**Supplemental Table 1.** Foods contained in the Food Frequency Questionnaire (FFQ) of the EPITeen and the 1982 Pelotas Cohorts, according to the NOVA Food Classification System.

|  |  |
| --- | --- |
| **EPITeen Cohort** | **Pelotas Cohort** |
| **Group 1. Unprocessed or minimally processed foods** |
| Milk; eggs; meats (steak, chicken, turkey, rabbit, pork, lamb, viscera, fish, and seafood); rice; spaghetti; fried potato; potatoes; cabbages; broccoli; cauliflower; brussels sprout; spinach; green beans; lettuce; onion; carrot; turnip; tomato; bell pepper; cucumber; beans, chickpeas; pea, fava beans; apple, pear; orange, tangerine; banana; kiwi; strawberry; cherry; peach, plum; watermelon or melon; persimmon; fig, loquats, apricots; grape; nuts; coffee; tea; pudding, candies; and vegetable soup. | Rice; bean; spaghetti; manioc flour; home bread; cake; polenta; fried potato; boiled potatoes; cassava; popcorn; lentil, pea, chickpeas; lettuce; collard greens; cabbage; orange, tangerine; banana; papaya; apple; watermelon, melon; pineapple; avocado; mango; strawberry; grape; peach; guava; pear; tomato; chayote; pumpkin; natural cucumber; green beans; carrot; beet; cauliflower; milk, eggs; meats (steak, pork, chicken, fish, and shrimp); snacks (kibe, filled pastry, empanada); pudding, candies; coffee; orange juice; lemonade; and fruit juice or fruit pulp juice.  |
| **Group 2. Processed culinary ingredients** |
| Olive oil; vegetable oils; butter; and sugar. | Sugar. |
| **Group 3. Processed foods** |
| Cheese; canned fish; white bread or toasts; whole-grain bread or toasts; marmalade, compote, jelly, honey; canned fruits; snacks (croissants, pastries, donut or cakes, croquettes, cod dumplings, etc.); olive; wine, and beer. | Whole grain bread; white bread; cheese; beer; and wine. |
| **Group 4. Ultra-processed foods** |
| Yogurt; ice cream; processed meats (ham, chorizo, sausage, bacon, etc.); margarine; breakfast ‘cereals’; sweet cookies, salty cracker; chocolate powder, chocolate bar; soft drinks, sugar-sweetened beverages; mayonnaise; ‘instant’ sauces; pizza; hamburger; packaged fried potato; and distilled drinks. | Sweet cookies; salty cracker; yogurt; Bauru or cheeseburger; ground meat (hamburger); processed meats (sausage, salami); hot dog; pizza; mayonnaise; ice cream; candies; chocolate powder; chocolate bar or bonbon; and soft drinks. |



**Supplemental Figure 1.** Direct acyclic graph of the effect of ultra-processed-foods consumption on interleukin-6 in the EPITeen and 1982 Pelotas cohort.

¹Variable included only in the Pelotas Cohort model; ²Parental education in the EPITeen Cohort; and fasting time was also analyzed as post confounders in the Pelotas Cohort.

**Supplemental Table 2.** Median interleukin-6 concentration and interquartile range (IQR) according to independent variables in the EPITeen and the 1982 Pelotas Cohorts, stratified by sex.

|  |  |
| --- | --- |
|   | **Interleukin-6 (pg/mL)**  |
|  | **Males**  | **Females** |
|  | Median (IQR) | p-value  | Median (IQR) | p-value  |
| **EPITeen** |  |  |  |  |
| *Socio-economic characteristics at 21 years* |  |  |  |  |
| Parental education, n (%)  |  | 0.13 |  | 0.34 |
| Low  | 2.85 (1.73; 4.47) |  | 2.85 (1.57; 4.55) |  |
| Intermediate | 2.30 (1.23; 3.46) |  | 2.84 (1.92; 4.70) |  |
| High  | 2.57 (1.24; 4.13) |  | 2.41 (1.47; 3.90) |  |
| *Health-related behaviors at 21 years* |  |  |  |  |
| Current smoker, n (%)  |  |  |  |  |
| No |  | **0.02** |  | 0.36 |
| Yes | 2.86 (1.59; 4.40) |  | 2.92 (1.78; 4.48) |  |
| Leisure physical activity, n (%)  | 2.32 (1.19; 3.55) |  | 2.54 (1.42; 4.21) |  |
| Low |  | 0.94 |  | 0.23 |
| Moderate  | 2.65 (1.41; 4.16) |  | 2.52 (1.35; 3.79) |  |
| High | 2.52 (1.54; 3.84) |  | 2.98 (1.90; 4.84) |  |
| **Pelotas** |  |  |  |  |
| *Socio-economic characteristics at perinatal and 23 years* |  |  |  |  |
| Skin color, n (%)  |  | **0.03** |  | **0.007** |
| White | 1.37 (0.98; 2.06) |  | 1.38 (0.94; 2.21) |  |
| Black | 1.27 (0.88; 2.04) |  | 1.66 (1.07; 2.55) |  |
| Brown/Indigenous/Asian  | 1.54 (1.12; 2.09) |  | 1.66 (1.01; 2.40) |  |
| Monthly income, n (%)  |  | **0.05** |  | **<0.001** |
| 1st (poorer) | 1.41 (1.04; 2.21) |  | 1.59 (1.02; 2.36) |  |
| 2nd | 1.33 (0.98; 1.92) |  | 1.42 (0.98; 2.32) |  |
| 3rd (richer) | 1.34 (0.93; 2.13) |  | 1.30 (0.90; 2.04) |  |
| Education, n (%)  |  | **<0.001** |  | **<0.001** |
| Low | 1.43 (1.04; 2.13) |  | 1.67 (1.08; 2.44) |  |
| Intermediate | 1.34 (0.95; 2.13) |  | 1.34 (0.96; 2.14) |  |
| High | 1.20 (0.91; 1.70) |  | 1.37 (0.85; 2.16) |  |
| *Health-related behaviors at 23 years* |  |  |  |  |
| Current smoker, n (%)  |  | **<0.001** |  | 0.11 |
| No | 1.33 (0.97; 1.99) |  | 1.40 (0.95; 2.26) |  |
| Yes | 1.50 (1.02; 2.31) |  | 1.57 (1.03; 2.30) |  |
| Leisure physical activity, n (%)  |  | 0.81 |  | 0.66 |
| Low | 1.37 (0.99; 2.06) |  | 1.44 (0.97; 2.22) |  |
| Intermediate | 1.37 (0.98; 2.02) |  | 1.50 (0.96; 2.47) |  |
| High | 1.35 (0.98; 2.09) |  | 1.36 (0.93; 2.27) |  |

Median (IQR): median and interquartile range.

The differences between median interleukin-6 concentrations according to variables were tested using the Wilcoxon or Kruskal-Wallis test.

**Supplemental Table 3.** Characteristics of participants according to the consumption of ultra-processed foods in the EPITeen and the 1982 Pelotas Cohorts, stratified by sex.

|  |  |  |
| --- | --- | --- |
|  | **Males** | **Females**    |
|  | 1sta | 2nd | 3rd | 4th | p-value\*  | 1sta | 2nd | 3rd | 4th | p-value¹  |
| **EPITeen Cohort** |  |  |  |  |  |  |  |  |  |  |
| *Socio-economic characteristics at 21 years* |  |  |  |  |  |  |  |  |  |  |
| Parental education, n (%)  |  |  |  |  | 0.39 |  |  |  |  | 0.29 |
| Low  | 16 (21.3) | 14 (18.7) | 21 (28.0) | 24 (32.0) |  | 31 (29.8) | 21 (20.2) | 23 (22.1) | 29 (27.9) |  |
| Intermediate  | 15 (22.7) | 17 (25.8) | 14 (21.2) | 20 (30.3) |  | 19 (23.4) | 23 (28.4) | 23 (28.4) | 16 (19.8) |  |
| High  | 30 (31.6) | 23 (24.2) | 23 (24.2) | 19 (20.0) |  | 20 (19.5) | 33 (32.0) | 27 (26.2) | 23 (22.3) |  |
| *Health-related behaviors at 21 years* |  |  |  |  |  |  |  |  |  |  |
| Current smoker, n (%)  |  |  |  |  | 0.71 |  |  |  |  | 0.87 |
|  No | 39 (26.9) | 30 (20.7) | 38 (26.2) | 38 (26.2) |  | 47 (23.6) | 56 (28.1) | 51 (25.6) | 45 (22.7) |  |
| Yes | 22 (24.2) | 24 (26.4) | 20 (22.0) | 25 (27.4) |  | 23 (26.1) | 21 (23.9) | 22 (25.0) | 22 (25.0) |  |
| Leisure physical activity, n (%)  |  |  |  |  | 0.62 |  |  |  |  | 0.31 |
| Low | 20 (23.5) | 21 (24.7) | 21 (24.7) | 23 (27.1) |  | 27 (26.2) | 23 (22.4) | 26 (25.2) | 27 (26.2) |  |
| Moderate  | 24 (23.8) | 26 (25.7) | 23 (22.8) | 28 (27.7) |  | 28 (21.1) | 40 (30.0) | 39 (29.3) | 26 (19.6) |  |
| High | 17 (34.0) | 07 (14.0) | 14 (28.0) | 12 (24.0) |  | 15 (28.8) | 14 (26.9) | 08 (15.4) | 15 (28.9) |  |
| **Pelotas Cohort** |  |  |  |  |  |  |  |  |  |  |
| *Socio-economic characteristics at 23 years* |  |  |  |  |  |  |  |  |  |  |
| Skin color, n (%)  |  |  |  |  | 0.18 |  |  |  |  | **0.003** |
| White | 267 (25.5) | 266 (25.4) | 269 (25.7) | 245 (23.4) |  | 234 (21.2) | 258 (23.3) | 288 (26.0) | 327 (29.5) |  |
| Black | 64 (28.9) | 57 (25.8) | 55 (24.9) | 45 (20.4) |  | 72 (28.8) | 64 (25.6) | 61 (24.4) | 53 (21.2) |  |
|    Brown/Indigenous/Asian  | 46 (34.3) | 39 (29.1) | 27 (20.2) | 22 (16.4) |  | 39 (30.1) | 38 (29.5) | 22 (17.1) | 30 (23.3) |  |
| Monthly income, n (%)  |  |  |  |  | **<0.001** |  |  |  |  | **<0.001** |
| 1st (poorer) | 174 (41.9) | 99 (23.9) | 86 (20.7) | 56 (13.5) |  | 186 (34.2) | 135 (24.9) | 108 (19.9) | 114 (21.0) |  |
| 2nd | 127 (26.1) | 134 (27.6) | 123 (25.3) | 102 (21.0) |  | 105 (21.0) | 125 (25.1) | 133 (26.7) | 136 (27.2) |  |
| 3rd (richer) | 76 (15.2) | 129 (25.8) | 142 (28.3) | 154 (30.7) |  | 54 (12.2) | 100 (22.5) | 130 (29.3) | 160 (36.0) |  |
| Education, n (%)  |  |  |  |  | **<0.001** |  |  |  |  | **<0.001** |
| Low | 191 (35.5) | 134 (24.9) | 125 (23.2) | 88 (16.4) |  | 183 (41.3) | 105 (23.7) | 80 (18.1) | 75 (16.9) |  |
| Intermediate | 167 (24.0) | 192 (27.6) | 175 (25.2) | 161 (23.2) |  | 141 (18.2) | 189 (24.3) | 209 (26.9) | 238 (30.6) |  |
| High | 19 (11.2) | 36 (21.3) | 51 (30.2) | 63 (37.3) |  | 21 (7.9) | 66 (24.8) | 82 (30.8) | 97 (36.5) |  |
| *Health-related behaviors at 23 years* |  |  |  |  |  |  |  |  |  |  |
| Current smoker, n (%)  |  |  |  |  | 0.29 |  |  |  |  | **0.001** |
| No | 270 (25.9) | 264 (25.3) | 267 (25.6) | 241 (23.2) |  | 244 (21.2) | 279 (24.3) | 310 (27.0) | 317 (27.5) |  |
| Yes | 107 (29.7) | 98 (27.2) | 84 (23.3) | 71 (19.8) |  | 101 (30.0) | 81 (24.1) | 61 (18.2) | 93 (27.7) |  |
| Leisure physical activity, n (%)  |  |  |  |  | 0.05 |  |  |  |  | 0.16 |
| Low | 120 (30.5) | 103 (26.2) | 93 (23.7) | 77 (19.6) |  | 240 (25.0) | 231 (24.1) | 231 (24.1) | 257 (26.8) |  |
| Intermediate | 111 (29.8) | 94 (25.3) | 81 (21.8) | 86 (23.1) |  | 65 (22.0) | 77 (26.0) | 71 (24.0) | 83 (28.0) |  |
| High | 146 (22.9) | 165 (25.9) | 177 (27.8) | 149 (23.4) |  | 40 (17.3) | 52 (22.5) | 69 (29.9) | 70 (30.3) |  |
| ¹p-value chi-squared test. |  |  |  |  |  |  |  |  |  |  |

**Supplemental Table 4.** Unadjusted and adjusted linear regressions between consumption of ultra-processed foods (in grams, energy, and % of total energy) and log-transformed interleukin-6, by sex in the EPITeen and the 1982 Pelotas Cohorts.

|  |  |  |
| --- | --- | --- |
|  | **EPITeen Cohort** | **Pelotas Cohort** |
|   | **Males**  | **Females**  | **Males**  | **Females**   |
| Ultra-processed food consumption | β (95% IC) | p-value | β (95% IC) | p-value | β (95% IC) | p-value | β (95% IC) | p-value |
| Grams |  |  |  |  |  |  |  |  |
| Crude | -0.016 (-0.057; 0.026) | 0.46 | 0.038 (-0.016; 0.091) | 0.17 | 0.009 (0.003; 0.016) | **0.006** | -0.003 (-0.010; 0.004) | 0.44 |
| Model 1 | -0.013 (-0.054; 0.028) | 0.54 | 0.044 (-0.014; 0.102) | 0.14 | 0.010 (0.003; 0.017) | **0.004** | -0.002 (-0.009; 0.006) | 0.66 |
| Model 2 | -0.013 (-0.055; 0.028) | 0.52 | 0.043 (-0.015; 0.102) | 0.15 | 0.011 (0.005; 0.018) | **0.001** | -0.001 (-0.008; 0.007) | 0.81 |
| Energy (kcal) |  |  |  |  |  |  |  |  |
| Crude | 0.006 (-0.045; 0.058) | 0.81 | 0.080 (0.020; 0.140) | **0.009** | 0.002 (-0.003; 0.007) | 0.38 | -0.004 (-0.010; 0.001) | 0.13 |
| Model 1 | 0.008 (-0.044; 0.059) | 0.77 | 0.083 (0.022; 0.145) | **0.01** | 0.003 (-0.002; 0.008) | 0.28 | -0.003 (-0.009; 0.002) | 0.24 |
| Model 2 | 0.003 (-0.050; 0.055) | 0.92 | 0.086 (0.022; 0.149) | **0.01** | 0.005 (-0.001; 0.010) | 0.10 | -0.003 (-0.009; 0.003) | 0.34 |
| % Energy (% kcal) |  |  |  |  |  |  |  |  |
| Crude | -0.004 (-0.021; 0.013) | 0.64 | 0.025 (0.007; 0.043) | **0.007** | 0.003 (-0.0001; 0.006) | 0.06 | -0.002 (-0.005; 0.0003) | 0.09 |
| Model 1 | -0.004 (-0.021; 0.013) | 0.64 | 0.025 (0.007; 0.044) | **0.006** | 0.004 (0.001; 0.007) | **0.005** | -0.001 (-0.004; 0.002) | 0.67 |
| Model 2 | -0.001 (-0.020; 0.017) | 0.87 | 0.029 (0.010; 0.048) | **0.003** | 0.004 (0.001; 0.007) | **0.011** | -0.001 (-0.004; 0.002) | 0.56 |

Grams and calories are on a scale of 100 for better interpretation.

Model 1: adjusted for socio-economic and health-related behavior characteristics (EPITeen: parental education, smoking status and leisure physical activity; Pelotas: skin color, monthly income, education, smoking status, leisure physical activity and fasting time).

Model 2: adjusted as in model 1 plus energy intake from food sources other than ultra-processed.

|  |
| --- |
| **Supplemental Table 5.** Sensitivity analyses of the consumption of ultra-processed foods (% of total energy) and interleukin-6, by sex in the EPITeen and the 1982 Pelotas Cohorts. |
|  | **Interleukin-6 (pg/mL)** |
|  | **EPITeen Cohort** | **Pelotas Cohort** |
| Quartile of consumption of UPF | 1st1 | 2nd | 3rd | 4th |  | 1st1 | 2nd | 3rd | 4th |  |
|  | mean (95% CI) | mean (95% CI) | mean (95% CI) | mean (95% CI) | p-value² | mean (95% CI) | mean (95% CI) | mean (95% CI) | mean (95% CI) | p-value² |
| Including bread in the UPF group |  |  |  |  |  |  |  |  |  |  |
| **Males** | 1.85 (1.33; 2.56) | 1.87 (1.33; 2.62) | 1.73 (1.21; 2.47) | 2.04 (1.47; 2.82) | 0.77 | 1.42 (1.33; 1.51) | 1.41 (1.32; 1.49) | 1.50 (1.41; 1.60) | 1.57 (1.47; 1.67) | **0.01** |
| **Females** | 1.29 (0.93; 1.80) | 1.88 (1.38; 2.57) | 1.86 (1.38; 2.52) | 3.05 (2.15; 4.32) | **<0.01** | 1.60 (1.51; 1.71) | 1.51 (1.42; 1.61) | 1.48 (1.39; 1.58) | 1.51 (1.41; 1.61) | 0.17 |
| Ultra-processed foods, UPF.Regressions performed with IL-6 on logarithmic scale – results presented in exponential means.1Reference category2p-values for the linear trend.Model adjusted for socio-economic and health-related behavior characteristics (EPITeen: parental education, smoking status, leisure physical activity and energy intake from food sources other than ultra-processed; Pelotas: skin color, monthly income, education, smoking status, leisure physical activity, fasting time and energy intake from food sources other than ultra-processed). |

**Supplemental Table 6.** Unadjusted and adjusted linear regressions between consumption of ultra-processed foods and fat mass percentage by sex in the EPITeen and the Pelotas Cohorts.

|  |
| --- |
| **Fat mass percentage** |
|  | **EPITeen Cohort** | **Pelotas Cohort** |
| Quartile of consumption of UPF | 2nd | 3rd | 4th |   | 2nd | 3rd | 4th |   |
|  | β (95% CI) | β (95% CI) | β (95% CI) | p-value¹ | β (95% CI) | β (95% CI) | β (95% CI) | p-value¹ |
| **Males** |  |  |  |  |  |  |  |  |
| Crude | -0.51 (-3.07; 2.05) | -1.58 (-4.11; 0.94) | -0.75 (-3.21; 1.71) | 0.42 | 0.95 (-0.35; 2.25) | 2.28 (0.98; 3.59) | 3.10 (1.75; 4.46) | **<0.001** |
| Model 1 | -1.03 (-3.55; 1.50) | -1.93 (-4.40; 0.54) | -1.42 (-3.85; 1.02) | 0.19 | 0.54 (-0.75; 1.82) | 1.82 (0.53; 3.12) | 2.40 (1.03; 3.77) | **<0.001** |
| Model 2 | -1.22 (-3.69; 1.24) | -2.28 (-4.70; 0.14) | -2.66 (-5.14; -0.19) | **0.02** | 0.40 (-0.88; 1.68) | 1.54 (0.23; 2.84) | 1.91 (0.51; 3.30) | **<0.01** |
| **Females** |  |  |  |  |  |  |  |  |
| Crude | -1.65 (-3.54; 0.23) | -0.48 (-2.39; 1.43) | -0.20 (-2.14; 1.75) | 0.83 | 0.53 (-0.75; 1.81) | 0.84 (-0.42; 2.11) | 1.07 (-0.17; 2.31) | 0.08 |
| Model 1 | -1.25 (-3.10; 0.60) | -0.26 (-2.13; 1.61) | -0.11 (-2.00; 1.78) | 0.81 | 0.25 (-1.04; 1.55) | 0.40 (-0.90; 1.70) | 0.77 (-0.52; 2.06) | 0.23 |
| Model 2 | -1.40 (-3.26; 0.45) | -0.48 (-2.37; 1.41) | -0.49 (-2.44; 1.47) | 0.89 | 0.18 (-1.10; 1.47) | 0.26 (-1.03; 1.55) | 0.33 (-0.97; 1.62) | 0.62 |

Reference category is 1st quartile.

¹p-values for the linear trend.

Model 1: adjusted for socio-economic and health-related behavior characteristics (EPITeen: parental education, smoking status and leisure physical activity; Pelotas: skin color, monthly income, education, smoking status and leisure physical activity).

Model 2: adjusted as model 1 plus energy intake from food sources other than ultra-processed.