

## SUPPLEMENTAL MATERIALS

### SUPPLEMENTAL TABLES

**Supplemental Table 1.** Power analyses

|                           | Volunteers<br>(control<br>diet) | MedDiets combined vs. control diet |  |  | MedDiet-EVOO vs. control diet |                                  |  | MedDiet-Nuts vs. control diet          |       |                                      |  |
|---------------------------|---------------------------------|------------------------------------|--|--|-------------------------------|----------------------------------|--|--|-------|--------------------------------------|--|
|                           |                                 | Volunteers<br>(MedDiet-<br>EVOO)   | Cases<br>(control +<br>MedDiet-<br>EVOO) | HR<br>detectable<br>with ≥80%<br>power |                               | Volunteers<br>(MedDiet-<br>Nuts) | Cases<br>(control +<br>MedDiet-<br>Nuts) | HR<br>detectable<br>with ≥80%<br>power |       | Volunteers<br>(MedDiets<br>combined) | Cases<br>(control +<br>MedDiets<br>combined) |
|                           |                                 |                                    |  | <1                                     | >1                            |                                  |  | <1                                     | >1    |                                      |  |
| Onset of thrombocytopenia | 988                             | 2,098                              | 41                                       | ≤0.42                                  | ≥3.55                         | 1,128                            | 32                                       | ≤0.35                                  | ≥3.09 | 970                                  | 31   |
| Onset of thrombocytosis   | 988                             | 2,098                              | 58                                       | ≤0.48                                  | ≥2.68                         | 1,128                            | 42                                       | ≤0.40                                  | ≥2.60 | 970                                  | 34   |

HR: hazard ratio; MedDiet-EVOO: Mediterranean diet enriched with extra-virgin olive oil; MedDiet-Nuts: Mediterranean diet enriched with mixed nuts.

**Supplemental Table 2.** Associations of platelet count alterations at baseline with the risk of all-cause mortality stratified by Mediterranean diet intervention group.

|  |                            | Thrombocytopenia     |                      |                       | Thrombocytosis       |                      |                       |
|--|----------------------------|----------------------|----------------------|-----------------------|----------------------|----------------------|-----------------------|
| Association of platelet count alterations (at baseline) with all-cause mortality |                            |                      |                      |                       |                      |                      |                       |
|  | Presence of the alteration | Cases/Total          | HR [95% CI]          | P-value               | Cases/Total          | HR [95% CI]          | P-value               |
|  | No                         | 154/3,997<br>(3.85%) | 1 (Ref.)             |                       | 154/3,997<br>(3.85%) | 1 (Ref.)             |                       |
|  | Yes                        | 16/81<br>(19.8%)     | 4.71<br>[2.69; 8.24] | <0.001                | 10/111<br>(9.01%)    | 1.71<br>[0.87; 3.37] | 0.120                 |
| Stratification in PREDIMED intervention groups                                   |                            |                      |                      |                       |                      |                      |                       |
| Control diet   | Presence of the alteration | Cases/Total          | HR [95% CI]          | Interaction (P-value) | Cases/Total          | HR [95% CI]          | Interaction (P-value) |
|  | No                         | 47/1,360<br>(3.46%)  | 1 (Ref.)             |                       | 47/1,360<br>(3.46%)  | 1 (Ref.)             |                       |
| MedDiet groups   | Yes                        | 9/27<br>(33.3%)      | 10.9<br>[5.26; 22.8] |                       | 2/28<br>(7.14%)      | 0.82<br>[0.26; 2.63] |                       |
|  | No                         | 107/2,637<br>(4.06%) | 1 (Ref.)             |                       | 107/2,637<br>(4.06%) | 1 (Ref.)             |                       |
|  | Yes                        | 7/54<br>(13.0%)      | 2.18<br>[0.95; 5.00] | 0.018                 | 8/83<br>(9.64%)      | 1.75<br>[0.75; 4.08] | 0.437                 |

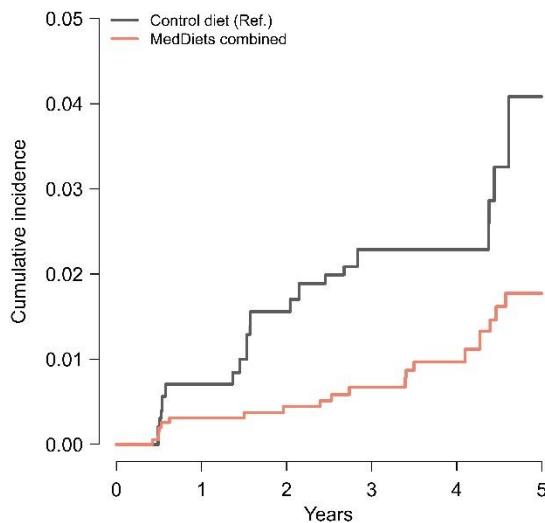
Hazard ratios were estimated by multivariable Cox proportional hazards regression models stratified by sex, recruitment site, and educational level; and adjusted for age, baseline platelet count, diabetes, hypercholesterolemia, hypertriglyceridemia, hypertension, antiplatelet drug use, smoking habit, white blood cells, leisure-time physical activity, body mass index, intake of alcohol, folates, and iron (at baseline, all); and two propensity scores that used 30 baseline variables to estimate the probability of assignment to each of the intervention groups. We used robust standard errors to account for intra-cluster correlations.

*MedDiet:* Mediterranean diet.

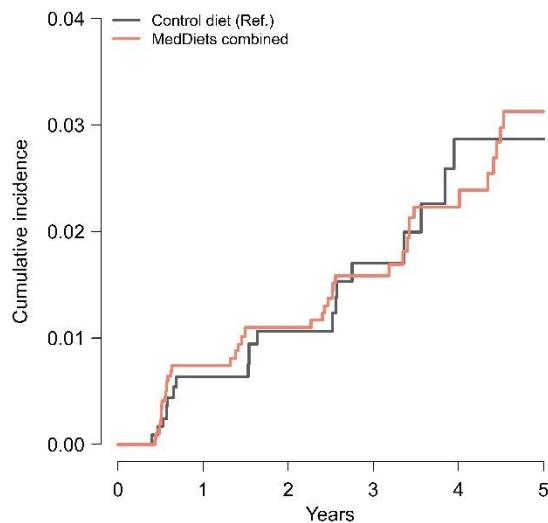
## SUPPLEMENTAL FIGURES

**Supplemental Figure 1.** Weighted Kaplan-Meier estimates of the cumulative incidence of thrombocytopenia (A) and thrombocytosis (B) in intervention groups.

A. Thrombocytopenia



B. Thrombocytosis



No. at risk

|              |      |      |      |      |     |     |
|--------------|------|------|------|------|-----|-----|
| Control diet | 988  | 891  | 575  | 442  | 291 | 141 |
| MedDiets     | 2098 | 1871 | 1403 | 1063 | 713 | 367 |

No. at risk

|              |      |      |      |      |     |     |
|--------------|------|------|------|------|-----|-----|
| Control diet | 988  | 890  | 576  | 442  | 289 | 143 |
| MedDiets     | 2098 | 1862 | 1402 | 1065 | 714 | 365 |

Kaplan-Meier curves weighted by inverse probability weighting using a propensity score model of assignment to intervention or control group based on: platelet count at baseline, age, sex, recruitment site, educational level, diabetes, hypercholesterolemia, hypertriglyceridemia, hypertension, smoking habit, leisure-time physical activity, body mass index, white blood cell counts, intake of alcohol, folates, and iron (baseline values, all), and two propensity scores that used 30 baseline variables to estimate the probability of assignment to each of the intervention groups.

*MedDiet-EVOO:* Mediterranean diet enriched with extra-virgin olive oil; *MedDiet-Nuts:* Mediterranean diet enriched with mixed nuts.

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