Supplemental Table 1: Age-standardized characteristics of person-years according to quintiles of **flavonols** intake in the Nurses' Health Study and in the Health Professionals Follow-Up Study

|  |  |  |
| --- | --- | --- |
|   | Health Professionals Follow-up Study  | Nurses' Health Study  |
|   | Quintile 1 | Quintile 3 | Quintile 5 | Quintile 1 | Quintile 3 | Quintile 5 |
| Age at baseline (y) | 52.0(9.6) | 52.3(9.3) | 52.8(9.2) | 49.7(7.2) | 50.2(7.1) | 50.1(7.1) |
| BMI (kg/m2) | 26.1(3.7) | 25.8(3.4) | 25.9(3.6) | 26.5(5.5) | 26.0(5.1) | 26.1(5.1) |
| Physical activity, METs/per week | 28.0(35.2) | 34.5(39.1) | 36.8(43.4) | 13.2(18.5) | 17.9(22.2) | 18.9(23.9) |
| Current/past smokers (%) | 8.0 | 4.9 | 4.9 | 18.8 | 12.3 | 12.0 |
| Pack-years of smoking before age 30 | 11.2(6.5) | 10.7(6.5) | 11.1(6.8) | 7.2(5.2) | 6.9(5.3) | 6.9(5.5) |
| Family history (%) | 11.1 | 12 | 12.2 | 13.0 | 13.3 | 13.3 |
| History of previous endoscopy (%) | 19.6 | 21.8 | 21.3 | 18.6 | 20.2 | 19.8 |
| Regular aspirin or NSAID use (%) | 38.9 | 40.7 | 41.0 | 41.8 | 41.5 | 41.9 |
| Dietary intake of |  |  |  |  |  |  |
| Alcohol (gm/day) | 7.8(13.0) | 11.6(14.2) | 12.8(16.9) | 4.6(9.8) | 6.0(9.9) | 5.8(10.6) |
| Calcium (mgm/day) | 979.2(478.5) | 960.6(449.2) | 962.1(469.2) | 1120.5(600.4) | 1186.5(585.5) | 1181.9(603.2) |
| Vitamin D (IU/day) | 431.5(303.2) | 450.6(304.0) | 459.5(330.7) | 402.6(301.6) | 430.0(302.1) | 429.0(312.9) |
| Red meat (g/day) | 70.1(53.6) | 60.0(46.1) | 55.0(47.3) | 59.2(43.2) | 54.0(38.7) | 51.7(39.4) |
| Processed meat (g/day) | 12.6(16.1) | 10.3(12.8) | 8.7(12.2) | 9.7(11.8) | 7.9(9.5) | 7.4(9.8) |
| Total flavonoids (mg/day) | 150.4(67.5) | 284.4(102.7) | 690.3(415.8) | 135.2(76.2) | 268.7(107.6) | 743.8(452.0) |
| Flavonols (mg/day) | 7.7(2.3) | 15.7(3.0) | 36.1(14.4) | 6.7(1.9) | 14.1(2.2) | 35.3(13.1) |
| Flavones (mg/d) | 1.8(1.3) | 2.8(1.8) | 3.4(2.7) | 1.5(1.2) | 2.3(1.5) | 2.5(2.0) |
| Flavanones (mg/day) | 40.3(37.5) | 56.3(44.9) | 59.3(50.6) | 32.8(33.6) | 45.2(37.6) | 45.0(40.1) |
| Flavan-3ols (mg/day) | 13.1(7.9) | 31.6(18.4) | 114.5(97.0) | 11.1(7.0) | 29.9(18.8) | 135.9(106.7) |
| Anthocyanins (mg/day) | 7.2(8.0) | 15.3(16.1) | 22.2(31.9) | 7.3(8.1) | 15.4(16.2) | 19.7(27.3) |
| Polymers (mg/day) | 79.9(43.8) | 163.5(74.8) | 459.7(321.4) | 70.2(38.5) | 157.1(68.8) | 516.2(346.8) |

NOTE: All variables (except age) are age-standardized; Continuous variables are described as mean (standard deviation); Physical activity is described by the product sum of the metabolic equivalen (MET) of each specific recreational activity and hours spent on the activity per week. Regular aspirin use is defined as ≥2 standard (325-mg) tablets of aspirin or ≥2 tablets of non-steriodal anti-inflammatory drugs (NSAIDs) per week.

Supplemental Table 2:Age-standardized characteristics of person-years according to quintiles of **flavones** intake in the Nurses' Health Study and in the Health Professionals Follow-Up Study

|  |  |  |
| --- | --- | --- |
|   | Health Professionals Follow-up Study  | Nurses' Health Study  |
|   | Quintile 1 | Quintile 3 | Quintile 5 | Quintile 1 | Quintile 3 | Quintile 5 |
| Age at baseline (y) | 51.1(9.2) | 52.5(9.3) | 53.5(9.5) | 49.0(7.1) | 49.9(7.1) | 51.5(7.0) |
| BMI (kg/m2) | 26.2(3.7) | 25.9(3.5) | 25.7(3.4) | 26.5(5.5) | 26.3(5.2) | 25.7(4.9) |
| Physical activity, METs/per week | 28.7(37.1) | 34.0(39.1) | 37.1(42.1) | 13.4(19.4) | 17.6(22.1) | 19.5(24.3) |
| Current/past smokers (%) | 9.3 | 5.0 | 3.7 | 19.7 | 12.0 | 11.6 |
| Pack-years of smoking before age 30 | 11.7(6.7) | 10.5(6.3) | 10.8(6.6) | 7.4(5.4) | 6.8(5.3) | 6.9(5.4) |
| Family history (%) | 11.3 | 12.2 | 12.1 | 12.9 | 13.5 | 13.2 |
| History of previous endoscopy (%) | 19.1 | 21.5 | 22.3 | 18.8 | 20.1 | 19.6 |
| Regular aspirin or NSAID use (%) | 39.4 | 40.7 | 41.7 | 41.7 | 41.6 | 41.3 |
| Dietary intake of |  |  |  |  |  |  |
| Alcohol (gm/day) | 10.1(15.9) | 11.0(14.0) | 12.7(16.1) | 4.8(10.7) | 5.5(9.4) | 7.0(11.4) |
| Calcium (mgm/day) | 940.5(481.0) | 965.4(440.0) | 994.3(473.8) | 1091.0(602.9) | 1175.5(573.5) | 1225.9(613.5) |
| Vitamin D (IU/day) | 421.5(309.5) | 447.0(303.1) | 478.9(328.7) | 399.6(311.2) | 423.8(296.8) | 441.3(313.6) |
| Red meat (g/day) | 71.9(55.2) | 64.3(47.3) | 46.4(40.2) | 60.8(44.7) | 57.6(40.2) | 44.6(33.8) |
| Processed meat (g/day) | 12.8(16.4) | 10.9(13.1) | 7.6(11.2) | 9.7(12.2) | 8.7(10.3) | 6.2(8.5) |
| Total flavonoids (mg/day) | 265.4(299.4) | 330.1(249.2) | 446.6(281.1) | 286.0(344.4) | 334.6(289.8) | 413.5(305.7) |
| Flavonols (mg/day) | 14.8(11.4) | 18.1(11.1) | 22.8(13.3) | 14.2(11.9) | 17.1(11.2) | 20.1(12.2) |
| Flavones (mg/d) | 0.8(0.3) | 2.4(0.4) | 5.5(2.7) | 0.6(0.2) | 1.9(0.3) | 4.4(2.1) |
| Flavanones (mg/day) | 14.1(16.8) | 48.4(21.3) | 106.8(58.7) | 10.1(14.6) | 37.4(18.2) | 86.9(46.3) |
| Flavan-3ols (mg/day) | 43.5(66.8) | 43.6(53.1) | 50.6(57.5) | 48.7(77.8) | 47.2(63.6) | 51.7(66.1) |
| Anthocyanins (mg/day) | 9.0(14.7) | 14.9(19.7) | 21.5(25.6) | 9.3(14.4) | 14.7(18.1) | 19.2(23.0) |
| Polymers (mg/day) | 184.3(227.2) | 202.9(187.9) | 243.1(209.9) | 200.7(259.6) | 212.2(216.4) | 235.2(227.8) |

NOTE: All variables (except age) are age-standardized; Continuous variables are described as mean (standard deviation); Physical activity is described by the product sum of the metabolic equivalen (MET) of each specific recreational activity and hours spent on the activity per week. Regular aspirin use is defined as ≥2 standard (325-mg) tablets of aspirin or ≥2 tablets of non-steriodal anti-inflammatory drugs (NSAIDs) per week.

Supplemental Table 3: Age-standardized characteristics of person-years according to quintiles of **flavanones** intake in the Nurses' Health Study and in the Health Professionals Follow-Up Study

|  |  |  |
| --- | --- | --- |
|   | Health Professionals Follow-up Study  | Nurses' Health Study  |
|   | Quintile 1 | Quintile 3 | Quintile 5 | Quintile 1 | Quintile 3 | Quintile 5 |
| Age at baseline (y) | 51.0(9.0) | 52.4(9.4) | 53.9(9.6) | 49.1(7.1) | 49.7(7.1) | 51.8(6.9) |
| BMI (kg/m2) | 26.2(3.7) | 25.9(3.5) | 25.6(3.4) | 26.4(5.5) | 26.3(5.2) | 25.7(4.9) |
| Physical activity, METs/per week | 29.8(37.9) | 34.4(39.1) | 35.7(41.1) | 14.5(20.5) | 17.8(22.3) | 18.3(23.6) |
| Current/past smokers (%) | 8.9 | 5 | 3.5 | 19.1 | 12.1 | 11.8 |
| Pack-years of smoking before age 30 | 11.7(6.8) | 10.6(6.3) | 10.7(6.6) | 7.4(5.5) | 6.8(5.3) | 6.8(5.4) |
| Family history (%) | 11.3 | 11.7 | 12 | 13.0 | 13.5 | 13.1 |
| History of previous endoscopy (%) | 19.9 | 21.3 | 22.1 | 19.3 | 20.2 | 19.2 |
| Regular aspirin or NSAID use (%) | 39.7 | 40.8 | 40.7 | 41.8 | 41.9 | 41.1 |
| Dietary intake of |  |  |  |  |  |  |
| Alcohol (gm/day) | 11.7(16.7) | 12.0(15.4) | 8.8(12.0) | 5.5(11.0) | 5.9(10.1) | 5.0(8.8) |
| Calcium (mgm/day) | 938.7(483.7) | 959.5(430.2) | 1008.6(484.4) | 1108.5(604.8) | 1161.7(557.8) | 1228.2(629.9) |
| Vitamin D (IU/day) | 429.5(318.7) | 442.5(299.1) | 481.0(330.3) | 406.2(316.7) | 417.7(289.0) | 443.3(317.9) |
| Red meat (g/day) | 70.0(54.8) | 67.1(49.4) | 44.8(38.7) | 60.3(45.1) | 59.7(40.7) | 42.6(32.0) |
| Processed meat (g/day) | 12.3(16.1) | 11.5(13.7) | 7.3(10.6) | 9.4(12.2) | 9.1(10.6) | 5.9(7.7) |
| Total flavonoids (mg/day) | 282.2(306.4) | 328.3(250.7) | 433.1(281.9) | 299.5(348.2) | 330.2(278.0) | 407.6(316.3) |
| Flavonols (mg/day) | 17.1(12.8) | 18.1(11.4) | 20.2(12.3) | 16.1(13.0) | 17.1(11.0) | 18.3(11.7) |
| Flavones (mg/d) | 1.3(1.6) | 2.5(1.7) | 4.7(2.1) | 1.0(1.3) | 2.0(1.1) | 3.8(1.7) |
| Flavanones (mg/day) | 7.6(5.0) | 46.1(7.0) | 122.0(48.0) | 5.1(3.8) | 34.8(6.9) | 99.0(37.9) |
| Flavan-3ols (mg/day) | 45.8(66.7) | 43.5(53.6) | 47.5(58.4) | 50.1(77.7) | 46.4(60.5) | 50.9(69.3) |
| Anthocyanins (mg/day) | 11.9(20.2) | 14.8(18.1) | 18.0(23.4) | 11.9(19.0) | 14.7(17.5) | 16.4(21.1) |
| Polymers (mg/day) | 199.1(232.2) | 202.2(188.3) | 227.2(210.4) | 212.2(261.7) | 209.3(205.8) | 227.3(237.2) |

NOTE: All variables (except age) are age-standardized; Continuous variables are described as mean (standard deviation); Physical activity is described by the product sum of the metabolic equivalen (MET) of each specific recreational activity and hours spent on the activity per week. Regular aspirin use is defined as ≥2 standard (325-mg) tablets of aspirin or ≥2 tablets of non-steriodal anti-inflammatory drugs (NSAIDs) per week.

Supplemental Table 4: Age-standardized characteristics of person-years according to quintiles of **flavan-3ols** intake in the Nurses' Health Study and in the Health Professionals Follow-Up Study

|  |  |  |
| --- | --- | --- |
|   | Health Professionals Follow-up Study  | Nurses' Health Study  |
|   | Quintile 1 | Quintile 3 | Quintile 5 | Quintile 1 | Quintile 3 | Quintile 5 |
| Age at baseline (y) | 52.4(9.5) | 52.2(9.2) | 52.5(9.3) | 49.7(7.1) | 50.4(7.1) | 49.9(7.2) |
| BMI (kg/m2) | 26.3(3.8) | 25.8(3.5) | 25.8(3.5) | 26.6(5.6) | 26.0(5.0) | 26.0(5.1) |
| Physical activity, METs/per week | 28.6(36.2) | 36.2(40.0) | 33.3(39.2) | 14.0(19.7) | 18.7(23.0) | 17.1(21.8) |
| Current/past smokers (%) | 9.4 | 4.2 | 4.8 | 20.3 | 11.4 | 11.9 |
| Pack-years of smoking before age 30 | 11.5(6.6) | 10.6(6.4) | 10.7(6.5) | 7.4(5.4) | 6.8(5.4) | 6.9(5.4) |
| Family history (%) | 11.3 | 11.9 | 11.9 | 12.9 | 13.4 | 13.3 |
| History of previous endoscopy (%) | 19.4 | 22 | 21.6 | 18.8 | 20.2 | 19.7 |
| Regular aspirin or NSAID use (%) | 39.5 | 40.8 | 41.3 | 41.4 | 40.8 | 42.1 |
| Dietary intake of |  |  |  |  |  |  |
| Alcohol (gm/day) | 8.3(13.7) | 12.1(14.0) | 11.1(15.5) | 5.1(10.3) | 6.2(10.0) | 5.1(9.6) |
| Calcium (mgm/day) | 977.3(477.7) | 978.3(455.7) | 943.9(455.9) | 1125.6(602.1) | 1204.6(597.2) | 1160.9(599.0) |
| Vitamin D (IU/day) | 431.4(305.0) | 460.3(313.5) | 447.9(316.1) | 401.5(303.2) | 435.8(308.2) | 425.9(310.6) |
| Red meat (g/day) | 72.6(55.1) | 55.4(44.2) | 58.4(46.6) | 61.0(43.6) | 50.4(37.3) | 52.5(39.1) |
| Processed meat (g/day) | 12.7(16.1) | 9.6(12.7) | 9.4(12.3) | 9.8(11.9) | 7.4(9.2) | 7.6(9.7) |
| Total flavonoids (mg/day) | 140.2(64.8) | 266.4(83.1) | 742.7(372.8) | 125.7(74.1) | 248.2(88.3) | 796.4(403.0) |
| Flavonols (mg/day) | 10.7(7.6) | 16.7(8.6) | 31.0(14.1) | 9.7(7.2) | 14.7(7.4) | 31.2(13.7) |
| Flavones (mg/d) | 2.1(1.9) | 2.9(2.0) | 2.9(2.1) | 1.8(1.7) | 2.4(1.6) | 2.2(1.7) |
| Flavanones (mg/day) | 46.3(46.9) | 56.4(44.0) | 54.5(46.0) | 37.9(39.8) | 45.2(36.9) | 42.9(38.2) |
| Flavan-3ols (mg/day) | 8.9(3.2) | 25.5(3.6) | 133.0(83.8) | 7.3(2.7) | 23.2(4.6) | 152.1(92.2) |
| Anthocyanins (mg/day) | 5.9(5.8) | 16.2(12.4) | 20.7(33.7) | 5.8(5.6) | 17.0(13.5) | 18.0(27.4) |
| Polymers (mg/day) | 66.3(34.0) | 149.9(56.6) | 506.0(283.8) | 57.8(29.5) | 142.1(49.7) | 560.2(304.6) |

NOTE: All variables (except age) are age-standardized; Continuous variables are described as mean (standard deviation); Physical activity is described by the product sum of the metabolic equivalen (MET) of each specific recreational activity and hours spent on the activity per week. Regular aspirin use is defined as ≥2 standard (325-mg) tablets of aspirin or ≥2 tablets of non-steriodal anti-inflammatory drugs (NSAIDs) per week.Supplemental Table 5: Age-standardized characteristics of person-years according to quintiles of **anthocyanins** intake in the Nurses' Health Study and in the Health Professionals Follow-Up Study

|  |  |  |
| --- | --- | --- |
|   | Health Professionals Follow-up Study  | Nurses' Health Study  |
|   | Quintile 1 | Quintile 3 | Quintile 5 | Quintile 1 | Quintile 3 | Quintile 5 |
| Age at baseline (y) | 52.1(9.5) | 52.3(9.4) | 52.7(9.3) | 50.0(7.2) | 50.0(7.1) | 50.3(7.0) |
| BMI (kg/m2) | 26.2(3.8) | 25.9(3.5) | 25.7(3.4) | 26.5(5.5) | 26.2(5.2) | 25.8(4.9) |
| Physical activity, METs/per week | 28.1(37.0) | 33.9(38.8) | 37.4(41.6) | 13.0(19.5) | 17.5(21.9) | 20.5(25.4) |
| Current/past smokers (%) | 9.4 | 4.7 | 3.5 | 21.6 | 12.0 | 10.4 |
| Pack-years of smoking before age 30 | 11.5(6.6) | 10.8(6.5) | 10.7(6.5) | 7.3(5.3) | 6.8(5.3) | 6.9(5.5) |
| Family history (%) | 11.4 | 11.6 | 12.3 | 12.9 | 13.5 | 13.4 |
| History of previous endoscopy (%) | 19 | 21 | 22.9 | 17.9 | 19.9 | 20.8 |
| Regular aspirin or NSAID use (%) | 40.3 | 40.3 | 40.5 | 42.4 | 41.7 | 40.3 |
| Dietary intake of |  |  |  |  |  |  |
| Alcohol (gm/day) | 11.3(17.1) | 10.7(13.9) | 11.9(15.4) | 5.9(11.9) | 5.4(9.3) | 6.1(10.4) |
| Calcium (mgm/day) | 935.1(463.8) | 962.8(446.0) | 1001.4(482.9) | 1066.2(578.3) | 1181.2(585.7) | 1254.8(633.5) |
| Vitamin D (IU/day) | 417.0(300.2) | 444.4(306.1) | 489.6(339.6) | 385.0(294.9) | 421.7(298.9) | 463.1(331.3) |
| Red meat (g/day) | 72.1(55.3) | 62.2(48.6) | 44.3(37.9) | 62.5(45.2) | 56.3(40.6) | 42.6(32.9) |
| Processed meat (g/day) | 13.2(16.6) | 10.7(13.6) | 7.0(10.1) | 10.2(12.4) | 8.5(10.3) | 5.8(8.0) |
| Total flavonoids (mg/day) | 247.3(278.8) | 335.7(259.2) | 462.4(296.7) | 268.6(327.7) | 336.2(294.1) | 444.9(321.6) |
| Flavonols (mg/day) | 14.6(11.6) | 18.3(11.3) | 23.0(13.0) | 14.1(11.8) | 17.1(11.1) | 20.9(12.5) |
| Flavones (mg/d) | 2.0(1.8) | 2.6(1.8) | 3.5(2.2) | 1.7(1.6) | 2.2(1.5) | 2.7(1.8) |
| Flavanones (mg/day) | 43.9(46.0) | 53.2(43.7) | 62.5(47.5) | 36.3(39.4) | 42.3(36.0) | 49.0(39.8) |
| Flavan-3ols (mg/day) | 38.1(62.9) | 44.1(56.5) | 57.1(60.2) | 43.8(74.5) | 47.3(65.4) | 59.3(69.6) |
| Anthocyanins (mg/day) | 2.3(1.5) | 10.1(4.3) | 39.8(33.3) | 2.1(1.4) | 9.9(3.9) | 38.6(29.5) |
| Polymers (mg/day) | 147.2(209.4) | 208.3(194.5) | 281.8(219.4) | 167.7(246.1) | 214.4(219.8) | 279.6(239.5) |

NOTE: All variables (except age) are age-standardized; Continuous variables are described as mean (standard deviation); Physical activity is described by the product sum of the metabolic equivalen (MET) of each specific recreational activity and hours spent on the activity per week. Regular aspirin use is defined as ≥2 standard (325-mg) tablets of aspirin or ≥2 tablets of non-steriodal anti-inflammatory drugs (NSAIDs) per week.

Supplemental table 6. Multivariable relative risks (RRs, 95% CIs) of colorectal cancer according to quintiles (Q) of flavonoid intake at baseline

|  |  |  |
| --- | --- | --- |
|  | Men | Women |
| No. of cases | 1061 | 1458 |
|   | RR | (95% CI) | RR | (95% CI) |
| Flavonols |  |  |  |  |
| Quintile 1 | 1 | Ref. | 1 | Ref. |
| Quintile 2 | 0.86 | (0.70, 1.04) | 1.10 | (0.94, 1.30) |
| Quintile 3 | 0.92 | (0.76, 1.13) | 1.02 | (0.86, 1.20) |
| Quintile 4 | 1.02 | (0.84, 1.24) | 1.05 | (0.89, 1.25) |
| Quintile 5 | 1.00 | (0.82, 1.22) | 1.13 | (0.96, 1.34) |
| p for trend |  | 0.38 |  | 0.23 |
| Flavones |  |  |  |  |
| Quintile 1 | 1 | Ref. | 1 | Ref. |
| Quintile 2 | 0.91 | (0.74, 1.11) | 0.89 | (0.74, 1.06) |
| Quintile 3 | 0.92 | (0.76, 1.13) | 0.98 | (0.82, 1.17) |
| Quintile 4 | 1.10 | (0.91, 1.33) | 0.86 | (0.72, 1.04) |
| Quintile 5 | 1.02 | (0.83, 1.24) | 0.89 | (0.74, 1.07) |
| p for trend |  | 0.33 |  | 0.25 |
| Flavanones |  |  |  |  |
| Quintile 1 | 1 | Ref. | 1 | Ref. |
| Quintile 2 | 1.03 | (0.84, 1.25) | 0.99 | (0.83, 1.19) |
| Quintile 3 | 1.10 | (0.91, 1.34) | 1.02 | (0.85, 1.22) |
| Quintile 4 | 1.04 | (0.86, 1.27) | 0.93 | (0.78, 1.12) |
| Quintile 5 | 1.00 | (0.82, 1.22) | 0.97 | (0.81, 1.17) |
| p for trend |  | 0.95 |  | 0.63 |
| Flavan-3ols |  |  |  |  |
| Quintile 1 | 1 | Ref. | 1 | Ref. |
| Quintile 2 | 0.93 | (0.76, 1.13) | 0.80 | (0.66, 0.96) |
| Quintile 3 | 0.99 | (0.82, 1.21) | 1.05 | (0.89, 1.25) |
| Quintile 4 | 1.09 | (0.89, 1.32) | 0.95 | (0.79, 1.13) |
| Quintile 5 | 1.02 | (0.84, 1.24) | 0.99 | (0.83, 1.18) |
| p for trend |  | 0.56 |  | 0.54 |
| Anthocyanidins |  |  |  |
| Quintile 1 | 1 | Ref. | 1 | Ref. |
| Quintile 2 | 0.94 | (0.77, 1.13) | 0.99 | (0.83, 1.18) |
| Quintile 3 | 0.82 | (0.68, 1.00) | 0.85 | (0.71, 1.02) |
| Quintile 4 | 1.09 | (0.90, 1.31) | 0.90 | (0.75, 1.08) |
| Quintile 5 | 0.86 | (0.71, 1.05) | 0.93 | (0.78, 1.12) |
| p for trend |  | 0.60 |  | 0.53 |

Multivariable relative risks were adjusted for age (in months), smoking before age 30, history of colorectal cancer in a parent or sibling (yes or no), history of endoscopy (yes or no), regular aspirin use (yes, no), postmenopausal hormone use (yes or no, in women only), body mass index (<25, 25 to <30, ≥30 kg/m2), physical activity (low, medium, high), alcohol consumption (0 to <5, 5 to <10, 10 to <15, or ≥15 g/day), total calories (quintiles), energy-adjusted total vitamin D intake (quintiles), total calcium intake (quintiles), red meat intake (quintiles), processed meat intake (quintiles)

Supplemental table 7. Multivariable relative risks (RRs, 95% CIs) of colorectal cancer according to quintiles (Q) of flavonoid intake (cumulative updated average with different lags)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   | Recent (0-4 year lag) | 4-8 year lag | 8-12 year lag | 12-16 year lag |
|  | Men | Women | Men | Women | Men | Women | Men | Women |
| No. of cases | 1061 | 1458 | 877 | 1183 | 689 | 1084 | 473 | 960 |
|   | RR | (95% CI) | RR | (95% CI) | RR | (95% CI) | RR | (95% CI) | RR | (95% CI) | RR | (95% CI) | RR | (95% CI) | RR | (95% CI) |
| Flavonols |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Quintile 1 | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. |
| Quintile 2 | 1.03 | (0.84, 1.25) | 1.20 | (1.01, 1.41) | 0.93 | (0.75, 1.17) | 0.94 | (0.78, 1.14) | 1.02 | (0.80, 1.30) | 0.95 | (0.78, 1.15) | **0.73** | **(0.54, 0.98)** | 1.00 | (0.82, 1.23) |
| Quintile 3 | 0.95 | (0.78, 1.17) | 1.09 | (0.92, 1.30) | 0.94 | (0.75, 1.17) | 0.97 | (0.81, 1.17) | 0.90 | (0.70, 1.16) | 1.00 | (0.82, 1.21) | 0.91 | (0.69, 1.21) | 1.03 | (0.84, 1.26) |
| Quintile 4 | 1.05 | (0.86, 1.28) | 1.15 | (0.97, 1.36) | 1.19 | (0.96, 1.48) | 1.00 | (0.83, 1.21) | 1.16 | (0.91, 1.47) | 1.03 | (0.85, 1.24) | 0.91 | (0.69, 1.22) | 1.06 | (0.86, 1.30) |
| Quintile 5 | 1.11 | (0.91, 1.34) | 1.22 | (1.03, 1.44) | 1.05 | (0.84, 1.30) | 1.04 | (0.86, 1.25) | 1.03 | (0.80, 1.31) | 0.97 | (0.79, 1.17) | 0.84 | (0.63, 1.12) | 1.00 | (0.81, 1.23) |
| p for trend |  | 0.23 |  | 0.07 |  | 0.23 |  | 0.44 |  | 0.57 |  | 0.93 |  | 0.64 |  | 0.96 |
| Flavones |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Quintile 1 | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. |
| Quintile 2 | 0.91 | (0.75, 1.11) | 0.96 | (0.81, 1.13) | 0.91 | (0.73, 1.13) | 0.99 | (0.82, 1.19) | 0.88 | (0.69, 1.12) | 0.90 | (0.74, 1.09) | 0.96 | (0.71, 1.29) | 1.06 | (0.87, 1.30) |
| Quintile 3 | 0.98 | (0.81, 1.19) | 1.01 | (0.85, 1.19) | 1.07 | (0.87, 1.32) | 0.99 | (0.82, 1.19) | 1.07 | (0.85, 1.36) | 0.95 | (0.78, 1.15) | 1.19 | (0.90, 1.59) | 0.97 | (0.79, 1.19) |
| Quintile 4 | 0.95 | (0.78, 1.15) | 0.98 | (0.83, 1.16) | 0.98 | (0.79, 1.22) | 0.92 | (0.76, 1.12) | 0.92 | (0.72, 1.17) | 0.90 | (0.74, 1.09) | 1.05 | (0.78, 1.42) | 0.98 | (0.79, 1.21) |
| Quintile 5 | 0.99 | (0.82, 1.21) | 0.96 | (0.82, 1.14) | 0.98 | (0.78, 1.22) | 0.98 | (0.81, 1.18) | 0.85 | (0.66, 1.09) | 0.94 | (0.77, 1.14) | 0.98 | (0.72, 1.33) | 1.05 | (0.85, 1.29) |
| p for trend |  | 0.87 |  | 0.76 |  | 0.95 |  | 0.66 |  | 0.28 |  | 0.64 |  | 0.99 |  | 0.89 |
| Flavanones |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Quintile 1 | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. |
| Quintile 2 | 1.03 | (0.84, 1.26) | 0.86 | (0.73, 1.02) | 0.93 | (0.75, 1.16) | 0.96 | (0.80, 1.15) | 0.86 | (0.68, 1.10) | 0.94 | (0.77, 1.14) | **0.71** | **(0.53, 0.96)** | 1.05 | (0.86, 1.29) |
| Quintile 3 | 1.14 | (0.94, 1.39) | 0.92 | (0.78, 1.08) | 1.14 | (0.93, 1.41) | 0.96 | (0.80, 1.16) | 0.99 | (0.78, 1.25) | 0.95 | (0.78, 1.15) | 1.08 | (0.83, 1.42) | 1.11 | (0.91, 1.36) |
| Quintile 4 | 1.11 | (0.91, 1.35) | 0.96 | (0.82, 1.13) | 0.96 | (0.77, 1.20) | 0.88 | (0.73, 1.07) | 0.95 | (0.74, 1.20) | 0.96 | (0.79, 1.16) | 0.87 | (0.65, 1.16) | 0.90 | (0.72, 1.11) |
| Quintile 5 | 1.05 | (0.86, 1.29) | 0.92 | (0.78, 1.08) | 0.98 | (0.79, 1.23) | 0.97 | (0.81, 1.17) | 0.83 | (0.65, 1.07) | 1.01 | (0.83, 1.23) | **0.73** | **(0.54, 1.00)** | 1.08 | (0.88, 1.33) |
| p for trend |  | 0.57 |  | 0.74 |  | 0.93 |  | 0.66 |  | 0.30 |  | 0.76 |  | 0.17 |  | 0.92 |
| Flavan-3ols |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Quintile 1 | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. |
| Quintile 2 | 0.89 | (0.73, 1.08) | 0.90 | (0.76, 1.06) | 1.11 | (0.89, 1.38) | 0.89 | (0.74, 1.08) | 0.96 | (0.74, 1.23) | 0.90 | (0.74, 1.10) | 0.95 | (0.70, 1.28) | 0.85 | (0.69, 1.05) |
| Quintile 3 | 1.05 | (0.86, 1.27) | 0.94 | (0.80, 1.10) | 1.13 | (0.90, 1.41) | 0.91 | (0.76, 1.10) | 1.26 | (0.99, 1.61) | 1.01 | (0.84, 1.22) | 1.14 | (0.85, 1.52) | 1.03 | (0.84, 1.26) |
| Quintile 4 | 0.96 | (0.79, 1.16) | 0.91 | (0.77, 1.08) | 1.24 | (1.00, 1.55) | 0.94 | (0.78, 1.13) | 1.12 | (0.88, 1.44) | 0.94 | (0.77, 1.14) | 1.06 | (0.79, 1.42) | 0.96 | (0.79, 1.18) |
| Quintile 5 | 1.03 | (0.85, 1.24) | 1.02 | (0.87, 1.20) | 1.17 | (0.94, 1.45) | 1.00 | (0.83, 1.19) | 1.13 | (0.89, 1.45) | 0.98 | (0.81, 1.18) | 1.02 | (0.76, 1.37) | 0.95 | (0.77, 1.16) |
| p for trend |  | 0.54 |  | 0.27 |  | 0.27 |  | 0.46 |  | 0.41 |  | 0.93 |  | 0.92 |  | 0.94 |
| Anthocyanidins |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Quintile 1 | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. | 1 | Ref. |
| Quintile 2 | 0.97 | (0.80, 1.17) | 0.98 | (0.83, 1.15) | 0.93 | (0.75, 1.15) | 1.01 | (0.84, 1.21) | 0.94 | (0.75, 1.19) | 0.86 | (0.71, 1.04) | **0.68** | **(0.51, 0.91)** | 1.00 | (0.81, 1.22) |
| Quintile 3 | 0.93 | (0.76, 1.12) | 1.00 | (0.85, 1.18) | 0.97 | (0.79, 1.20) | 1.10 | (0.91, 1.32) | 0.80 | (0.63, 1.02) | 0.82 | (0.68, 1.00) | 0.84 | (0.63, 1.11) | 0.96 | (0.78, 1.18) |
| Quintile 4 | 0.99 | (0.82, 1.20) | 0.98 | (0.83, 1.16) | 0.95 | (0.77, 1.17) | 1.01 | (0.83, 1.22) | 0.89 | (0.70, 1.13) | 0.86 | (0.71, 1.05) | 0.89 | (0.68, 1.18) | 0.96 | (0.78, 1.18) |
| Quintile 5 | 0.90 | (0.74, 1.10) | 1.09 | (0.92, 1.28) | 0.92 | (0.74, 1.15) | 1.04 | (0.86, 1.26) | 0.83 | (0.65, 1.07) | 0.94 | (0.78, 1.14) | **0.70** | **(0.52, 0.95)** | 1.08 | (0.88, 1.34) |
| p for trend |   | 0.41 |   | 0.26 |   | 0.57 |   | 0.83 |   | 0.20 |   | 0.90 |   | 0.19 |   | 0.41 |

Multivariable relative risks were adjusted for age (in months), smoking before age 30, history of colorectal cancer in a parent or sibling (yes or no), history of endoscopy (yes or no), regular aspirin use (yes, no), postmenopausal hormone use (yes or no, in women only), body mass index (<25, 25 to <30, ≥30 kg/m2), physical activity (low, medium, high), alcohol consumption (0 to <5, 5 to <10, 10 to <15, or ≥15 g/day), total calories (quintiles), energy-adjusted total vitamin D intake (quintiles), total calcium intake (quintiles), red meat intake (quintiles), processed meat intake (quintiles)

Statistically significant results are shown in **bold**.

Supplemental table 8: Relative risks (RRs, 95% CIs) of colorectal cancer according to categories of selected flavonoid-rich foods (cumulative updated average intake)

|  |  |  |  |
| --- | --- | --- | --- |
|   | Colorectal | Colon | Rectum |
|   | Men | Women | Men | Women | Men | Women |
|   | No. of cases | RR | (95% CI) | No. of cases | RR | (95% CI) | No. of cases | RR | (95% CI) | No. of cases | RR | (95% CI) | No. of cases | RR | (95% CI) | No. of cases | RR | (95% CI) |
| Blueberries |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| <1 svg/mo | 778 | 1.00 | (Ref.) | 593 | 1.00 | (Ref.) | 619 | 1.00 | (Ref.) | 473 | 1.00 | (Ref.) | 159 | 1.00 | (Ref.) | 778 | 1.00 | (Ref.) |
| 1-3 svg/mo | 193 | 1.02 | (0.86-1.20) | 528 | 1.08 | (0.95-1.22) | 145 | 0.95 | (0.79-1.14) | 418 | 1.08 | (0.93-1.25) | 48 | 1.28 | (0.92-1.79) | 193 | 1.02 | (0.86-1.20) |
| ≥1 svg/wk | 68 | 0.95 | (0.74-1.23) | 333 | 1.10 | (0.95-1.27) | 51 | 0.89 | (0.66-1.20) | 256 | 1.06 | (0.90-1.25) | 17 | 1.22 | (0.72-2.04) | 68 | 0.95 | (0.74-1.23) |
| p for trend |  |  | 0.67 |  |  | 0.33 |  |  | 0.86 |  |  | 0.28 |  |  | 0.18 |  |  | 0.67 |
| Oranges |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| <1 svg/mo | 216 | 1.00 | (Ref.) | 178 | 1.00 | (Ref.) | 167 | 1.00 | (Ref.) | 138 | 1.00 | (Ref.) | 49 | 1.00 | (Ref.) | 216 | 1.00 | (Ref.) |
| 1-3 svg/mo | 245 | 1.10 | (0.92-1.33) | 297 | 0.97 | (0.80-1.17) | 190 | 1.12 | (0.91-1.39) | 236 | 1.01 | (0.81-1.25) | 55 | 1.05 | (0.71-1.55) | 245 | 1.10 | (0.92-1.33) |
| 1 svg/wk | 314 | 1.12 | (0.93-1.34) | 535 | 0.96 | (0.81-1.15) | 246 | 1.15 | (0.94-1.41) | 422 | 0.98 | (0.81-1.20) | 68 | 1.01 | (0.69-1.48) | 314 | 1.12 | (0.93-1.34) |
| ≥2 svg/wk | 269 | 1.08 | (0.89-1.30) | 446 | 1.00 | (0.83-1.21) | 213 | 1.11 | (0.90-1.38) | 354 | 1.03 | (0.84-1.27) | 56 | 0.95 | (0.63-1.43) | 269 | 1.08 | (0.89-1.30) |
| p for trend |  |  | 0.42 |  |  | 0.98 |  |  | 0.53 |  |  | 0.85 |  |  | 0.61 |  |  | 0.42 |
| Tea |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| <1 svg/mo | 414 | 1.00 | (Ref.) | 274 | 1.00 | (Ref.) | 314 | 1.00 | (Ref.) | 215 | 1.00 | (Ref.) | 100 | 1.00 | (Ref.) | 414 | 1.00 | (Ref.) |
| 1-3 svg/mo | 124 | 1.10 | (0.90-1.35) | 191 | 0.79 | (0.65-0.96) | 98 | 1.13 | (0.90-1.43) | 150 | 0.80 | (0.64-0.99) | 26 | 1.01 | (0.65-1.56) | 124 | 1.10 | (0.90-1.35) |
| 1 svg/wk | 167 | 1.06 | (0.88-1.28) | 271 | 0.90 | (0.76-1.06) | 136 | 1.15 | (0.93-1.41) | 223 | 0.94 | (0.78-1.14) | 31 | 0.81 | (0.54-1.22) | 167 | 1.06 | (0.88-1.28) |
| 2-4 svg/wk | 130 | 1.11 | (0.90-1.35) | 171 | 0.84 | (0.69-1.02) | 106 | 1.18 | (0.94-1.48) | 142 | 0.88 | (0.71-1.09) | 24 | 0.85 | (0.54-1.34) | 130 | 1.11 | (0.90-1.35) |
| ≥5 svg/wk | 204 | 1.10 | (0.92-1.30) | 548 | 0.95 | (0.82-1.11) | 162 | 1.14 | (0.94-1.38) | 418 | 0.93 | (0.79-1.10) | 42 | 0.97 | (0.67-1.41) | 204 | 1.10 | (0.92-1.30) |
| p for trend |  |  | 0.51 |  |  | 0.32 |  |  | 0.61 |  |  | 0.43 |  |  | 0.66 |  |  | 0.51 |

Multivariable relative risks were adjusted for age (in months), smoking before age 30, history of colorectal cancer in a parent or sibling (yes or no), history of endoscopy (yes or no), regular aspirin use (yes, no), body mass index (<25, 25 to <30, ≥30 kg/m2), physical activity (low, medium, high), alcohol consumption (0 to <5, 5 to <10, 10 to <15, or ≥15 g/day), total calories (quintiles), energy-adjusted total vitamin D intake (quintiles), and total calcium intake (quintiles) and total red meat intake (quintiles)

p for trend based on continuous variables (servings/day)

Numbers of cases are slightly different by food type due to missing values

svg/mo=servings per month; svg/wk=servings per week