**Supplementary Table 13. Total duration of statin use and colorectal cancer incidence in the pooled NHS and HPFS (sensitivity analyses, among participants with hypercholesterolemia)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **NHS+HPFS (Pooled)** | **Total Duration of Statin Use (Years)** | ***P*-trend** e | **Per 5-year increment****HR (95% CI)**  | ***P*-trend** f |
| **0** | **1 to 5** | **6 to 10** \* | **11 to 15** | **>15** |
| **Colorectal cancer** |  |  |  |  |  |  |  |  |
| No. of cases (1495 in total) a | 700 | 395 | 283 | 74 | 43 |  |  |  |
| Age-adjusted b | 1 [Ref] | 1.10 (0.97-1.25) | 1.05 (0.91-1.22) | 1.04 (0.80-1.34) | 1.44 (1.04-2.02) | .19 | 1.03 (0.97-1.11) | .31 |
| MV c | 1 | 1.09 (0.96-1.24) | 1.04 (0.90-1.22) | 1.03 (0.79-1.33) | 1.44 (1.03-2.02) | .22 | 1.03 (0.96-1.10) | .36 |
| MV + screening d | 1 | 1.10 (0.97-1.25) | 1.05 (0.90-1.22) | 1.04 (0.80-1.34) | 1.46 (1.04-2.04) | .18 | 1.04 (0.97-1.11) | .31 |
|  |  |  |  |  |  |  |  |  |
| **Colon cancer** |  |  |  |  |  |  |  |  |
| No. of cases (1115 in total) a | 495 | 301 | 225 | 55 | 39 |  |  |  |
| Age-adjusted b | 1 | 1.18 (1.02-1.37) | 1.17 (0.99-1.39) | 1.09 (0.81-1.46) | 1.88 (1.32-2.69) | .009 | 1.09 (1.01-1.17) | .03 |
| MV c | 1 | 1.18 (1.02-1.37) | 1.16 (0.98-1.39) | 1.08 (0.80-1.45) | 1.86 (1.29-2.67) | .01 | 1.08 (1.00-1.17) | .04 |
| MV + screening d | 1 | 1.18 (1.02-1.37) | 1.17 (0.99-1.40) | 1.09 (0.81-1.47) | 1.88 (1.31-2.71) | .03 | 1.09 (1.01-1.18) | .03 |
|  |  |  |  |  |  |  |  |  |
| **Proximal colon cancer** |  |  |  |  |  |  |  |  |
| No. of cases (702 in total) a | 287 | 194 | 148 | 42 | 31 |  |  |  |
| Age-adjusted b | 1 | 1.26 (1.05-1.52) | 1.23 (0.99-1.52) | 1.27 (0.90-1.80) | 2.27 (1.51-3.43) | .002 | 1.14 (1.04-1.25) | .005 |
| MV c | 1 | 1.25 (1.03-1.51) | 1.20 (0.97-1.50) | 1.24 (0.87-1.76) | 2.20 (1.45-3.34) | .005 | 1.13 (1.03-1.24) | .01 |
| MV + screening d | 1 | 1.26 (1.04-1.52) | 1.22 (0.98-1.51) | 1.26 (0.88-1.78) | 2.25 (1.48-3.41) | .003 | 1.13 (1.03-1.24) | .008 |
|  |  |  |  |  |  |  |  |  |
| **Distal Colon cancer** |  |  |  |  |  |  |  |  |
| No. of cases (367 in total) a | 189 | 94 | 84 | -- | -- |  |  |  |
| Age-adjusted b | 1 | 1.06 (0.83-1.37) | 1.05 (0.79-1.40) | -- | -- | .77 | 0.98 (0.85-1.14) | .82 |
| MV c | 1 | 1.07 (0.83-1.39) | 1.08 (0.81-1.45) | -- | -- | .64 | 1.00 (0.86-1.16) | .96 |
| MV + screening d | 1 | 1.07 (0.83-1.39) | 1.09 (0.81-1.46) | -- | -- | .61 | 1.00 (0.86-1.16) | .99 |
|  |  |  |  |  |  |  |  |  |
| **Rectal cancer** |  |  |  |  |  |  |  |  |
| No. of cases (303 in total) a | 169 | 74 | 60 | -- | -- |  |  |  |
| Age-adjusted b | 1 | 0.89 (0.67-1.18) | 0.76 (0.55-1.05) | -- | -- | .10 | 0.86 (0.73-1.02) | .08 |
| MV c | 1 | 0.90 (0.68-1.20) | 0.76 (0.55-1.06) | -- | -- | .11 | 0.87 (0.73-1.03) | .10 |
| MV + screening d | 1 | 0.91 (0.68-1.21) | 0.77 (0.55-1.07) | -- | -- | .12 | 0.87 (0.73-1.03) | .11 |

Abbreviations: NHS, Nurses’ Health Study; HPFS, Health Professionals Follow-up Study; MV, multivariate; HR, hazard ratio; CI, confidence interval.

a The number of proximal colon cancer, distal colon cancer and rectal cancer cases does not sum to the total number of colorectal cancer cases due to some of the colorectal cancer cases have missing subsite information.

b Stratified by age and follow-up cycle.

c Stratified by age and follow-up cycle; adjusted for sex, race, pack-years of smoking, physical activity, BMI, alcohol consumption, AHEI, regular use of aspirin, family history of colorectal cancer, history of diabetes mellitus, multivitamin use, total calorie intake, red or processed meat intake, fiber intake, folate intake, calcium intake, and vitamin D intake.

d Controlled for the same sets of covariates as denoted above, and were additionally adjusted for screening colonoscopy or sigmoidoscopy.

e *P*-value for trend was calculated using the mid-point of each category of statin use in years.

f *P*-value for trend was the *P* value for variables modeled as continuous.

\* 6 to 10 for colorectal cancer, colon cancer, and proximal colon cancer, ≥ 6 for distal colon cancer and rectal cancer.