Appendix Table A. Proportional Hazards analysis of the relationship between decaf coffee consumption and incident colorectal cancer.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Cancer Site | Level |  |  | Unadjusted1 | Multivariate Adjusted1,2 |
|  |  | **Events** | **Ann Rate** | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** |
| All Colorectal | None | 877 | 0.119 | 1.00 (ref) | 0.78 | 1.00 (ref) | 0.95 |
|  | >0 - <4 cups / day | 360 | 0.117 | 1.01 (0.89, 1.14) |  | 0.99 (0.88, 1.12) |  |
|  | 4+ cups / day | 44 | 0.123 | 1.06 (0.79, 1.44) |  | 1.02 (0.75, 1.38) |  |
| Colon | None | 732 | 0.100 | 1.00 (ref) | 0.42 | 1.00 (ref) | 0.69 |
|  | >0 - <4 cups / day | 312 | 0.102 | 1.04 (0.92, 1.19) |  | 1.02 (0.89, 1.17) |  |
|  | 4+ cups / day | 38 | 0.106 | 1.10 (0.80, 1.53) |  | 1.05 (0.76, 1.45) |  |
| Rectum | None | 115 | 0.016 | 1.00 (ref) | 0.53 | 1.00 (ref) | 0.50 |
|  | >0 - <4 cups / day | 39 | 0.013 | 0.83 (0.58, 1.19) |  | 0.83 (0.58, 1.20) |  |
|  | 4+ cups / day | 6 | 0.017 | 1.10 (0.49, 2.51) |  | 1.05 (0.46, 2.39) |  |
| Rectosigmoid | None | 54 | 0.007 | 1.00 (ref) | 0.09 | 1.00 (ref) | 0.13 |
|  | >0 - <4 cups / day | 14 | 0.005 | 0.64 (0.36, 1.15) |  | 0.68 (0.38, 1.23) |  |
|  | 4+ cups / day | 1 | 0.003 | 0.40 (0.06, 2.88) |  | 0.40 (0.06, 2.89) |  |

1All models are adjusted for enrollment in WHI extension periods

2Adjusted for age, ethnicity, education, alcohol, smoking/pack years, BMI, physical activity, energy intake, red meat intake, fruit/vegetable intake, percent calories from fat, fiber intake, calcium intake, hormone use, NSAID use, history of treated diabetes, and family history of colorectal cancer

3Trend p-value calculated from a separate model with the outcome of interest as a function of linear coffee level (None=1, >0-4=2, ≥4=3)

Appendix Table B. Proportional Hazards analysis of the relationship between total coffee consumption and incident colorectal cancer.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Cancer Site | Level |  |  | Unadjusted1 | Multivariate Adjusted1,2 |
|  |  | **Events** | **Ann Rate** | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** |
| All Colorectal | None | 321 | 0.104 | 1.00 (ref) | 0.004 | 1.00 (ref) | 0.07 |
|  | >0 - <4 cups / day | 746 | 0.124 | 1.19 (1.05, 1.36) |  | 1.12 (0.98, 1.28) |  |
|  | 4+ cups / day | 215 | 0.129 | 1.27 (1.06, 1.50) |  | 1.17 (0.97, 1.40) |  |
| Colon | None | 272 | 0.088 | 1.00 (ref) | 0.004 | 1.00 (ref) | 0.07 |
|  | >0 - <4 cups / day | 624 | 0.103 | 1.18 (1.02, 1.36) |  | 1.10 (0.95, 1.27) |  |
|  | 4+ cups / day | 187 | 0.112 | 1.30 (1.08, 1.57) |  | 1.19 (0.98, 1.45) |  |
| Rectum | None | 39 | 0.013 | 1.00 (ref) | 0.50 | 1.00 (ref) | 0.88 |
|  | >0 - <4 cups / day | 98 | 0.016 | 1.29 (0.89, 1.87) |  | 1.20 (0.82, 1.76) |  |
|  | 4+ cups / day | 23 | 0.014 | 1.11 (0.66, 1.86) |  | 0.98 (0.58, 1.67) |  |
| Rectosigmoid | None | 19 | 0.006 | 1.00 (ref) | 0.52 | 1.00 (ref) | 0.66 |
|  | >0 - <4 cups / day | 37 | 0.006 | 1.00 (0.58, 1.74) |  | 0.99 (0.56, 1.74) |  |
|  | 4+ cups / day | 13 | 0.008 | 1.30 (0.64, 2.64) |  | 1.21 (0.58, 2.56) |  |

1All models are adjusted for enrollment in WHI extension periods

2Adjusted for age, ethnicity, education, alcohol, smoking/pack years, BMI, physical activity, energy intake, red meat intake, fruit/vegetable intake, percent calories from fat, fiber intake, calcium intake, hormone use, NSAID use, history of treated diabetes, and family history of colorectal cancer

3Trend p-value calculated from a separate model with the outcome of interest as a function of linear coffee level (None=1, >0-4=2, ≥4=3)

Appendix Table C. Colorectal Cancer by Regular Coffee Consumption1 (3-level) Full Model Results

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | Level | HR (95% CI) | p-value |
| Coffee |  |  | 0.07 |
|  | None | 1.0 (ref) |  |
|  | >0 - <4 cups / day | 1.15 (1.02, 1.29) |  |
|  | 4+ cups / day | 1.14 (0.93, 1.38) |  |
| Age (5-year increase) |  | 1.32 (1.26, 1.37) | <0.001 |
| Ethnicity |  |  | 0.29 |
|  | White (ref) | 1.00 (ref) |  |
|  | African American | 1.12 (0.90, 1.39) |  |
|  | Asian | 0.81 (0.55, 1.21) |  |
|  | Hispanic | 0.84 (0.58, 1.22) |  |
|  | Other/Unknown | 0.72 (0.44, 1.17) |  |
| Education |  |  | 0.01 |
|  | ≤ High school / GED | 1.00 (ref) |  |
|  | School after high school | 1.26 (1.08, 1.47) |  |
|  | College degree or higher | 1.23 (1.05, 1.44) |  |
| Physical Activity (5 MET-hr/wk increase) |  | 0.98 (0.96, 1.01) | 0.13 |
| Alcohol |  |  | 0.59 |
|  | Never/Past | 1.00 (ref) |  |
|  | <1 drink/day | 1.07 (0.94, 1.22) |  |
|  | ≥1 drink/day | 1.02 (0.83, 1.25) |  |
| Smoking2 |  |  | <0.001 |
|  | Never | 1.00 (ref) |  |
|  | Past, <20 pack-years | 1.00 (0.87, 1.14) |  |
|  | Past, ≥20 pack-years | 1.34 (1.15, 1.56) |  |
|  | Current, <20 pack-years | 1.05 (0.70, 1.58) |  |
|  | Current, ≥20 pack-years | 1.63 (1.26, 2.11) |  |
| Body Mass Index (5 kg/m2 increase)  |  | 1.10 (1.05, 1.15) | <.001 |
| Total Energy Intake (500kcal/day increase) |  | 0.99 (0.91, 1.08) | 0.87 |
| Red Meat Intake (1 oz increase) |  | 1.03 (0.97, 1.08) | 0.34 |
| Fruit / Vegetable Intake (1 cup increase) |  | 0.98 (0.92, 1.04) | 0.42 |
| Fiber Intake (10g/day increase) |  | 1.05 (0.89, 1.23) | 0.58 |
| Calcium Intake (500 mg/day increase) |  | 1.00 (0.96, 1.04) | 0.93 |
| Percent Caloric Intake from Fat (5 percent increase) |  | 1.02 (0.98, 1.07) | 0.31 |
| Hormone Use |  |  | <0.001 |
|  | Never | 1.00 (ref) |  |
|  | Past | 0.89 (0.76, 1.04) |  |
|  | Current, E-Alone | 0.72 (0.62, 0.84) |  |
|  | Current, E+P | 0.75 (0.64, 0.89) |  |
| NSAID use |  | 0.87 (0.77, 0.97) | 0.02 |
| History of treated diabetes |  | 1.27 (0.99, 1.63) | 0.06 |
| Family History of Colorectal Cancer3 |  |  | 0.003 |
|  | No | 1.0 (ref) |  |
|  | Yes | 1.24 (1.08, 1.43) |  |

1Model additionally adjusted for enrollment in WHI extension periods

2 Smoking has an additional categorical level indicating missing pack-years data. P-value based on contrast of known responses.

3Family history of colorectal cancer has an additional categorical level indicating missing data. p-value based on contrast of ‘Yes’ vs. ‘No’ responses.

Appendix Table D. Coffee Consumption on Colorectal Cancer by Subgroups

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | Cups of Regular Coffee per Day |  |
|  |  | ***Events (Ann %)*** | ***HR (95% CI0 vs. 0*** | ***Interaction*** |
| *Variable* | ***Level*** | ***0*** | ***>0 - <4*** | ***≥ 4*** | ***>0 - <4*** | ***≥ 4*** | ***trend p-value1*** |
| All Participants |  | 513 (0.11) | 634 (0.13) | 135 (0.13) | 1.15 (1.02, 1.29) | 1.14 (0.93, 1.38) |  |
| Age |  |  |  |  |  |  | 0.112 |
|  | 50 – 59 | 83 (0.05) | 105 (0.06) | 34 (0.09) | 1.25 (0.94, 1.67) | 1.63 (1.09, 2.44) |  |
|  | 60 – 69 | 236 (0.11) | 294 (0.13) | 68 (0.14) | 1.14 (0.96, 1.35) | 1.10 (0.84, 1.45) |  |
|  | 70 – 79 | 194 (0.19) | 235 (0.22) | 33 (0.19) | 1.12 (0.92, 1.35) | 0.89 (0.61, 1.29) |  |
| Ethnicity |  |  |  |  |  |  | 0.89 |
|  | White | 430 (0.11) | 554 (0.13) | 126 (0.13) | 1.15 (1.01, 1.31) | 1.12 (0.92, 1.38) |  |
|  | African American | 53 (0.13) | 44 (0.18) | 4 (0.24) | 1.25 (0.84, 1.87) | 1.53 (0.55, 4.24) |  |
|  | Hispanic | 13 (0.11) | 13 (0.08) | 3 (0.15) | 0.67 (0.31, 1.45) | 1.23 (0.35, 4.32) |  |
|  | Asian | 11 (0.09) | 14 (0.11) | 1 (0.12) | 1.20 (0.55, 2.65) | 1.35 (0.17, 10.47) |  |
|  | Other / Unknown | 6 (0.08) | 9 (0.11) | 1 (0.07) | 1.35 (0.48, 3.78) | 0.79 (0.10, 6.53) |  |
| Alcohol Use  |  |  |  |  |  |  | 0.433 |
|  | No | 186(0.12) | 157 (0.14) | 29 (0.13) | 1.17 (0.95, 1.45) | 1.03 (0.69, 1.53) |  |
|  | <1 drink/day | 285 (0.11) | 382 (0.12) | 77 (0.12) | 1.13 (0.97, 1.31) | 1.05 (0.82, 1.36) |  |
|  | ≥ 1 drink/day | 42 (0.09) | 95 (0.11) | 29 (0.16) | 1.24 (0.86, 1.79) | 1.70 (1.06, 2.74) |  |
| Smoking |  |  |  |  |  |  | 0.61 |
|  | Never | 279 (0.10) | 297 (0.12) | 39 (0.10) | 1.17 (0.99, 1.38) | 0.97 (0.69, 1.36) |  |
|  | Past, <20 pack-years | 119 (0.10) | 154 (0.11) | 30 (0.12) | 1.14 (0.90, 1.45) | 1.24 (0.83, 1.86) |  |
|  | Past, ≥20 pack-years | 83 (0.15) | 128 (0.17) | 31 (0.15) | 1.15 (0.87, 1.52) | 1.07 (0.71, 1.62) |  |
|  | Current, <20 pack-years | 4 (0.06) | 12 (0.09) | 9 (0.20) | 1.63 (0.53, 5.06) | 3.69 (1.14, 12.01) |  |
|  | Current, ≥20 pack-years | 15 (0.18) | 32 (0.21) | 22 (0.20) | 1.12 (0.61, 2.07) | 1.16 (0.60, 2.23) |  |
| Current HT Use |  |  |  |  |  |  | 0.52 |
|  | No | 335 (0.13) | 409 (0.16) | 99 (0.17) | 1.15 (0.99, 1.33) | 1.21 (0.96, 1.53) |  |
|  | Yes | 178 (0.08) | 225 (0.09) | 36 (0.08) | 1.15 (0.94, 1.40) | 0.98 (0.68, 1.41) |  |
| Current HT Type4 |  |  |  |  |  |  | 0.49 |
|  | E-Alone | 111 (0.09) | 121 (0.09) | 20 (0.09) | 1.00 (0.77, 1.30) | 0.99 (0.61, 1.61) |  |
|  | E+P | 67 (0.07) | 104 (0.09) | 16 (0.07) | 1.33 (0.98, 1.81) | 0.99 (0.57, 1.72) |  |
| BMI |  |  |  |  |  |  | 0.392 |
|  | Normal | 180 (0.09) | 226 (0.11) | 51 (0.12) | 1.17 (0.96, 1.43) | 1.26 (0.92, 1.73) |  |
|  | Overweight | 188 (0.12) | 217 (0.12) | 43 (0.11) | 1.00 (0.82, 1.22) | 0.91 (0.65, 1.27) |  |
|  | Obese | 145 (0.13) | 191 (0.17) | 41 (0.17) | 1.31 (1.05, 1.63) | 1.28 (0.90, 1.82) |  |
| Coffee Type4 |  |  |  |  |  |  | 0.06 |
|  | Non-drip | 513 (0.11) | 172 (0.13) | 35 (0.18) | 1.05 (0.89, 1.25) | 1.43 (1.01, 2.02) |  |
|  | Drip | 457 (0.13) | 100 (0.12) | 1.20 (1.05, 1.36) | 1.08 (0.86, 1.34) |  |

1Interaction p-values were calculated in a separate model with colorectal cancer as a function of the subgroup of interest, linear coffee level (0 cups=1, >0-<4 cups=2, ≥4 cups=3) and their interaction, with adjustment for all variables in Table 3.

2Interactions for continuous markers were evaluated with the interaction between coffee level by the continuous version of the subgroup of interest

3interaction tests linear alcohol trend (1=”No”, 2=”<1 drink/day”, 3=”≥1 drink/day” by linear coffee level

3Among participants reporting current HT at baseline only

4Both coffee type subgroups share a reference group of participants with no regular coffee consumption