**Supplementary Table 1.** Complete-case analysis: association between lifestyle changes from baseline to follow-up and risk of colorectal cancer

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| --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | **By sex** | **By age at baseline** | **By site** |
|  |  |  | **Overall** | **Males** | **Females** | **Age ≤55** | **Age >55** | **Proximal** | **Distal** | **Rectal** |
|  | **N (CRC events)** | **137302 (1219)** | **47669 (584)** | **89633 (635)** | **94563 (533)** | **42739 (686)** | **137302 (367)** | **137302 (361)** | **137302 (418)** |
| **Model 1** | Difference in continuous HLI score | 1unit increase | **0.95 (0.92-0.99)** | 0.96 (0.92-1.00) | **0.95 (0.90-0.99)** | **0.93 (0.89-0.98)** | 0.97 (0.93-1.02) | **0.93 (0.87-0.98)** | 0.96 (0.90-1.02) | 0.98 (0.93-1.04) |
| **Model 2** | Difference in categorical HLI score | ≤ -3 vs 0 | **1.43 (1.17-1.75)** | 1.31 (0.97-1.77) | **1.54 (1.17-2.02)** | **1.67 (1.23-2.28)** | 1.28 (0.99-1.67) | **1.80 (1.24-2.61)** | **1.70 (1.17-2.48)** | 1.06 (0.76-1.49) |
|  |  | -2 vs 0 | 0.94 (0.76-1.16) | 0.86 (0.62-1.18) | 1.01 (0.76-1.35) | 1.29 (0.95-1.75) | **0.72 (0.53-0.97)** | 1.41 (0.97-2.07) | 0.92 (0.61-1.39) | **0.69 (0.48-0.999)** |
|  |  | -1 vs 0 | 1.07 (0.89-1.27) | 0.94 (0.72-1.23) | 1.18 (0.93-1.50) | 1.01 (0.77-1.35) | 1.09 (0.87-1.38) | **1.47 (1.06-2.06)** | 1.04 (0.74-1.47) | 0.90 (0.67-1.20) |
|  |  | 1 vs 0 | 1.05 (0.88-1.26) | 0.95 (0.74-1.24) | 1.16 (0.90-1.49) | 1.17 (0.89-1.54) | 0.98 (0.77-1.25) | 1.24 (0.87-1.77) | 1.15 (0.82-1.60) | 0.88 (0.65-1.19) |
|  |  | 2 vs 0 | 1.01 (0.81-1.26) | 1.01 (0.75-1.35) | 0.98 (0.70-1.37) | 1.00 (0.71-1.40) | 1.02 (0.76-1.37) | 1.47 (0.99-2.20) | 1.20 (0.82-1.77) | 0.70 (0.47-1.05) |
|  |  | ≥ 3 vs 0 | 0.83 (0.65-1.07) | 0.74 (0.54-1.03) | 0.97 (0.64-1.45) | 0.89 (0.61-1.30) | 0.80 (0.57-1.12) | 0.91 (0.55-1.50) | 0.97 (0.63-1.49) | 0.74 (0.48-1.13) |
| **Model 3** | Difference in continuous smoking score | 1unit increase | 1.07 (0.93-1.22) | 1.08 (0.91-1.28) | 1.07 (0.85-1.34) | 1.15 (0.96-1.37) | 0.99 (0.81-1.22) | 1.04 (0.81-1.33) | 1.24 (0.98-1.57) | 0.95 (0.76-1.20) |
|  | Difference in continuous alcohol score | 1unit increase | 0.96 (0.89-1.02) | 0.96 (0.89-1.05) | 0.95 (0.85-1.06) | **0.85 (0.77-0.94)** | 1.04 (0.96-1.14) | 0.93 (0.82-1.05) | 0.95 (0.84-1.07) | 0.98 (0.88-1.10) |
|  | Difference in continuous BMI score | 1unit increase | 0.95 (0.87-1.05) | 0.97 (0.83-1.12) | 0.94 (0.83-1.06) | 1.02 (0.89-1.18) | 0.90 (0.79-1.02) | 0.98 (0.83-1.16) | 0.87 (0.73-1.04) | 0.99 (0.84-1.16) |
|  | Difference in continuous physical activity score | 1 unit increase | **0.94 (0.89-0.98)** | 0.94 (0.88-1.00) | 0.94 (0.88-1.00) | **0.92 (0.86-0.99)** | 0.95 (0.89-1.01) | **0.88 (0.81-0.96)** | 0.96 (0.88-1.05) | 0.99 (0.92-1.08) |

CRC: colorectal cancer. HLI: healthy lifestyle index. BMI: body mass index. Bold font indicates statistical significance (p<0.05). Models 1 and 2 are stratified by study centre, age and sex, and adjusted for education, diet score at baseline, continuous healthy lifestyle index (HLI) score at baseline, and calendar year of follow-up questionnaire. Model 3 is stratified by study centre, age and sex, and adjusted for education, diet score at baseline, continuous index components scores at baseline, and date of follow-up questionnaire; differences for the single index components are mutually adjusted. \* p-values for heterogeneity between males and females: difference in continuous HLI score, p=0.698; difference in categorical HLI score, p=0.899; smoking, p=0.952; alcohol, p=0.832; BMI, p=0.739; physical activity, p=0.990. ° p-values for heterogeneity between age groups: continuous HLI score, p=0.230; categorical HLI score, p=0.207; smoking, p=0.298; alcohol p=0.003; BMI, p=0.178; physical activity, p=0.591.