**Supplementary table S1. The components of empirical dietary index for hyperinsulinemia (EDIH) in the study participants a**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Cases (n=923)** | **Controls (n=1,846)** | ***P*-value b** |
| EDIH score |  |  |  |
|  Mean ± SD | 14.37 ± 24.98 | 17.49 ± 194.91 | 0.001 |
| EDIH component |  |  |  |
| *Positive associations* |  |  |  |
| Red meat | 44.20 ± 40.09 | 62.66 ± 64.89 | < 0.001 |
|  Processed meat | 1.47 ± 18.43 | 2.65 ± 14.85  | < 0.001 |
| Margarine | 0.01 ± 0.02 | 0.02 ± 0.08 | < 0.001 |
| Poultry | 5.47 ± 35.21 | 11.34 ± 56.69 | < 0.001 |
| Butter | 0.01 ± 0.05 | 0.06 ± 0.21 | < 0.001 |
|  Fish and other sea food | 38.15 ± 220.16 | 74.67 ± 510.85 | < 0.001 |
| High energy beverages | 14.30 ± 70.54 | 59.55 ± 554.41 | < 0.001 |
| Tomatoes | 14.84 ± 29.52 | 32.19 ± 77.10 | < 0.001 |
| Low fat dairy products | 33.53 ± 119.51 | 250.06 ± 2,566.04 | < 0.001 |
|  Eggs | 14.47 ± 14.60 | 19.71 ± 21.18 | < 0.001 |
|  |  |  |  |
| *Inverse associations* |  |  |  |
|  Wine | 0.02 ± 0.34 | 0.16 ± 0.94 | < 0.001 |
| Coffee | 3.95 ± 4.21 | 5.37 ± 5.90 | < 0.001 |
| Whole fruits | 122.37 ± 157.63 | 247.48 ± 413.01 | < 0.001 |
| High fat dairy products | 112.43 ± 1,109.87 | 473.87 ± 4,882.16 | < 0.001 |
|  Green leafy vegetables | 21.90 ± 27.29 | 43.46 ± 66.29 | < 0.001 |

a All components were adjusted for total energy intake using the residual method. b The Wilcoxon signed-rank test was used for significant *P*-values that met the 5% level.

**Supplementary table S2. The components of empirical lifestyle index for hyperinsulinemia (ELIH) in the study participants a**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Cases (n=923)** | **Controls (n=1,846)** | ***P*-value b** |
| ELIH score |  |  |  |
|  Mean ± SD | -4.49 ± 56.78 | -25.47 ± 262.57 | < 0.001 |
| ELIH component |  |  |  |
| *Positive associations* |  |  |  |
| BMI | 24.03 ± 3.35 | 24.26 ± 2.86 | 0.07 |
| Margarine | 0.01 ± 0.02 | 0.02 ± 0.08 | < 0.001 |
| Liquor | 19.25 ± 98.19 | 15.20 ± 51.17 | 0.10 |
| Butter | 0.01 ± 0.05 | 0.06 ± 0.21 | < 0.001 |
|  Red meat | 44.20 ± 40.09 | 62.66 ± 64.89 | < 0.001 |
| Fruit juice | 30.08 ± 159.60 | 62.86 ± 211.62 | < 0.001 |
|  |  |  |  |
| *Inverse associations* |  |  |  |
|  Coffee | 3.95 ± 4.21 | 5.37 ± 5.90 | < 0.001 |
| Whole fruits | 122.37 ± 157.63 | 247.48 ± 413.01 | < 0.001 |
|  Wine | 0.02 ± 0.34 | 0.16 ± 0.94 | < 0.001 |
| Physical activity (MET/week) | 2,236.69 ± 2,025.33 | 2,731.01 ± 2,945.47 | 0.10 |
| High fat dairy products | 112.43 ± 1,109.87 | 473.87 ± 4,882.16 | < 0.001 |
| Snacks | 12.17 ± 196.66 | 12.98 ± 103.28 | 0.83 |
|  Salad dressing | 1.18 ± 0.87 | 1.78 ± 1.53 | < 0.001 |

a All components were adjusted for total energy intake using the residual method. b The Wilcoxon signed-rank test was used for significant *P*-values that met the 5% level.

**Supplementary table S3. The components of empirical dietary index for insulin resistance (EDIR) in the study participants a**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Cases (n=923)** | **Controls (n=1,846)** | ***P*-value b** |
| EDIR score |  |  |  |
|  Mean ± SD | 79.08 ± 46.95 | 63.73 ± 307.74 | < 0.001 |
| EDIR component |  |  |  |
| *Positive associations* |  |  |  |
|  Margarine | 0.01 ± 0.02 | 0.02 ± 0.08 | < 0.001 |
| Red meat | 44.20 ± 40.09 | 62.66 ± 64.89 | < 0.001 |
| Refined grains | 660.30 ± 167.28 | 590.88 ± 206.41 | < 0.001 |
| Processed meats | 1.47 ± 18.43 | 2.65 ± 14.85 | < 0.001 |
|  Tomatoes | 14.84 ± 29.52 | 32.19 ± 77.10 | < 0.001 |
| Other vegetables | 15.22 ± 12.10 | 18.82 ± 22.58 | 0.06 |
| Fish and other sea food | 38.15 ± 220.16 | 74.67 ± 510.85 | < 0.001 |
| Fruit juice | 30.08 ± 159.60 | 62.86 ± 211.62 | < 0.001 |
|  |  |  |  |
| *Inverse associations* |  |  |  |
|  Coffee | 3.95 ± 4.21 | 5.37 ± 5.90 | < 0.001 |
|  Wine | 0.02 ± 0.34 | 0.16 ± 0.94 | < 0.001 |
| Liquor | 19.25 ± 98.19 | 15.20 ± 51.17 | 0.10 |
| Beer | 1.77 ± 8.51 | 1.55 ± 5.02 | 0.57 |
| Green leafy vegetables | 21.90 ± 27.29 | 43.46 ± 66.29 | < 0.001 |
|  High fat dairy products | 112.43 ± 1,109.87 | 473.87 ± 4,882.16 | < 0.001 |
|  Dark yellow vegetables | 10.05 ± 17.04 | 10.51 ± 25.28 | < 0.001 |
|  Nuts | 1.25 ± 2.64 | 4.33 ± 13.58 | < 0.001 |

a All components were adjusted for total energy intake using the residual method. b The Wilcoxon signed-rank test was used for significant *P*-values that met the 5% level.

**Supplementary table S4. The components of empirical lifestyle index for insulin resistance (ELIR) in the study participants a**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Cases (n=923)** | **Controls (n=1,846)** | ***P*-value b** |
| ELIR score |  |  |  |
|  Mean ± SD | 58.23 ± 70.19 | 45.22 ± 303.91 | 0.002 |
| ELIR component |  |  |  |
| *Positive associations* |  |  |  |
| BMI | 24.03 ± 3.35 | 24.26 ± 2.86 | 0.07 |
|  Refined grains | 660.30 ± 167.28 | 590.88 ± 206.41 | < 0.001 |
| Red meat | 44.20 ± 40.09 | 62.66 ± 64.89 | < 0.001 |
| Margarine | 0.01 ± 0.02 | 0.02 ± 0.08 | < 0.001 |
| Tomatoes | 14.84 ± 29.52 | 32.19 ± 77.10 | < 0.001 |
|  Fruit juice | 30.08 ± 159.60 | 62.86 ± 211.62 | < 0.001 |
| Potatoes | 37.29 ± 28.97 | 60.50 ± 203.08 | < 0.001 |
| Processed meat | 1.47 ± 18.43 | 2.65 ± 14.85 | < 0.001 |
| Other vegetables | 15.22 ± 12.10 | 18.82 ± 22.58 | 0.06 |
| Tea | 36.79 ± 169.30 | 215.14 ± 1427.75 | < 0.001 |
|  |  |  |  |
| *Inverse associations* |  |  |  |
|  Coffee | 3.95 ± 4.21 | 5.37 ± 5.90 | < 0.001 |
|  Wine | 0.02 ± 0.34 | 0.16 ± 0.94 | < 0.001 |
| Liquor | 19.25 ± 98.19 | 15.20 ± 51.17 | 0.10 |
| High fat dairy products | 112.43 ± 1,109.87 | 473.87 ± 4,882.16 | < 0.001 |
| Physical activity (MET/week) | 2,236.69 ± 2,025.33 | 2,731.01 ± 2,945.47 | 0.10 |
|  Green leafy vegetables | 21.90 ± 27.29 | 43.46 ± 66.29 | < 0.001 |

a All components were adjusted for total energy intake using the residual method. b The Wilcoxon signed-rank test was used for significant *P*-values that met the 5% level.

**Supplementary table S5. Interaction between ELIR score and rs2423279 polymorphism in relation to CRC risk by anatomic subsite**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| ***HAO1* rs2423279 (Dominant model)** | **T/T** | **T/T** | **T/C+C/C** | **T/C+C/C** |  |
| **ELIR** | **Low** | **High** | **Low** | **High** | ***P* for interaction** |
| **Colon cancer** |  |  |  |  |  |
| **No. of Cases/Controls** | 74/361 | 101/390 | 68/339 | 109/310 |  |
| **CrudeOR (95% CI)** | 1.0 (ref) | 1.26 (0.91-1.76) | 0.98 (0.68-1.40) | 1.72 (1.23-2.39) | 0.18 |
| **MultivariableOR (95% CI) a** | 1.0 (ref) | 1.93 (1.26-2.95) | 0.92 (0.60-1.42) | 2.83 (1.85-4.33) | 0.11 |
| **Rectal cancer** |  |  |  |  |  |
| **No. of Cases/Controls** | 67/361 | 92/390 | 68/339 | 104/310 |  |
| **CrudeOR (95% CI)** | 1.0 (ref) | 1.27 (0.90-1.80) | 1.08 (0.75-1.56) | 1.81 (1.28-2.55) | 0.27 |
| **MultivariableOR (95% CI) a** | 1.0 (ref) | 1.72 (1.11-2.66) | 0.95 (0.61-1.48) | 2.41 (1.57-3.72) | 0.19 |

EDIH, empirical dietary index for hyperinsulinemia; ELIH, empirical lifestyle index for hyperinsulinemia; EDIR, empirical dietary index for insulin resistance; ELIR, empirical lifestyle index for insulin resistance. The empirical indices were categorized into low and high groups based on the median level of their control group’s score (EDIH = 14.22, ELIH = -3.67, EDIR = 77.59, ELIR = 59.16). a Multivariable model was adjusted for age (< 50 years or ≥ 50 years), sex (male or female), BMI (< 25 kg/m2 or ≥ 25 kg/m2), prior BMI (< 25 kg/m2 or ≥ 25 kg/m2), education level, occupation, income, smoking status (never or ever), alcohol drinking status (never or ever), regular physical activity status (yes or no), first-degree family history of CRC (yes or no), diabetes mellitus status (yes or no), and total energy intake. Significant *P*-values that met the 5% level are in bold.