

| <b>Supplemental Table 1.</b> Spearman correlations between olive oil intake and other types of fat at the mid-point of follow-up (2000). |                  |                  |               |                   |                             |                  |                           |
|--|------------------|------------------|---------------|-------------------|-----------------------------|------------------|---------------------------|
| <b>NHS</b>   |                  |                  |               |                   |                             |                  |                           |
|  | <b>Olive oil</b> | <b>Margarine</b> | <b>Butter</b> | <b>Mayonnaise</b> | <b>Other vegetable oils</b> | <b>Dairy fat</b> | <b>All other diet fat</b> |
| <b>Olive oil</b>   | 1                | -0.10*           | 0.16*         | -0.04*            | -0.03*                      | -0.04*           | -0.10*                    |
| <b>Margarine</b>   | -0.10*           | 1                | -0.23*        | 0.11*             | 0.12*                       | -0.04*           | 0.72*                     |
| <b>Butter</b>  | 0.16*            | -0.23*           | 1             | 0.14*             | 0.09*                       | 0.41*            | 0.08*                     |
| <b>Mayonnaise</b>  | -0.04*           | 0.11*            | 0.14*         | 1                 | 0.77*                       | 0.21*            | 0.52*                     |
| <b>Other plant oils</b>  | -0.03*           | 0.12*            | 0.09*         | 0.77*             | 1                           | 0.15*            | 0.50*                     |
| <b>Dairy fat</b>   | -0.04*           | -0.04*           | 0.41*         | 0.21*             | 0.15*                       | 1                | 0.43*                     |
| <b>All other diet fat</b>  | -0.10*           | 0.72*            | 0.08*         | 0.52*             | 0.50*                       | 0.43*            | 1                         |
| <b>HPFS</b>  |                  |                  |               |                   |                             |                  |                           |
| <b>Olive oil</b>   | 1                | -0.11*           | 0.13*         | -0.02*            | -0.03*                      | -0.02*           | -0.08*                    |
| <b>Margarine</b>   | -0.11*           | 1                | -0.12*        | 0.19*             | 0.20*                       | 0.12*            | 0.69*                     |
| <b>Butter</b>  | 0.13*            | -0.12*           | 1             | 0.14*             | 0.07*                       | 0.39*            | 0.16*                     |
| <b>Mayonnaise</b>  | -0.02*           | 0.19*            | 0.14*         | 1                 | 0.74*                       | 0.28*            | 0.58*                     |
| <b>Other plant oils</b>  | -0.03*           | 0.20*            | 0.07*         | 0.74*             | 1                           | 0.25*            | 0.57*                     |
| <b>Dairy fat</b>   | -0.02*           | 0.12*            | 0.39*         | 0.28*             | 0.25*                       | 1                | 0.61*                     |
| <b>All other diet fat</b>  | -0.08*           | 0.69*            | 0.16*         | 0.58*             | 0.57*                       | 0.61*            | 1                         |

NHS, Nurses' Health Study; HPFS, Health Professionals Follow-up Study; \*, P value <0.001. *All other fat is the sum of dairy fat, other plant oils, margarine, butter and mayonnaise.*

| <b>Supplemental Table 2. Relative risk (95% CI) of ischemic stroke</b> |                   |                   |                   |
|--|-------------------|-------------------|-------------------|
|  | <b>NHS</b>        | <b>HPFS</b>       | <b>Pooled</b>     |
| <b>Age-adjusted model</b>  | 0.96 (0.89, 1.03) | 0.95 (0.84, 1.07) | 0.96 (0.90, 1.02) |
| <b>Multivariable model</b>   | 1.01 (0.94, 1.09) | 0.91 (0.80, 1.03) | 0.99 (0.93, 1.05) |

*Results are expressed as Hazard Ratios (HR) and 95% Confidence Intervals (95% CI) per 5g increment in olive oil intake. Abbreviations: CVD, cardiovascular disease; NHS, Nurses' Health Study, HPFS, Health Professionals Follow-up Study. The multivariable model was adjusted for age (years), ethnicity (white, non-white), Southern European/Mediterranean ancestry (yes, no), smoking status (never, former, current smoker 1-14 cigarettes per day, 15-24 cigarettes per day, or ≥ 25 cigarettes per day), alcohol intake (0, 0.1-4.9, 5.0-9.9, 10.0-14.9, and ≥ 15.0 g/d), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥27.00 metabolic equivalent task-h/week), family history of diabetes mellitus (yes/no), family history of myocardial infarction (yes/no), family history of cancer (yes/no), baseline diabetes mellitus (yes/no), baseline hypertension or antihypertensive medication use (yes/no), baseline hypercholesterolemia or cholesterol-lowering medication use (yes/no), multivitamin use (yes/no), aspirin use (yes/no), in women postmenopausal status and menopausal hormone use [premenopausal, postmenopausal (no, past, or current hormone use), total energy intake (kilocalories per day), body mass index (calculated as weight in kilograms divides by height in meters squared), for red meat, fruits and vegetables, nuts, soda, whole grains intake (in quintiles), and trans. Results were pooled with the use of fixed-effect models.*

| <b>Supplemental Table 3. Relative risk (95% CI) of cardiovascular disease mutually adjusting for other types of dietary fats</b> |                   |                   |                   |
|--|-------------------|-------------------|-------------------|
|  | <b>NHS</b>        | <b>HPFS</b>       | <b>Pooled</b>     |
| <b>Total Cardiovascular disease</b>  | 0.95 (0.91, 0.98) | 0.95 (0.91, 1.00) | 0.95 (0.93, 0.98) |
| <b>Coronary Heart Disease</b>  | 0.94 (0.89, 0.99) | 0.95 (0.90, 1.01) | 0.95 (0.91, 0.99) |
| <b>Stroke</b>  | 0.96 (0.91, 1.02) | 0.97 (0.88, 1.06) | 0.96 (0.92, 1.01) |

*Results are expressed as Hazard Ratios (HR) and 95% Confidence Intervals (95% CI) per 5g increment in olive oil intake. Abbreviations: CVD, cardiovascular disease; NHS, Nurses' Health Study, HPFS, Health Professionals Follow-up Study. The multivariable model was adjusted for age (years), ethnicity (white, non-white), Southern European/Mediterranean ancestry (yes, no), smoking status (never, former, current smoker 1-14 cigarettes per day, 15-24 cigarettes per day, or ≥ 25 cigarettes per day), alcohol intake (0, 0.1-4.9, 5.0-9.9, 10.0-14.9, and ≥ 15.0 g/d), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, ≥27.00 metabolic equivalent task-h/week), family history of diabetes (yes/no), family history of myocardial infarction (yes/no), family history of cancer (yes/no), baseline diabetes mellitus (yes/no), baseline hypertension or antihypertensive medication use (yes/no), baseline hypercholesterolemia or cholesterol-lowering medication use (yes/no), multivitamin use (yes/no), aspirin use (yes/no), in women postmenopausal status and menopausal hormone use [premenopausal, postmenopausal (no, past, or current hormone use), total energy intake (kilocalories per day), body mass index (calculated as weight in kilograms divides by height in meters squared), for red meat, fruits and vegetables, nuts, soda, whole grains intake (in quintiles), trans fat and mutually adjusted for other types of dietary fat (mayonnaise, margarine, dairy fat and other plant oils). Results were pooled with the use of fixed-effect models.*

**Supplemental table 4. Relative risk (95% CI) of fatal and nonfatal cardiovascular events according to categories of total olive oil intake**

|   |                        | Categories of olive oil intake     |  |                                |                   | <i>P</i> for trend | HR (95% CI)<br>for 5 g increase<br>in olive oil<br>intake |
|---|------------------------|------------------------------------|--|--------------------------------|-------------------|--------------------|---|
|   | Never or<br><1/month   | >0–≤4.5 g/d<br>(>0 to ≤1 teaspoon) | >4.5–≤ 7 g/d<br>>1 teaspoon to ≤1/2<br>tablespoon) | >7 g/d<br>(>1/2<br>Tablespoon) |                   |                    |   |
| <b>FATAL CVD: fatal myocardial infarction + fatal stroke</b>          |                        |                                    |  |                                |                   |                    |   |
| <b>NHS</b>  | Mean total olive oil   | 0                                  | 1.5 (± 1.2)  | 5.6 (± 0.7)                    | 11.7 (± 5.7)      |                    |   |
|   | N° cases/ Person-years | 727/399686                         | 772/638583   | 96/106313                      | 139/150743        |                    |   |
|   | Age-adjusted model     | 1 (Ref.)                           | 0.62 (0.56, 0.69)                                  | 0.53 (0.42, 0.65)              | 0.55 (0.46, 0.66) | <0.001             | 0.77 (0.71, 0.83)   |
|   | Multivariable model    | 1 (Ref.)                           | 0.77 (0.69, 0.85)                                  | 0.73 (0.59, 0.91)              | 0.84 (0.69, 1.02) | 0.18               | 0.90 (0.83, 0.97)   |
| <b>HPFS</b>   | Mean total olive oil   | 0                                  | 1.5 (± 1.2)  | 5.6 (± 0.7)                    | 11.2 (± 5.4)      |                    |   |
|   | N° cases/ Person-years | 945/191480                         | 957/308406   | 126/45995                      | 151/55468         |                    |   |
|   | Age-adjusted model     | 1 (Ref.)                           | 0.68 (0.62, 0.74)                                  | 0.63 (0.52, 0.76)              | 0.65 (0.54, 0.77) | <0.001             | 0.86 (0.80, 0.93)   |
|   | Multivariable model    | 1 (Ref.)                           | 0.77 (0.70, 0.85)                                  | 0.75 (0.62, 0.91)              | 0.79 (0.65, 0.94) | 0.02               | 0.93 (0.87, 1.00)   |
| <b>Pooled Model 3</b>   |                        | 1 (Ref.)                           | 0.77 (0.72, 0.83)                                  | 0.74 (0.64, 0.86)              | 0.81 (0.71, 0.93) | 0.01               | 0.92 (0.87, 0.97)   |
| <b>NONFATAL CVD: nonfatal myocardial infarction + nonfatal stroke</b> |                        |                                    |  |                                |                   |                    |   |
| <b>NHS</b>  | N° cases/ Person-years | 1348/399602                        | 1984/638521  | 280/106308                     | 368/150733        |                    |   |
|   | Age-adjusted model     | 1 (Ref.)                           | 0.92 (0.86, 0.99)                                  | 0.82 (0.71, 0.93)              | 0.77 (0.69, 0.86) | <0.001             | 0.90 (0.86, 0.95)   |
|   | Multivariable model    | 1 (Ref.)                           | 1.00 (0.93, 1.08)                                  | 0.95 (0.83, 1.08)              | 0.93 (0.82, 1.05) | 0.17               | 0.97 (0.92, 1.01)   |
| <b>HPFS</b>   | N° cases/ Person-years | 882/191510                         | 1214/308437  | 147/45999                      | 178/55475         |                    |   |
|   | Age-adjusted model     | 1 (Ref.)                           | 0.93 (0.85, 1.02)                                  | 0.77 (0.64, 0.91)              | 0.80 (0.67, 0.94) | 0.002              | 0.90 (0.84, 0.96)   |
|   | Multivariable model    | 1 (Ref.)                           | 0.96 (0.88, 1.06)                                  | 0.82 (0.68, 0.98)              | 0.86 (0.73, 1.03) | 0.03               | 0.93 (0.87, 0.99)   |
| <b>Pooled model 3</b>   |                        | 1 (Ref.)                           | 0.99 (0.93, 1.05)                                  | 0.90 (0.91, 1.00)              | 0.91 (0.82, 1.01) | 0.02               | 0.96 (0.92, 0.99)   |

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*Results are expressed as Hazard Ratios (HR) and 95% Confidence Intervals (95% CI). Abbreviations: NHS, Nurses' Health Study, HPFS, Health Professionals Follow-up Study. The multivariable model was adjusted for age (years), ethnicity (white, non-white), Southern European/Mediterranean ancestry (yes, no), smoking status (never, former, current smoker 1-14 cigarettes per day, 15-24 cigarettes per day, or  $\geq 25$  cigarettes per day), alcohol intake (0, 0.1-4.9, 5.0-9.9, 10.0-14.9, and  $\geq 15.0$  g/d), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9,  $\geq 27.00$  metabolic equivalent task-h/week), family history of diabetes (yes/no), family history of myocardial infarction (yes/no), family history of cancer (yes/no), baseline diabetes mellitus (yes/no), baseline hypertension or antihypertensive medication use (yes/no), baseline hypercholesterolemia or cholesterol-lowering medication use (yes/no), multivitamin use (yes/no), aspirin use (yes/no), in women postmenopausal status and menopausal hormone use [premenopausal, postmenopausal (no, past, or current hormone use), total energy intake (kilocalories per day), body mass index (calculated as weight in kilograms divided by height in meters squared), red meat, fruits and vegetables, nuts, soda, whole grains intake (in quintiles), and trans fat. Results were pooled with the use of fixed-effect models.*

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**Supplemental Table 5. Relative risk (95% CI) of cardiovascular events according to categories of total olive oil intake adjusted for diet quality**

|  |                     | Categories of olive oil intake |                                    |  |                      | <i>P</i> for trend | HR (95% CI)<br>for 5 g increase<br>in olive oil<br>intake |
|--|---------------------|--------------------------------|------------------------------------|--|----------------------|--------------------|---|
|  |                     | Never or<br><1/month           | >0–≤4.5 g/d<br>(>0 to ≤1 teaspoon) | >4.5–≤7 g/d<br>>1 teaspoon to ≤1/2<br>TBS) | >7 g/d<br>(>1/2 TBS) |                    |   |
| <b>TOTAL CVD: fatal and nonfatal myocardial infarction + fatal and nonfatal stroke</b> |                     |                                |                                    |  |                      |                    |   |
| <b>NHS</b>   |                     |                                |                                    |  |                      |                    |   |
|  | Multivariable model | 1 (Ref.)                       | 0.91 (0.85, 0.97)                  | 0.87 (0.77, 0.98)                          | 0.88 (0.78, 0.97)    | 0.04               | 0.94 (0.91, 0.98)   |
| <b>HPFS</b>  |                     |                                |                                    |  |                      |                    |   |
|  | Multivariable model | 1 (Ref.)                       | 0.86 (0.80, 0.92)                  | 0.78 (0.68, 0.89)                          | 0.84 (0.73, 0.95)    | 0.001              | 0.94 (0.89, 0.98)   |
|  | <b>Pooled Model</b> | 1 (Ref.)                       | 0.89 (0.85, 0.93)                  | 0.83 (0.76, 0.91)                          | 0.86 (0.79, 0.94)    | <0.001             | 0.94 (0.92, 0.97)   |
| <b>CORONARY HEART DISEASE: fatal and nonfatal myocardial infarction</b>                |                     |                                |                                    |  |                      |                    |   |
| <b>NHS</b>   |                     |                                |                                    |  |                      |                    |   |
|  | Multivariable model | 1 (Ref.)                       | 0.90 (0.83, 0.98)                  | 0.84 (0.71, 0.99)                          | 0.88 (0.76, 1.02)    | 0.05               | 0.94 (0.89, 0.99)   |
| <b>HPFS</b>  |                     |                                |                                    |  |                      |                    |   |
|  | Multivariable model | 1 (Ref.)                       | 0.81 (0.75, 0.87)                  | 0.79 (0.68, 0.93)                          | 0.76 (0.65, 0.89)    | 0.003              | 0.93 (0.87, 0.98)   |
|  | <b>Pooled model</b> | 1 (Ref.)                       | 0.85 (0.80, 0.90)                  | 0.82 (0.73, 0.92)                          | 0.82 (0.74, 0.92)    | <0.001             | 0.93 (0.90, 0.97)   |
| <b>STROKE: fatal and nonfatal stroke</b>   |                     |                                |                                    |  |                      |                    |   |
| <b>NHS</b>   |                     |                                |                                    |  |                      |                    |   |
|  | Multivariable model | 1 (Ref.)                       | 0.94 (0.86, 1.03)                  | 0.91 (0.77, 1.07)                          | 0.89 (0.76, 1.04)    | 0.17               | 0.95 (0.90, 1.01)   |
| <b>HPFS</b>  |                     |                                |                                    |  |                      |                    |   |
|  | Multivariable model | 1 (Ref.)                       | 1.02 (0.89, 1.17)                  | 0.75 (0.57, 0.98)                          | 1.06 (0.84, 1.34)    | 0.65               | 0.96 (0.88, 1.05)   |
|  | <b>Pooled model</b> | 1 (Ref.)                       | 0.97 (0.90, 1.04)                  | 0.86 (0.75, 0.99)                          | 0.94 (0.83, 1.07)    | 0.16               | 0.96 (0.91, 1.00)   |

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*Results are expressed as Hazard Ratios (HR) and 95% Confidence Intervals (95% CI). Abbreviations: NHS, Nurses' Health Study, HPFS, Health Professionals Follow-up Study. Model was adjusted for age (years), ethnicity (white, non-white), Southern European/Mediterranean ancestry (yes, no), smoking status (never, former, current smoker 1-14 cigarettes per day, 15-24 cigarettes per day, or  $\geq 25$  cigarettes per day), alcohol intake (0, 0.1-4.9, 5.0-9.9, 10.0-14.9, and  $\geq 15.0$  g/d), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9,  $\geq 27.00$  metabolic equivalent task-h/week), family history of diabetes (yes/no), family history of myocardial infarction (yes/no), family history of cancer (yes/no), baseline diabetes mellitus (yes/no), baseline hypertension or antihypertensive medication use (yes/no), baseline hypercholesterolemia or cholesterol-lowering medication use (yes/no), multivitamin use (yes/no), aspirin use (yes/no), in women postmenopausal status and menopausal hormone use [premenopausal, postmenopausal (no, past, or current hormone use), total energy intake (kilocalories per day) and body mass index (calculated as weight in kilograms divides by height in meters squared) and quintiles of the Alternative Healthy Eating index (AHEI) without the polyunsaturated:saturated fat ratio. Results were pooled with the use of fixed-effect models.*

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## Supplementary Figure 2. Associations between olive oil intake at baseline and blood lipid levels in the NHS, NHS2, and HPFS.

Linear regressions were used to analyze the association between olive oil intake categories (cumulative average scores of 1990 and 1994 in NHS and HPFS, and 1991 and 1995 in NHSII) and blood lipid levels assessed using blood samples (1989-1990 in NHS, 1993-1995 in HPFS, and 1996-1999 in NHSII). Analysis were conducted only on participants not taking lipid-lowering medication and without self-reported hypercholesterolemia. Multivariable models were adjusted for study cohort, age, fasting status, body mass index, ethnicity (white, non-white), Southern European/Mediterranean ancestry, smoking status, alcohol intake, physical activity, family history of diabetes, family history of myocardial infarction, baseline diabetes mellitus, baseline hypertension, steroid use, multivitamin use, aspirin use, in women postmenopausal status and menopausal hormone use [premenopausal, postmenopausal (no, past, or current hormone use), total energy intake, trans, saturated and polyunsaturated fatty acids, and case-control status in original sub-studies. CI, confidence interval; SD, standard deviation; LDL-C, low-density lipoprotein cholesterol; and HDL-C, high-density lipoprotein cholesterol.

