to estimate the effect size and P value.