**Supplementary Materials**

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| **Supplementary Table 1. Age-adjusted characteristics of participants in the Men’s Lifestyle Validation Study (n=293) compared to the full HPFS cohort in 2010** | | |
|  | **MLVS** | **HPFS** |
| Participants, n | 293 | 22772 |
| Age, yr | 65.9 (1.8) | 73.6 (8.0) |
| BMI, kg/m2 | 25.5 (3.3) | 25.0 (5.9) |
| Physical activity, MET-hour/week | 50.0 (40.2) | 36.9 (37.3) |
| Comorbidity | 0.8 (0.8) | 1.3 (1.1) |
| Calorie intake, kcal/day | 2144 (622) | 2022 (650) |
| NSAID use, % | 68.6 | 61.8 |
| Smoking status, % |  |  |
| Never | 57.3 | 41.7 |
| Past | 41.3 | 55.6 |
| Current | 1.4 | 2.7 |
| BMI & physical activity combination |  |  |
| Lean and active | 24.9 | 15.9 |
| Lean and sedentary | 20.5 | 29.5 |
| Overweight/obese and active | 24.9 | 16.5 |
| Overweight/obese and sedentary | 29.7 | 38.1 |
| EDIHa | 0.3 (0.4) | 0.4 (0.4) |
| Dietary insulin indexa | 37.3 (5.4) | 38.8 (5.7) |
| Dietary insulin loada | 801.5 (262.5) | 784.5 (280.9) |
| Food items included in EDIH |  |  |
| Processed meat | 1.4 (2.1) | 1.7 (2.3) |
| Read meat | 3.6 (2.7) | 3.7 (2.9) |
| Other fish | 1.7 (1.3) | 1.7 (1.5) |
| Poultry | 2.2 (2.1) | 1.9 (1.9) |
| Eggs | 2.2 (3.1) | 2.1 (2.8) |
| Butter | 1.8 (3.2) | 1.9 (4.0) |
| Margarine | 1.2 (2.8) | 1.5 (3.6) |
| Low-fat dairy products | 6.2 (6.5) | 6.9 (7.4) |
| High-fat dairy products | 6.4 (5.2) | 6.0 (6.7) |
| Wine | 4.7 (5.6) | 2.9 (4.7) |
| Coffee | 14.9 (14.8) | 15.4 (17.7) |
| Fruits | 16.3 (13.4) | 19.4 (19.6) |
| Tomatoes | 5.7 (4.7) | 5.4 (5.0) |
| Leafy green vegetables | 5.6 (4.2) | 5.0 (4.5) |
| French fries | 0.5 (0.7) | 0.5 (0.8) |
| High-energy beverages | 1.4 (2.8) | 1.7 (3.6) |
| Low-energy beverages | 14.3 (21.5) | 18.0 (28.3) |
| Cream soup | 0.3 (0.4) | 0.4 (0.7) |
| Data are presented as mean (SD) for continuous variables and percentage for categorical variables.  Abbreviation: BMI, body mass index, EDIH, empirical dietary index for hyperinsulinemia, HPFS, Health Professionals Follow-up Study, MET, metabolic equivalent task, MLVS, Men’s Life Style Validation Study.  a Unadjusted for calorie intake. | | |

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| **Supplementary Table 2. Spearman correlations of empirical dietary index for hyperinsulinemia (EDIH) with dietary insulin index and dietary insulin load (n=293)** | | |
|  | EDIH (single, 2010) | EDIH (average of 2010 and 2012) |
| Dietary insulin index (single, 2010) | 0.205 | 0.230 |
| Dietary insulin index (average of 2010 and 2012) | 0.229 | 0.227 |
| Dietary insulin load (single, 2010) | 0.183 | 0.200 |
| Dietary insulin load (average of 2010 and 2012) | 0.191 | 0.196 |
| Correlations were adjusted for calorie intake. | | |

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| **Supplementary Table 3. Association of cumulative averages (2010 and 2012) of empirical dietary index for hyperinsulinemia (EDIH), dietary insulin index, and dietary insulin load with 24-hour urinary C-peptide in the Men’s Lifestyle Validation Study (n=293)a** | | | | | | |
|  | **EDIH** | |  | | |  |
| Mean (95% CI) | **Tertile 1** | **Tertile 2** | | **Tertile 3** | **1-SD increasec** | **P-trend** |
| Age-adjusted | 35.7 (30.6, 41.7) | 44.7 (38.3, 52.2) | | 48.9 (41.9, 57.1)\* | 1.15 (1.06, 1.26) | 0.002 |
| Multivariable adjustedb | 36.4 (31.1, 42.5) | 45.2 (38.7, 52.7) | | 47.5 (40.6, 55.5)\* | 1.13 (1.03, 1.24) | 0.008 |
| Multivariable adjustedb + BMI | 38.8 (33.4, 45.1) | 44.5 (38.3, 51.6) | | 45.2 (38.9, 52.6) | 1.07 (0.98, 1.17) | 0.13 |
|  | **Dietary insulin index** | | |  |  |  |
| Mean (95% CI) | **Tertile 1** | **Tertile 2** | | **Tertile 3** | **1-SD increasec** |  |
| Age-adjusted | 34.7 (29.7, 40.5) | 43.6 (37.4, 50.8) | | 51.6 (44.2, 60.1)\* | 1.17 (1.07, 1.28) | <.001 |
| Multivariable adjustedb | 34.8 (29.8, 40.7) | 43.3 (37.2, 50.5) | | 51.7 (44.3, 60.5)\* | 1.16 (1.06, 1.28) | 0.001 |
| Multivariable adjustedb + BMI | 35.5 (30.6, 41.3) | 42.9 (37.1, 49.7) | | 51.2 (44.1, 59.4)\* | 1.16 (1.06, 1.26) | 0.001 |
|  | **Dietary insulin load** | | |  |  |  |
| Mean (95% CI) | **Tertile 1** | **Tertile 2** | | **Tertile 3** | **1-SD increasec** |  |
| Age-adjusted | 33.5 (28.7, 39.1) | 49.5 (42.5, 57.7)\* | | 47.0 (40.3, 54.8)\* | 1.15 (1.05, 1.26) | 0.002 |
| Multivariable adjustedb | 33.5 (28.6, 39.2) | 49.2 (42.2, 57.3)\* | | 47.3 (40.6, 55.2)\* | 1.15 (1.05, 1.26) | 0.003 |
| Multivariable adjustedb + BMI | 34.7 (29.9, 40.3) | 47.6 (41.1, 55.1)\* | | 47.2 (40.7, 54.8)\* | 1.13 (1.03, 1.23) | 0.008 |
| Values are absolute 24-hour urinary C-peptide and its 95% CI (ng/mL).  Abbreviation: BMI, body mass index, CI, confidence interval.  a EDIH, dietary insulin index, and dietary insulin load were adjusted for calorie intake using residual method.  b Multivariable-adjusted models included age (continuous), physical activity (continuous), comorbidity score (continuous), NSAID use (yes or no), and smoking status (never, past or current). Multivariable-adjusted + BMI models further included BMI (continuous).  c Relative concentrations (or relative ratio) with 95% CI of 24-hour urinary C-peptide per 1-SD increase in dietary index.  \* Significantly different from tertile 1 (P<0.05). | | | | | | |

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| **Supplementary Table 4. Association of empirical dietary index for hyperinsulinemia (EDIH) and empirical lifestyle index for hyperinsulinemia (ELIH) with 24-hour urinary C-peptide in the Men’s Lifestyle Validation Study (n=293)a** | | | | | |
|  | **EDIH (adjusted for BMI using residual method)** | | |  |  |
| Mean (95% CI) | **Tertile 1** | **Tertile 2** | **Tertile 3** | **1-SD increased** | **P-trend** |
| Age-adjusted | 38.2 (32.7, 44.7) | 45.6 (39.0, 53.3) | 44.8 (38.3, 52.4) | 1.08 (0.99, 1.18) | 0.10 |
| Multivariable adjustedb | 38.8 (33.1, 45.3) | 46.1 (39.4, 53.8) | 43.7 (37.4, 51.1) | 1.06 (0.98, 1.16) | 0.22 |
|  | **ELIH** |  |  |  |  |
| Mean (95% CI) | **Tertile 1** | **Tertile 2** | **Tertile 3** | **1-SD increasec** |  |
| Age-adjusted | 34.4 (29.5, 40.1) | 42.4 (36.4, 49.4) | 53.4 (45.9, 62.2) | 1.26 (1.16, 1.38) | <.001 |
| Multivariable adjustedc | 34.3 (29.4, 40.1) | 42.8 (36.7, 49.9) | 53.1 (45.6, 61.9) | 1.26 (1.16, 1.38) | <.001 |
| Values are absolute 24-hour urinary C-peptide and its 95% CI (ng/mL).  Abbreviation: BMI, body mass index, CI, confidence interval.  a EDIH and ELIH were adjusted for calorie intake using residual method.  b Multivariable-adjusted model included age (continuous), physical activity (continuous), comorbidity score (continuous), NSAID use (yes or no), and smoking status (never, past or current).  c Multivariable-adjusted model included age (continuous), comorbidity score (continuous), NSAID use (yes or no), and smoking status (never, past or current).  d Relative concentrations (or relative ratio) with 95% CI of 24-hour urinary C-peptide per 1-SD increase in dietary index.  \* Significantly different from tertile 1 (P<0.05). | | | | | |