

### Supplemental Online Material

**Supplemental Table 1.** Plasma pyridoxal-5-phosphate (PLP<sup>1</sup>) concentrations by tertile category of inflammatory biomarker in 2605 participants of the 7<sup>th</sup> examination of the Framingham Offspring Study.

| Inflammatory Biomarker   | Tertile Category of Inflammatory Marker |             |             | <i>P</i> -trend <sup>2</sup> |
|--------------------------|---|-------------|-------------|------------------------------|
|                          | 1                                       | 2           | 3           |                              |
| plasma CRP               | 75(71, 79)                              | 70 (66, 74) | 59 (56, 62) | <0.001                       |
| <i>n</i>                 | 869                                     | 876         | 861         |                              |
| Plasma CD40L             | 66 (63, 70)                             | 67 (66, 71) | 67 (63, 71) | 0.80                         |
| <i>n</i>                 | 863                                     | 872         | 871         |                              |
| Plasma Fibrinogen        | 72(68, 76)                              | 68 (64, 72) | 63 (60, 66) | <0.001                       |
| <i>n</i>                 | 862                                     | 866         | 878         |                              |
| Serum IL-6 <sup>3</sup>  | 74 (70, 78)                             | 68 (65, 72) | 61 (60, 67) | <0.001                       |
| <i>n</i>                 | 871                                     | 876         | 859         |                              |
| Urinary Isoprostanes     | 76 (72, 81)                             | 67 (63, 71) | 63 (59, 67) | <0.001                       |
| <i>n</i>                 | 748                                     | 750         | 735         |                              |
| Plasma LPLP-A2 Activity  | 69 (65, 73)                             | 70 (66, 74) | 63 (60, 66) | 0.002                        |
| <i>n</i>                 | 868                                     | 873         | 865         |                              |
| Plasma LPLP-A2 Mass      | 70 (66., 74)                            | 66 (63, 70) | 65 (62, 69) | 0.02                         |
| <i>n</i>                 | 871                                     | 880         | 855         |                              |
| Serum Myeloperoxidase    | 68 (64, 72)                             | 68 (64, 72) | 65 (62, 69) | 0.10                         |
| <i>n</i>                 | 863                                     | 868         | 878         |                              |
| Plasma Osteoprotegerin   | 71 (67, 75)                             | 67 (63, 70) | 65 (61, 68) | 0.006                        |
| <i>n</i>                 | 864                                     | 871         | 866         |                              |
| Plasma P-selectin        | 69 (66, 73)                             | 67 (64, 71) | 65 (61, 68) | 0.21                         |
| <i>n</i>                 | 869                                     | 865         | 872         |                              |
| Plasma TNFR-2            | 76 (72, 80)                             | 68 (65, 72) | 59 (56, 63) | <0.001                       |
| <i>n</i>                 | 868                                     | 862         | 876         |                              |
| Plasma TNFα <sup>3</sup> | 72 (67, 76)                             | 70 (66, 75) | 62 (58, 66) | <0.001                       |
| <i>n</i>                 | 656                                     | 656         | 661         |                              |

<sup>1</sup> Values are geometric mean (95% CI) from participants with valid dietary intake data who were not missing data on inflammatory biomarkers or other covariates stratified by tertile category of inflammatory indices and adjusted for sex, age, BMI, circulating homocysteine, folate, vitamin B-12, creatinine, and total cholesterol, vitamin B-6, protein, and energy intakes, and NSAID, cigarette, and multivitamin use. CD40L=CD40 ligand, CRP=C-reactive protein, IL-6=interleukin-6: LPLP-A2=lipoprotein phospholipase A2, NSAID=Non-steroidal anti-inflammatory drug, PLP=Pyridoxal-5-phosphate, TNFα=tumor necrosis factor α, TNFR-2=tumor necrosis factor receptor-2.

<sup>2</sup> *P*-value of the regression coefficient for the independent variable (i.e., inflammation score or biomarker) derived by entering this variable into the model as a continuous variable.

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**Supplemental Table 2.** Plasma pyridoxal-5-phosphate (PLP<sup>1</sup>) concentrations by tertile category of significant inflammatory biomarkers from supplemental Table 1 additionally adjusted for CRP, in 2605 participants of the 7<sup>th</sup> examination of the Framingham Offspring Study.

| Inflammatory Biomarker  | Tertile Category of Inflammatory Marker |             |             | P-trend <sup>2</sup> |
|-------------------------|---|-------------|-------------|----------------------|
|                         | 1                                       | 2           | 3           |                      |
| Plasma Fibrinogen       | 69 (65, 73) <sup>3</sup>                | 68 (64, 71) | 67 (63, 70) | 0.22                 |
| <i>n</i>                | 862                                     | 866         | 878         |                      |
| Serum IL-6              | 71 (67, 75)                             | 69 (65, 72) | 64 (61, 68) | 0.002                |
| <i>n</i>                | 871                                     | 876         | 859         |                      |
| Urinary Isoprostanes    | 76 (72, 81)                             | 67 (63, 71) | 64 (60, 67) | <0.001               |
| <i>n</i>                | 748                                     | 750         | 735         |                      |
| Plasma LPLP-A2 Activity | 71 (67, 75)                             | 69 (66, 74) | 65 (60, 67) | <0.001               |
| <i>n</i>                | 868                                     | 873         | 865         |                      |
| Plasma LPLP-A2 Mass     | 71 (67, 75)                             | 67 (66, 71) | 66 (63, 70) | 0.02                 |
| <i>n</i>                | 871                                     | 880         | 855         |                      |
| Plasma Osteoprotegerin  | 71 (67, 75)                             | 67 (64, 71) | 66 (63, 70) | 0.04                 |
| <i>n</i>                | 864                                     | 871         | 866         |                      |
| Plasma TNFR-2           | 75 (71, 80)                             | 68 (65, 72) | 61 (58, 65) | <0.001               |
| <i>n</i>                | 868                                     | 862         | 876         |                      |
| Plasma TNF $\alpha$     | 71 (67, 76)                             | 70 (67, 75) | 63 (60, 68) | <0.001               |
| <i>n</i>                | 656                                     | 656         | 661         |                      |

<sup>1</sup> Values are geometric mean (95% CI) from participants with valid dietary intake data who were not missing data on inflammatory biomarkers or other covariates stratified by tertile category of inflammatory indices and adjusted for sex, age, BMI, circulating homocysteine, folate, vitamin B-12, creatinine, and total cholesterol, vitamin B-6, protein, and energy intakes, and NSAID, cigarette, and multivitamin use. CD40L=CD40 ligand, CRP=C-reactive protein, ICAM-1=intracellular adhesion molecule-1, IL-6=interleukin-6; LPLP-A2=lipoprotein phospholipase A2, MCP-1=monocyte chemoattractant protein-1, NSAID=Non-steroidal anti-inflammatory drug, PLP=Pyridoxal-5-phosphate, TNF $\alpha$ =tumor necrosis factor  $\alpha$ , TNFR-2=tumor necrosis factor receptor-2.

<sup>2</sup> P-value of the regression coefficient for the independent variable (i.e., inflammation score or biomarker) derived by entering this variable into the model as a continuous variable.

## Supplemental Online Material

**Supplemental Table 3.** Plasma pyridoxal-5-phosphate (PLP) concentrations by tertile category of inflammatory indices in 2135 participants of the 7<sup>th</sup> examination of the Framingham Offspring Study. Analyses excluded 470 participants with known CVD<sup>1</sup> or diabetes

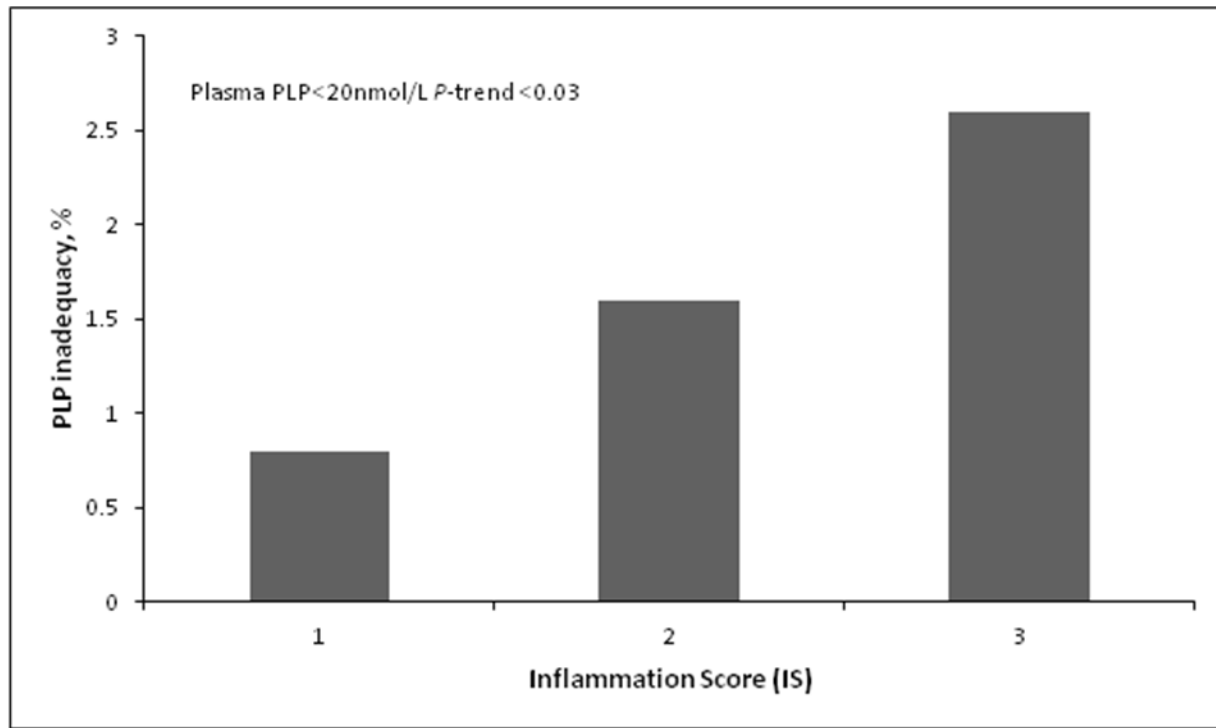
| Inflammatory Index                     | Tertile Category of Inflammatory Index |             |             | P-trend <sup>2</sup> |
|--|--|-------------|-------------|----------------------|
|  | 1                                      | 2           | 3           |                      |
|  | Plasma PLP (nmol/L)                    |             |             |                      |
| IS <sup>3</sup>                        | 81(75, 88) <sup>4</sup>                | 75 (70, 81) | 64 (59, 68) | <0.001               |
| <i>n</i>                               | 512                                    | 513         | 502         |                      |
| IS- Acute Phase Reactants <sup>3</sup> | 75 (71, 80)                            | 70 (66, 75) | 63 (59, 67) | <0.001               |
| <i>n</i>                               | 707                                    | 721         | 708         |                      |
| IS- Cytokines <sup>3</sup>             | 77 (71, 83)                            | 74 (69, 79) | 62 (58, 67) | <0.001               |
| <i>n</i>                               | 536                                    | 532         | 535         |                      |
| IS- Oxidative Stress <sup>3</sup>      | 76 (70, 81)                            | 73 (68, 78) | 65 (61, 69) | <0.001               |
| <i>n</i>                               | 608                                    | 621         | 601         |                      |
| IS- Selectins <sup>3</sup>             | 71 (67, 76)                            | 69 (65, 74) | 67 (63, 71) | 0.05                 |
| <i>n</i>                               | 705                                    | 717         | 703         |                      |
| Serum ICAM-1                           | 72 (68, 77)                            | 70 (66, 75) | 66 (63, 70) | 0.01                 |
| <i>n</i>                               | 716                                    | 712         | 708         |                      |
| Serum MCP-1                            | 67 (63, 72)                            | 72 (67, 76) | 68 (64, 72) | 0.79                 |
| <i>n</i>                               | 703                                    | 717         | 716         |                      |

<sup>1</sup> Values are geometric mean (95% CI) from participants with valid dietary intake data who were not missing data on inflammatory biomarkers or other covariates stratified by tertile category of inflammatory indices and adjusted for sex, age, BMI, circulating homocysteine, folate, vitamin B-12, creatinine, and total cholesterol, vitamin B-6, protein, and energy intakes, and NSAID, cigarette, and multivitamin use. CD40L=CD40 ligand, CRP=C-reactive protein, CVD= cardiovascular disease, ICAM-1=intracellular adhesion molecule-1, IL-6=interleukin-6: LPLP-A2=lipoprotein phospholipase A2, MCP-1=monocyte chemoattractant protein-1, NSAID=Non-steroidal anti-inflammatory drug, PLP=Pyridoxal-5-phosphate, TNF $\alpha$ =tumor necrosis factor  $\alpha$ , TNFR-2=tumor necrosis factor receptor-2.

<sup>2</sup> P-value of the regression coefficient for the independent variable (i.e., inflammation score or biomarker) derived by entering this variable into the model as a continuous variable.

<sup>3</sup>IS= summed Z-scores of: CRP, fibrinogen, IL-6, TNF $\alpha$ , TNFR-2, osteoprotegerin, P-selectin, CD40L, ICAM-1, MCP-1, myeloperoxidase, LPLP-A2 mass, LPLP-A2 activity, and isoprostanes, IS- acute phase reactants= summed Z-scores of: CRP and Fibrinogen, IS- Cytokines= summed Z-scores of: IL-6, TNF $\alpha$ , TNFR-2, and osteoprotegerin, IS-Oxidative Stress= summed Z-scores of: myeloperoxidase, LPLP-A2 mass, LPLP- A2 activity, and isoprostanes, IS-Selectins= summed Z-scores of: P-selectin and CD40L.

## Supplemental Online Material



**Supplemental Figure 1.** Prevalence of major (<20 nmol/L) plasma pyridoxal 5'-phosphate (PLP) insufficiency (%) from participants of the 7<sup>th</sup> examination of the Framingham Offspring Study ( $n=1965$ ) according to tertile category of the inflammation score. Prevalence is adjusted for sex, age, BMI, plasma homocysteine, folate, vitamin B-12, creatinine, total cholesterol, protein intake, energy intake, NSAID use, and cigarette use. *P*-trend for the relation between plasma PLP inadequacy and the inflammation score was derived by entering the inflammation score into the regression model as a continuous, rather than categorical, variable. The inflammation score is the sum of Z-scores of CRP, fibrinogen, IL-6, TNF $\alpha$ , TNFR-2, osteoprotegerin, P-selectin, CD40L, ICAM-1, MCP-1, myeloperoxidase, LPLP-A2 mass, LPLP-A2 activity, and isoprostanes.

Author Defined Abbreviations: CD40L=CD40 ligand, CRP=C-reactive protein, ICAM-1=intracellular adhesion molecule-1, IL-6=interleukin-6; LPLP-A2=lipoprotein phospholipase A2, MCP-1=monocyte chemoattractant protein-1, NSAID=non-steroidal anti-inflammatory drug, PLP=pyridoxal-5-phosphate, TNF $\alpha$ =tumor necrosis factor  $\alpha$ , TNFR-2=tumor necrosis factor receptor-2.