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| **Table S2.** Associations of circulating levels of sex hormones and SHBG (quartiles) with colon cancer in EPIC and NSHDS. |
|  | **Quartile 1** | **Quartile 2** | **Quartile 3** | **Quartile 4** | **Ptrend** | **Continuousd** |
| **Androstenedione**Quartile cutpoints, pg/mLn (case/control)Unadjusted model OR (95% CI)Multivariable-adjusted OR (95% CI)aMultivariable-adjusted OR (95% CI)b | ≤ 548.2195/1731.001.001.00 | > 548.2 - 720.8162/1720.82 (0.61-1.11)0.81 (0.59-1.10)0.80 (0.58-1.09) | > 720.8 - 922.7147/1720.74 (0.54-1.03)0.72 (0.52-1.00)0.74 (0.53-1.03) | > 922.7186/1730.94 (0.67-1.31)0.91 (0.64-1.29)0.99 (0.70-1.41) | 0.830.730.87 | 0.98 (0.79-1.22)0.97 (0.78-1.22)1.03 (0.83-1.29) |
| **Dehydroepiandrosterone**Quartile cutpoints, ng/mLn (case/control)Unadjusted model OR (95% CI)Multivariable-adjusted OR (95% CI)aMultivariable-adjusted OR (95% CI)b | ≤ 1.50185/1731.001.001.00 | > 1.50 - 2.34173/1720.93 (0.70-1.25)0.91 (0.68-1.24)0.92 (0.68-1.25) | > 2.34 - 3.47152/1720.81 (0.59-1.12)0.81 (0.58-1.14)0.86 (0.62-1.21) | > 3.47180/1730.95 (0.67-1.33)0.97 (0.68-1.38)1.12 (0.78-1.60) | 0.790.940.45 | 0.99 (0.85-1.14)0.99 (0.86-1.15)1.05 (0.91-1.23) |
| **Estrone**Quartile cutpoints, pg/mLn (case/control)Unadjusted model OR (95% CI)Multivariable-adjusted OR (95% CI)aMultivariable-adjusted OR (95% CI)b | ≤ 22.4169/1721.001.001.00 | > 22.4 - 28.2156/1720.94 (0.69-1.28)0.94 (0.69-1.30)0.91 (0.66-1.26) | > 28.2 - 35.8174/1711.06 (0.78-1.44)1.07 (0.78-1.47)1.02 (0.74-1.41) | > 35.8191/1721.15 (0.83-1.61)1.18 (0.83-1.66)1.10 (0.77-1.56) | 0.270.240.43 | 1.18 (0.92-1.52)1.19 (0.92-1.54)1.13 (0.87-1.47) |
| **Estradiol**Quartile cutpoints, pg/mLn (case/control)Unadjusted model OR (95% CI)Multivariable-adjusted OR (95% CI)aMultivariable-adjusted OR (95% CI)b | ≤ 14.9165/1731.001.001.00 | > 14.9 - 19.1189/1721.16 (0.86-1.57)1.15 (0.85-1.57)1.14 (0.84-1.56) | > 19.1 - 24.1167/1721.01 (0.73-1.39)1.00 (0.72-1.38)0.96 (0.69-1.34) | > 24.1167/1730.99 (0.70-1.41)0.98 (0.68-1.39)0.89 (0.62-1.38) | 0.760.690.36 | 0.83 (0.64-1.09)0.83 (0.63-1.09)0.76 (0.58-1.01) |
| **Progesterone**Quartile cutpoints, pg/mLN (case/control)Unadjusted model OR (95% CI)Multivariable-adjusted OR (95% CI)aMultivariable-adjusted OR (95% CI)b | ≤ 56.1197/1731.001.001.00 | > 56.1 - 78.3175/1720.88 (0.65-1.18)0.89 (0.66-1.20)0.92 (0.68-1.24) | > 78.3 - 112.1160/1720.78 (0.57-1.08)0.82 (0.59-1.13)0.90 (0.65-1.26) | > 112.1158/1730.76 (0.55-1.05)0.79 (0.56-1.10)0.89 (0.64-1.26) | 0.100.170.58 | 0.96 (0.81-1.14)0.98 (0.82-1.17)1.06 (0.89-1.28) |
| **Testosterone**Quartile cutpoints, ng/mLn (case/control)Unadjusted model OR (95% CI)Multivariable-adjusted OR (95% CI)aMultivariable-adjusted OR (95% CI)b | ≤ 3.47211/1731.001.001.00 | > 3.47 - 4.41189/1720.86 (0.65-1.15)0.87 (0.65-1.16)0.92 (0.68-1.24) | > 4.41 - 5.50145/1720.64 (0.47-0.88)0.66 (0.48-0.91) 0.74 (0.53-1.02) | > 5.50145/1730.62 (0.44-0.86)0.63. (0.45-0.89)0.75 (0.53-1.08) | 0.0020.0050.08 | 0.59 (0.45-0.76) 0.60 (0.46-0.78)0.68 (0.51-0.89) |
| **Free estradiol**Quartile cutpoints, pg/mLN (case/control)Unadjusted model OR (95% CI)Multivariable-adjusted OR (95% CI)aMultivariable-adjusted OR (95% CI)b | ≤ 0.38147/1731.001.001.00 | > 0.38 - 0.48175/1721.23 (0.90-1.69)1.25 (0.91-1.72)1.20 (0.86-1.66) | > 0.48 - 0.62210/1721.49 (1.09-2.05)1.50 (1.08-2.07) 1.40 (1.01-1.95) | > 0.62156/1731.09 (0.78-1.54)1.08 (0.76-1.52)0.91 (0.64-1.31) | 0.660.770.53 | 1.10 (0.85-1.43)1.09 (0.83-1.42)0.93 (0.70-1.23) |
| **Free Testosterone**Quartile cutpoints, pg/mLn (case/control)Unadjusted model OR (95% CI)Multivariable-adjusted OR (95% CI)aMultivariable-adjusted OR (95% CI)b | ≤ 65.1202/1731.001.001.00 | > 65.1 - 77.6167/1720.79 (0.58-1.07)0.77 (0.56-1.05)0.79 (0.58-1.09) | > 77.6 - 92.6166/1720.77 (0.56-1.06)0.77 (0.56-1.07)0.83 (0.59-1.15) | > 92.6155/1730.69 (0.49-0.98)0.69 (0.49-0.99)0.77 (0.53-1.10) | 0.050.060.21 | 0.73 (0.52-1.02)0.75 (0.53-1.05)0.83 (0.58-1.18) |
| **SHBG**Quartile cutpoints, nmol/Ln (case/control)Unadjusted model OR (95% CI)Multivariable-adjusted OR (95% CI)aMultivariable-adjusted OR (95% CI)bMultivariable-adjusted OR (95% CI)c | ≤ 28.6222/1731.001.001.001.00 | > 28.6 - 37.6153/1720.67 (0.50-0.90)0.68 (0.51-0.93)0.73 (0.54-1.00)0.78 (0.56-1.06) | > 37.6 - 51.0173/1720.72 (0.53-0.99)0.74 (0.54-1.03)0.85 (0.61-1.18)0.92 (0.64-1.32) | > 51.0142/1730.56 (0.40-0.79)0.57 (0.40-0.81)0.67 (0.46-0.97)0.80 (0.50-1.26) | 0.0030.0050.070.51 | 0.69 (0.57-0.84)0.70 (0.57-0.86)0.77 (0.62-0.96)0.83 (0.61-1.13) |

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

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

bAdditionally adjusted for BMI (continuous).

cAdditionally adjusted for levels of estradiol and testosterone.

dOR per 1-log2 unit increment