**Supplementary Table 17. Remote period duration of statin use a and colorectal cancer risk in the pooled NHS and HPFS**

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| --- | --- | --- | --- | --- | --- | --- |
| **NHS+HPFS (Pooled)** | **Remote Period Duration of Regular Statin Use (Years)** | | | ***P*-trend** f | **Per 5-year increment**  **HR (95% CI)** | ***P*-trend** g |
| **0** | **1 to 5** | **≥6** |
| **Colorectal cancer** |  |  |  |  |  |  |
| No. of cases (880 in total) b | 723 | 105 | 52 |  |  |  |
| Age-adjusted c | 1 [Ref] | 1.05 (0.85-1.29) | 1.25 (0.93-1.68) | .13 | 1.10 (0.92-1.31) | .31 |
| MV (including screening and hypercholesterolemia) d | 1 | 1.02 (0.82-1.26) | 1.19 (0.88-1.61) | .28 | 1.06 (0.87-1.27) | .57 |
| MV (including screening and hypercholesterolemia) d + recent period duration of statin use e | 1 | 1.05 (0.83-1.33) | 1.24 (0.90-1.71) | .19 | 1.08 (0.89-1.33) | .43 |
|  |  |  |  |  |  |  |
| **Colon cancer** |  |  |  |  |  |  |
| No. of cases (634 in total) b | 508 | 81 | 45 |  |  |  |
| Age-adjusted c | 1 | 1.11 (0.87-1.41) | 1.51 (1.10-2.08) | .01 | 1.24 (1.02-1.51) | .03 |
| MV (including screening and hypercholesterolemia) d | 1 | 1.06 (0.82-1.36) | 1.41 (1.01-1.95) | .045 | 1.17 (0.95-1.44) | .13 |
| MV (including screening and hypercholesterolemia) d + recent period duration of statin use e | 1 | 1.07 (0.82-1.40) | 1.43 (1.01-2.03) | .045 | 1.18 (0.95-1.48) | .14 |
|  |  |  |  |  |  |  |
| **Proximal colon cancer** |  |  |  |  |  |  |
| No. of cases (429 in total) b | 333 | 59 | 37 |  |  |  |
| Age-adjusted c | 1 | 1.18 (0.89-1.57) | 1.78 (1.24-2.54) | .001 | 1.38 (1.11-1.73) | .004 |
| MV (including screening and hypercholesterolemia) d | 1 | 1.15 (0.85-1.54) | 1.67 (1.15-2.42) | .007 | 1.33 (1.05-1.68) | .02 |
| MV (including screening and hypercholesterolemia) d + remote period duration of statin use e | 1 | 1.11 (0.81-1.53) | 1.62 (1.09-2.41) | .02 | 1.29 (1.00-1.67) | .046 |
|  |  |  |  |  |  |  |
| **Distal colon cancer** |  |  |  |  |  |  |
| No. of cases (174 in total) b | 150 | 18 | 6 |  |  |  |
| Age-adjusted c | 1 | 0.94 (0.57-1.55) | 0.83 (0.36-1.92) | .63 | 0.84 (0.51-1.37) | .48 |
| MV (including screening and hypercholesterolemia) d | 1 | 0.88 (0.52-1.46) | 0.78 (0.33-1.83) | .50 | 0.78 (0.47-1.30) | .34 |
| MV (including screening and hypercholesterolemia) d + remote period duration of statin use e | 1 | 0.95 (0.55-1.65) | 0.86 (0.35-2.09) | .72 | 0.84 (0.48-1.44) | .52 |
|  |  |  |  |  |  |  |
| **Rectal cancer** |  |  |  |  |  |  |
| No. of cases (108 in total) b | 100 | 6 | 2 |  |  |  |
| Age-adjusted c | 1 | 0.52 (0.22-1.20) | 0.39 (0.09-1.61) | .09 | 0.47 (0.20-1.09) | .08 |
| MV (including screening and hypercholesterolemia) d | 1 | 0.72 (0.41-1.25) | 0.45 (0.16-1.25) | .08 | 0.60 (0.33-1.07) | .08 |
| MV (including screening and hypercholesterolemia) d + recent period duration of statin use e | 1 | 0.74 (0.41-1.33) | 0.46 (0.16-1.33) | .12 | 0.62 (0.33-1.15) | .13 |

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

a Remote period duration of statin use: duration of regular statin use during every specific remote period (>10 years before every follow-up period, i.e. begin from 1994 (NHS) and 1990 (HPFS), and then was extended by every 2-year subsequent interval at a time, until 2004).

b 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.

c Stratified by age and follow-up cycle in the follow-up period.

d 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, history of hypercholesterolemia, screening colonoscopy or sigmoidoscopy, multivitamin use, total calorie intake, red or processed meat intake, fiber intake, folate intake, calcium intake, and vitamin D intake in the follow-up period.

e Recent period duration of statin use: duration of regular statin use during every specific subsequent 10-year period after the remote periods.

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.