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| **Supplementary Table 1.** Mean level of biomarkers of bacterial translocation according to selected characteristics among controls in a nested case-control study of the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) cohort | | | | | | | | | | | |
|  | **anti-flagellin** | |  |  | **anti-LPS** |  |  |  | **LBP** |  | **sCD14** |
|  | **IgA** | **IgG** | **IgM** |  | **IgA** | **IgG** | **IgM** |  |  |  |  |
|  | **Mean (SD)** | **Mean (SD)** | **Mean (SD)** |  | **Mean (SD)** | **Mean (SD)** | **Mean (SD)** |  | **Mean (SD)** |  | **Mean (SD)** |
| **Age at randomization** |  |  |  |  |  |  |  |  |  |  |  |
| ≤54 | 1.28 (0.47) | 1.37 (0.32) | 3.15 (0.26) |  | 1.33 (0.47) | 1.65 (0.46) | 2.42 (0.52) |  | 0.74 (0.24) |  | 0.61 (0.01) |
| 55 - 59 | 1.30 (0.47) | 1.28 (0.29) | 3.03 (0.46) |  | 1.31 (0.47) | 1.53 (0.45) | 2.45 (0.56) |  | 0.73 (0.24) |  | 0.62 (0.10) |
| 60 - 64 | 1.40 (0.48) | 1.33 (0.27) | 3.07 (0.41) |  | 1.37 (0.43) | 1.61 (0.42) | 2.49 (0.58) |  | 0.78 (0.25) |  | 0.62 (0.10) |
| ≥65 | 1.60 (0.51) | 1.41 (0.48) | 3.06 (0.38) |  | 1.60 (0.59) | 1.81 (0.61) | 2.49 (0.78) |  | 0.70 (0.26) |  | 0.62 (0.12) |
| *ptrend* | *0.11* | *0.21* | *0.32* |  | *0.20* | *0.12* | *0.92* |  | *0.58* |  | *0.87* |
| **Body mass index (kg/m2)** |  |  |  |  |  |  |  |  |  |  |  |
| <25.0 | 1.30 (0.50) | 1.29 (0.32) | 3.08 (0.39) |  | 1.34 (0.56) | 1.58 (0.55) | 2.49 (0.54) |  | 0.73 (0.22) |  | 0.61 (0.10) |
| 25.0 - <30.0 | 1.35 (0.44) | 1.36 (0.30) | 3.12 (0.30) |  | 1.34 (0.39) | 1.58 (0.41) | 2.49 (0.55) |  | 0.73 (0.26) |  | 0.63 (0.10) |
| ≥30.0 | 1.43 (0.57) | 1.33 (0.33) | 2.90 (0.62) |  | 1.36 (0.45) | 1.61 (0.40) | 2.24 (0.63) |  | 0.78 (0.21) |  | 0.61 (0.09) |
| *ptrend* | *0.43* | *0.25* | *0.03* |  | *0.98* | *0.94* | *0.08* |  | *0.53* |  | *0.47* |
| **Education1** |  |  |  |  |  |  |  |  |  |  |  |
| 1 | 1.29 (0.42) | 1.34 (0.33) | 3.10 (0.36) |  | 1.26 (0.43) | 1.53 (0.45) | 2.50 (0.53) |  | 0.73 (0.22) |  | 0.62 (0.11 ) |
| 2 | 1.37 (0.50) | 1.32 (0.32) | 3.02 (0.44) |  | 1.34 (0.48) | 1.58 (0.48) | 2.37 (0.60) |  | 0.73 (0.27) |  | 0.61 (0.09) |
| 3 | 1.36 (0.53) | 1.33 (0.28) | 3.16 (0.35) |  | 1.47 (0.49) | 1.68 (0.46) | 2.56 (0.50) |  | 0.78 (0.21) |  | 0.64 (0.10) |
| *ptrend* | *0.56* | *0.90* | *0.11* |  | *0.06* | *0.24* | *0.11* |  | *0.42* |  | *0.12* |
| **Cigarette smoking (pack-years)** | |  |  |  |  |  |  |  |  |  |  |
| >0 - 24 | 1.36 (0.48) | 1.33 (0.33) | 3.09 (0.37) |  | 1.37 (0.51) | 1.57 (0.55) | 2.53 (0.57) |  | 0.70 (0.21) |  | 0.61 (0.10) |
| 25 - 34 | 1.25 (0.42) | 1.29 (0.35) | 3.11 (0.34) |  | 1.26 (0.44) | 1.56 (0.47) | 2.43 (0.56) |  | 0.73 (0.24) |  | 0.61 (0.08) |
| 35 - 44 | 1.35 (0.55) | 1.34 (0.27) | 3.06 (0.35) |  | 1.37 (0.47) | 1.66 (0.42) | 2.43 (0.57) |  | 0.72 (0.30) |  | 0.62 (0.10) |
| ≥45 | 1.39 (0.47) | 1.35 (0.30) | 3.03 (0.54) |  | 1.35 (0.44) | 1.55 (0.38) | 2.39 (0.55) |  | 0.82 (0.21) |  | 0.64 (0.10) |
| *ptrend* | *0.44* | *0.72* | *0.77* |  | *0.50* | *0.63* | *0.58* |  | *0.04* |  | *0.19* |
| **Drinks of alcohol (per day)** |  |  |  |  |  |  |  |  |  |  |  |
| 0 | 1.57 (0.46) | 1.35 (0.37) | 2.83 (0.50) |  | 1.48 (0.58) | 1.49 (0.55) | 2.09 (0.73) |  | 0.73 (0.23) |  | 0.56 (0.09) |
| >0 - <1.0 | 1.29 (0.43) | 1.31 (0.33) | 3.10 (0.41) |  | 1.28 (0.45) | 1.56 (0.48) | 2.53 (0.56) |  | 0.73 (0.23) |  | 0.61 (0.09) |
| 1.0 - <2.0 | 1.36 (0.54) | 1.34 (0.29) | 3.08 (0.35) |  | 1.35 (0.44) | 1.63 (0.49) | 2.44 (0.49) |  | 0.74 (0.26) |  | 0.63 (0.10) |
| ≥2.0 | 1.38 (0.52) | 1.33 (0.25) | 3.11 (0.30) |  | 1.48 (0.51) | 1.58 (0.40) | 2.39 (0.59) |  | 0.78 (0.27) |  | 0.64 (0.10) |
| *ptrend* | *0.17* | *0.94* | *0.09* |  | *0.08* | *0.73* | *0.04* |  | *0.66* |  | *0.02* |
| **Coffee consumption (g/day)** |  |  |  |  |  |  |  |  |  |  |  |
| 0 - <200 | 1.40 (0.48) | 1.35 (0.29) | 3.11 (0.38) |  | 1.27 (0.35) | 1.45 (0.41) | 2.48 (0.64) |  | 0.77 (0.19) |  | 0.62 (0.08) |
| 200 - <500 | 1.40 (0.43) | 1.33 (0.29) | 3.08 (0.36) |  | 1.39 (0.44) | 1.58 (0.46) | 2.41 (0.56) |  | 0.73 (0.24) |  | 0.62 (0.11) |
| 500 - <1000 | 1.29 (0.51) | 1.30 (0.34) | 3.07 (0.43) |  | 1.35 (0.53) | 1.59 (0.52) | 2.49 (0.59) |  | 0.74 (0.25) |  | 0.62 (0.10) |
| ≥1000 | 1.32 (0.53) | 1.35 (0.28) | 3.07 (0.36) |  | 1.24 (0.42) | 1.57 (0.40) | 2.44 (0.53) |  | 0.76 (0.25) |  | 0.61 (0.08) |
| *ptrend* | *0.49* | *0.87* | *0.99* |  | *0.42* | *0.80* | *0.83* |  | *0.90* |  | *0.97* |
| Abbreviations: Ig, immunoglobulin; LBP, lipopolysaccharide-binding protein; LPS, lipopolysaccharide; sCD14, soluble CD14; SD, standard deviation. | | | | | | | | | | | |
| 1Levels of education: 1) elementary school or less, no vocation training; 2) elementary school or less, vocational training; 3) more than elementary school | | | | | | | | | | | |

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| **Supplementary Table 2.**  Associations between biomarkers of bacterial translocation and risk of hepatocellular carcinoma in a nested case-control study of the Alpha-tocopherol Beta-Carotene Cancer Prevention (ATBC) cohort | | | | |
|  | **Cases** | **Controls** | **Minimally-adjusted1** | **Multivariable-adjusted2** |
|  | **N** | **N** | **OR (95% CI)** | **OR (95% CI)** |
| **anti-flagellin IgA** |  |  |  |  |
| Quartile 1 | 28 | 42 | 1.00 (ref) | 1.00 (ref) |
| Quartile 2 | 28 | 37 | 1.17 (0.58, 2.40) | 1.23 (0.52, 2.92) |
| Quartile 3 | 40 | 39 | 1.81 (0.91, 3.60) | 1.43 (0.67, 3.05) |
| Quartile 4 | 60 | 37 | 4.79 (2.03, 11.31) | 4.18 (1.60, 10.92) |
| *ptrend* |  |  | *<0.01* | *<0.01* |
| **anti-flagellin IgG** |  |  |  |  |
| Quartile 1 | 41 | 38 | 1.00 (ref) | 1.00 (ref) |
| Quartile 2 | 32 | 43 | 0.71 (0.38, 1.31) | 0.64 (0.31, 1.31) |
| Quartile 3 | 35 | 39 | 0.86 (0.45, 1.67) | 0.87 (0.41, 1.87) |
| Quartile 4 | 48 | 35 | 1.78 (0.82, 3.87) | 1.95 (0.79, 4.86) |
| *ptrend* |  |  | *0.33* | *0.19* |
| **anti-flagellin IgM** |  |  |  |  |
| Quartile 1 | 46 | 39 | 1.00 (ref) | 1.00 (ref) |
| Quartile 2 | 42 | 36 | 0.9 (0.48, 1.66) | 0.83 (0.40, 1.70) |
| Quartile 3 | 30 | 38 | 0.63 (0.31, 1.26) | 0.57 (0.24, 1.34) |
| Quartile 4 | 39 | 42 | 0.77 (0.41, 1.41) | 0.86 (0.42, 1.75) |
| *ptrend* |  |  | *0.89* | *0.95* |
| **anti-LPS IgA** |  |  |  |  |
| Quartile 1 | 31 | 43 | 1.00 (ref) | 1.00 (ref) |
| Quartile 2 | 25 | 38 | 0.83 (0.42, 1.64) | 0.76 (0.35, 1.67) |
| Quartile 3 | 26 | 37 | 1.02 (0.53, 1.97) | 0.77 (0.36, 1.66) |
| Quartile 4 | 75 | 37 | 3.18 (1.65, 6.12) | 2.48 (1.16, 5.29) |
| *ptrend* |  |  | *<0.01* | *<0.01* |
| **anti-LPS IgG** |  |  |  |  |
| Quartile 1 | 41 | 37 | 1.00 (ref) | 1.00 (ref) |
| Quartile 2 | 25 | 44 | 0.53 (0.27, 1.03) | 0.5 (0.23, 1.09) |
| Quartile 3 | 35 | 42 | 0.88 (0.46, 1.71) | 0.74 (0.34, 1.60) |
| Quartile 4 | 55 | 32 | 1.66 (0.84, 3.25) | 1.21 (0.55, 2.69) |
| *ptrend* |  |  | *0.11* | *0.64* |
| **anti-LPS IgM** |  |  |  |  |
| Quartile 1 | 38 | 38 | 1.00 (ref) | 1.00 (ref) |
| Quartile 2 | 45 | 39 | 1.17 (0.60, 2.30) | 1.1 (0.51, 2.36) |
| Quartile 3 | 30 | 39 | 0.73 (0.35, 1.49) | 0.73 (0.31, 1.72) |
| Quartile 4 | 44 | 39 | 1.16 (0.54, 2.48) | 1.3 (0.55, 3.09) |
| *ptrend* |  |  | *0.98* | *0.69* |
| **LBP** |  |  |  |  |
| Quartile 1 | 41 | 39 | 1.00 (ref) | 1.00 (ref) |
| Quartile 2 | 40 | 42 | 0.91 (0.49, 1.68) | 1.06 (0.49, 2.28) |
| Quartile 3 | 27 | 41 | 1.00 (0.49, 2.02) | 0.92 (0.40, 2.14) |
| Quartile 4 | 49 | 34 | 1.57 (0.79, 3.14) | 1.25 (0.55, 2.87) |
| *ptrend* |  |  | *0.21* | *0.65* |
| **sCD14** |  |  |  |  |
| Quartile 1 | 46 | 36 | 1.00 (ref) | 1.00 (ref) |
| Quartile 2 | 26 | 43 | 0.70 (0.37, 1.30) | 0.60 (0.28, 1.27) |
| Quartile 3 | 37 | 38 | 0.87 (0.46, 1.65) | 0.59 (0.26, 1.30) |
| Quartile 4 | 48 | 39 | 1.21 (0.62, 2.36) | 1.11 (0.50, 2.50) |
| *ptrend* |  |  | *0.77* | *0.34* |
| 1Accounting for matching factors only (age at randomization assignment and date of blood collection) | | | | |
| 2Accounting for matching factors (age at randomization assignment and date of blood collection), and additionally adjusted for body mass index, education, smoking intensity, alcohol intake, and history of diabetes or hypertension at baseline. | | | | |
| P values for linear trend were calculated using the Wald test, by including the continuous form of each biomarker in the model | | | | |
| Abbreviations: CI, confidence interval; Ig, immunoglobulin; LBP, lipopolysaccharide-binding protein; LPS, lipopolysaccharide; OR, odds ratio; sCD14, soluble CD14. | | | | |