**Supplementary Table 11. Total duration of statin use and colorectal cancer incidence in the NHS**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **NHS** | **Total Duration of Statin Use (Years)** | ***P*-trend** f | **Per 5-year increment****HR (95% CI)**  | ***P*-trend** g |
| **0** | **1 to 5** | **6 to 10** \* | **11 to 15** | **>15** |
| **Colorectal cancer** |  |  |  |  |  |  |  |  |
| No. of cases (1687 in total) a | 1145 | 278 | 190 | 47 | 27 |  |  |  |
| Age-adjusted b | 1 [Ref] | 1.03 (0.90-1.18) | 1.01 (0.86-1.19) | 1.02 (0.75-1.38) | 1.64 (1.10-2.46) | .21 | 1.04 (0.97-1.12) | .31 |
| MV c | 1 | 1.02 (0.89-1.17) | 1.01 (0.85-1.19) | 1.00 (0.74-1.36) | 1.63 (1.09-2.45) | .27 | 1.03 (0.96-1.12) | .37 |
| MV + screening d | 1 | 1.04 (0.91-1.19) | 1.04 (0.88-1.22) | 1.04 (0.77-1.42) | 1.72 (1.15-2.59) | .12 | 1.05 (0.98-1.14) | .18 |
| MV + screening + hypercholesterolemia e | 1 | 1.09 (0.94-1.26) | 1.09 (0.91-1.30) | 1.09 (0.80-1.50) | 1.81 (1.20-2.73) | .049 | 1.08 (0.99-1.17) | .08 |
|  |  |  |  |  |  |  |  |  |
| **Colon cancer** |  |  |  |  |  |  |  |  |
| No. of cases (1343 in total) a | 887 | 231 | 161 | 39 | 25 |  |  |  |
| Age-adjusted b | 1 | 1.09 (0.94-1.26) | 1.09 (0.91-1.30) | 1.06 (0.76-1.48) | 1.87 (1.22-2.85) | .04 | 1.08 (0.99-1.17) | .07 |
| MV c | 1 | 1.07 (0.92-1.24) | 1.07 (0.89-1.28) | 1.03 (0.74-1.45) | 1.82 (1.19-2.78) | .08 | 1.07 (0.98-1.16) | .12 |
| MV + screening d | 1 | 1.09 (0.94-1.27) | 1.10 (0.92-1.32) | 1.08 (0.77-1.51) | 1.93 (1.26-2.95) | .03 | 1.09 (1.00-1.18) | .048 |
| MV + screening + hypercholesterolemia e | 1 | 1.16 (0.98-1.37) | 1.18 (0.97-1.43) | 1.15 (0.82-1.63) | 2.06 (1.33-3.17) | .009 | 1.11 (1.02-1.22) | .02 |
|  |  |  |  |  |  |  |  |  |
| **Proximal colon cancer** |  |  |  |  |  |  |  |  |
| No. of cases (869 in total) a | 551 | 157 | 113 | 30 | 18 |  |  |  |
| Age-adjusted b | 1 | 1.14 (0.95-1.37) | 1.13 (0.91-1.40) | 1.17 (0.80-1.72) | 1.90 (1.15-3.13) | .03 | 1.10 (1.01-1.21) | .04 |
| MV c | 1 | 1.13 (0.94-1.35) | 1.11 (0.89-1.38) | 1.14 (0.77-1.67) | 1.85 (1.12-3.06) | .06 | 1.09 (0.99-1.20) | .07 |
| MV + screening d | 1 | 1.15 (0.95-1.38) | 1.15 (0.92-1.43) | 1.19 (0.81-1.76) | 1.98 (1.20-3.27) | .02 | 1.11 (1.01-1.23) | .03 |
| MV + screening + hypercholesterolemia e | 1 | 1.27 (1.04-1.56) | 1.29 (1.02-1.63) | 1.34 (0.90-2.00) | 2.22 (1.33-3.71) | .004 | 1.16 (1.05-1.29) | .005 |
|  |  |  |  |  |  |  |  |  |
| **Distal colon cancer** |  |  |  |  |  |  |  |  |
| No. of cases (396 in total) a | 286 | 59 | 51 | -- | -- |  |  |  |
| Age-adjusted b | 1 | 0.98 (0.74-1.29) | 1.06 (0.77-1.45) | -- | -- | .74 | 1.02 (0.87-1.21) | .79 |
| MV c | 1 | 0.95 (0.72-1.26) | 1.04 (0.75-1.43) | -- | -- | .83 | 1.01 (0.86-1.20) | .88 |
| MV + screening d | 1 | 0.97 (0.73-1.29) | 1.08 (0.78-1.49) | -- | -- | .67 | 1.03 (0.87-1.22) | .73 |
| MV + screening + hypercholesterolemia e | 1 | 0.94 (0.69-1.27) | 1.04 (0.74-1.47) | -- | -- | .79 | 1.02 (0.85-1.22) | .85 |
|  |  |  |  |  |  |  |  |  |
| **Rectal cancer** |  |  |  |  |  |  |  |  |
| No. of cases (344 in total) a | 258 | 47 | 39 | -- | -- |  |  |  |
| Age-adjusted b | 1 | 0.82 (0.59-1.12) | 0.75 (0.53-1.08) | -- | -- | .11 | 0.86 (0.71-1.04) | .13 |
| MV c | 1 | 0.84 (0.61-1.16) | 0.78 (0.54-1.13) | -- | -- | .17 | 0.88 (0.72-1.07) | .20 |
| MV + screening d | 1 | 0.86 (0.62-1.18) | 0.80 (0.55-1.16) | -- | -- | .22 | 0.89 (0.73-1.09) | .26 |
| MV + screening + hypercholesterolemia e | 1 | 0.84 (0.60-1.19) | 0.78 (0.53-1.16) | -- | -- | .23 | 0.89 (0.72-1.10) | .28 |

Abbreviations: NHS, Nurses’ Health 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 race, pack-years of smoking, physical activity, BMI, alcohol consumption, AHEI, regular use of aspirin, family history of colorectal cancer, history of diabetes mellitus, menopausal status, 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 Controlled for the same sets of covariates as denoted above, and were additionally adjusted for screening colonoscopy or sigmoidoscopy and history of hypercholesterolemia.

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

g *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.