|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Table S4.** Associations of circulating levels of free and total testosterone and SHBG (quartiles) with colon cancer in EPIC and NSHDS separately | | | | | | |
|  | **Tertile 1** | **Tertile 2** | **Tertile 3** | **Ptrend** | **Continuousc** | **Pheterogeneity** |
| **Androstenedione**  **EPIC (n = 926)**  n (case/control)  Multivariable-adjusted OR (95% CI)a  **NSHDS (n = 454)**  n (case/control)  Multivariable-adjusted OR (95% CI)a | 207/204  1.00  34/26  1.00 | 145/159  0.86 (0.61-1.21)  55/71  0.64 (0.34-1.19) | 111/100  1.12 (0.76-1.66)  138/130  0.96 (0.53-1.76) | 0.71  0.58 | 0.92 (0.68-1.24)  1.04 (0.68-1.59) | 0.97 |
| **Dehydroepiandrosterone**  **EPIC (n = 926)**  n (case/control)  Multivariable-adjusted OR (95% CI)a  **NSHDS (n = 454)**  n (case/control)  Multivariable-adjusted OR (95% CI)a | 197/190  1.00  44/40  1.00 | 146/149  0.94 (0.68-1.30)  75/81  0.84 (0.49-1.44) | 120/124  1.02 (0.68-1.50)  108/106  0.96 (0.53-1.72) | 0.98  0.94 | 1.06 (0.88-1.28)  1.01 (0.77-1.34) | 0.84 |
| **Estrone**  **EPIC (n = 926)**  n (case/control)  Multivariable-adjusted OR (95% CI)a  **NSHDS (n = 454)**  n (case/control)  Multivariable-adjusted OR (95% CI)a | 193/202  1.00  24/28  1.00 | 167/169  0.90 (0.64-1.26)    68/59  1.54 (0.79-3.03) | 103/91  1.02 (0.70-1.50)  135/138  1.26 (0.67-2.36) | 1.00  0.98 | 1.13 (0.79-1.60)  1.08 (0.68-1.73) | 0.55 |
| **Estradiol**  **EPIC (n = 926)**  n (case/control)  Multivariable-adjusted OR (95% CI)a  **NSHDS (n = 454)**  n (case/control)  Multivariable-adjusted OR (95% CI)a | 205/208  1.00  27/22  1.00 | 174/166  1.04 (0.75-1.43)  66/64  0.87 (0.41-1.83) | 82/89  0.78 (0.52-1.17)  134/141  0.78 (0.39-1.55) | 0.34  0.43 | 0.79 (0.55-1.13)  0.83 (0.48-1.45) | 0.42 |
| **Progesterone**  **EPIC (n = 926)**  n (case/control)  Multivariable-adjusted OR (95% CI)a  **NSHDS (n = 454)**  n (case/control)  Multivariable-adjusted OR (95% CI)a | 201/190  1.00  45/40  1.00 | 157/152  0.98 (0.71-1.34)  77/78  0.87 (0.47-1.61) | 105/121  0.96 (0.66-1.40)  105/109  0.84 (0.45-1.58) | 0.82  0.65 | 1.05 (0.83-1.31)  1.05 (0.75-1.47) | 0.68 |
| **Testosterone**  **EPIC (n = 926)**  n (case/control)  Multivariable-adjusted OR (95% CI)a  **NSHDS (n = 454)**  n (case/control)  Multivariable-adjusted OR (95% CI)a | 232/194  1.00  52/36  1.00 | 150/161  0.83 (0.59-1.16)  58/69  0.48 (0.24-0.93) | 81/108  0.75 (0.50-1.10)  117/122  0.58 (0.30-1.14) | 0.12  0.35 | 0.64 (0.45-0.91)  0.95 (0.56-1.58) | 0.07 |
| **Free estradiol**  **EPIC (n = 926)**  n (case/control)  Multivariable-adjusted OR (95% CI)a  **NSHDS (n = 454)**  n (case/control)  Multivariable-adjusted OR (95% CI)a | 171/198  1.00  34/32  1.00 | 175/156  1.20 (0.86-1.66)  71/74  0.89 (0.47-1.71) | 109/115  0.98 (0.67-1.43)  122/121  0.87 (0.48-1.58) | 0.92  0.67 | 0.93 (0.64-1.33)  0.95 (0.59-1.55) | 0.33 |
| **Free testosterone**  **EPIC (n = 926)**  n (case/control)  Multivariable-adjusted OR (95% CI)a  **NSHDS (n = 454)**  n (case/control)  Multivariable-adjusted OR (95% CI)a | 210/180  1.00  57/50  1.00 | 140/152  0.78 (0.56-1.09)  56/78  0.65 (0.38-1.11) | 113/131  0.77 (0.52-1.12)  114/99  1.11 (0.64-1.92) | 0.14  0.38 | 0.69 (0.45-1.06)  1.10 (0.59-2.04) | 0.04 |
| **SHBG**  **EPIC (n = 926)**  n (case/control)  Multivariable-adjusted OR (95% CI)a  Multivariable-adjusted OR (95% CI)b  **NSHDS (n = 454)**  n (case/control)  Multivariable-adjusted OR (95% CI)a  Multivariable-adjusted OR (95% CI)b | 237/183  1.00  1.00  48/47  1.00  1.00 | 144/162  0.72 (0.53-1.00)  0.72 (0.51-1.03)  80/68  1.32 (0.74-2.36)  1.56 (0.83-2.92) | 82/118  0.62 (0.41-0.93)  0.60 (0.36-0.98)  99/112  0.98 (0.53-1.82)  1.21 (0.58-2.49) | 0.01  0.03  0.71  0.85 | 0.71 (0.54-0.94)  0.86 (0.58-1.28)  0.82 (0.55-1.23)  0.75 (0.42-1.36) | 0.16 |

Abbreviations: Number of (n), Odds Ratio (OR), Confidence Interval (CI).

aAdjusted for BMI (continuous), smoking status (current, former, never, unknown), physical activity (active, moderately active, moderately inactive, inactive), alcohol consumption (zero, below median, above median).

bAdditionally adjusted for levels of estradiol and testosterone.

cOR per 1-log2 unit increment