### Supplemental Table 1 Responses of BMD to intervention with low-dose B-vitamins for 2 years in males and females

Data presented as mean (95% CI), apart from Change which is presented as adjusted mean (95% CI).

|                      | Males (n=81) |             | Females (n=124) |             |
|----------------------|--------------|-------------|-----------------|-------------|
|                      | Active Placebo | B-vitamin Treatment | P value | Active Placebo | B-vitamin Treatment | P value |
| **Age (years)**      | 72.0 (69.4, 74.6) | 70.2 (68.1, 72.2) | 0.331 | 69.5 (67.8, 71.3) | 67.8 (65.9, 69.8) | 0.180 |
| **BMI (kg/m²)**      | 29.3 (27.8, 30.8) | 28.1 (26.9, 29.4) | 0.259 | 28.1 (26.8, 29.5) | 28.3 (27.1, 29.5) | 0.178 |
| **Baseline B-vitamin biomarkers** |             |             |             |             |
| Serum folate (nmol/L) | 15.6 (13.5, 17.8) | 16.6 (14.7, 18.5) | 0.322 | 16.4 (15.1, 17.7) | 17.2 (15.4, 19.0) | 0.823 |
| Serum total vitamin B12 (pmol/L) | 235 (211, 259) | 243 (219, 268) | 0.703 | 280 (256, 304) | 247 (226, 268) | 0.039 |
| Serum MMA (µmol/L)   | 0.31 (0.25, 0.37) | 0.34 (0.21, 0.47) | 0.758 | 0.25 (0.21, 0.29) | 0.28 (0.23, 0.33) | 0.425 |
| Plasma PLP (vitamin B6, nmol/L) | 42.3 (36.2, 49.0) | 47.4 (41.7, 53.1) | 0.125 | 47.2 (42.5, 51.9) | 42.9 (38.9, 46.8) | 0.208 |
| Riboflavin (EGRac)   | 1.33 (1.27, 1.40) | 1.36 (1.31, 1.41) | 0.434 | 1.34 (1.31, 1.37) | 1.36 (1.31, 1.41) | 0.608 |
| Serum total homocysteine (µmol/L) | 15.5 (12.9, 18.1) | 14.0 (12.4, 15.6) | 0.457 | 12.6 (11.8, 13.5) | 13.4 (12.3, 14.5) | 0.418 |
| **Bone mineral density (g/cm²)** |             |             |             |             |
| Total hip            |             |             |             |             |
| Pre                  | 1.043 (0.996, 1.089) | 1.043 (1.004, 1.082) | 0.914 (0.881, 0.946) | 0.913 (0.881, 0.945) |             |             |
| Post                 | 1.036 (0.990, 1.082) | 1.037 (0.995, 1.079) | 0.905 (0.873, 0.937) | 0.899 (0.867, 0.930) |             |             |
| Change               | -0.007 (-0.014, 0.000) | -0.007 (-0.015, 0.001) | 0.913 | -0.008 (-0.015, -0.002) | -0.014 (-0.020, -0.008) | 0.200 |
| % change             | -0.6 (-1.2, 0.0) | -0.6 (-1.5, 0.3) | -0.9 (-1.6, -0.2) | -1.5 (-2.2, -0.9) |             |             |
| Femoral neck         |             |             |             |             |
| Pre                  | 0.940 (0.896, 0.986) | 0.957 (0.917, 0.996) | 0.859 (0.831, 0.888) | 0.872 (0.839, 0.904) |             |             |
| Post                 | 0.939 (0.895, 0.984) | 0.957 (0.917, 0.997) | 0.849 (0.820, 0.877) | 0.860 (0.828, 0.892) |             |             |
| Change               | -0.003 (-0.010, 0.004) | 0.001 (-0.007, 0.008) | 0.507 | -0.011 (-0.018, -0.003) | -0.012 (-0.019, -0.004) | 0.937 |
| % change             | -0.1 (-0.9, 0.7) | 0.0 (-0.6, 0.6) | -1.2 (-2.0, -0.5) | -1.3 (-2.2, -0.3) |             |             |
| Lumbar spine         |             |             |             |             |
| Pre                  | 1.247 (1.180, 1.314) | 1.267 (1.195, 1.338) | 1.059 (1.009, 1.109) | 1.062 (1.017, 1.107) |             |             |
| Post                 | 1.240 (1.176, 1.305) | 1.256 (1.180, 1.331) | 1.053 (1.004, 1.101) | 1.046 (1.000, 1.090) |             |             |
| Change               | -0.008 (-0.023, 0.006) | -0.009 (-0.024, 0.006) | 0.940 | -0.008 (-0.017, 0.001) | -0.015 (-0.023, -0.007) | 0.219 |
| % change             | -0.4 (-1.3, 0.5) | -1.0 (-2.4, 0.4) | -0.5 (-1.3, 0.2) | -1.5 (-2.3, -0.6) |             |             |
1The treatment capsule contained a combination of 10µg vitamin D, along with B-vitamins (200µg folic acid, 10µg vitamin B12, 10mg vitamin B6 and 5mg riboflavin). The ‘active’ placebo capsule contained 10µg vitamin D only. Both treatments were administered to participants daily.

2Differences between groups were assessed using an independent samples t-test for continuous variables; P <0.05.

3Change in BMD was assessed on an intention-to-treat basis by ANCOVA (adjusted for age, sex, BMI, alcohol intake units/week), P <0.05; Analysis was conducted on log-transformed data where appropriate.

Abbreviations: BMI, body mass index; BMD, bone mineral density; EGRac, erythrocyte glutathione reductase activation coefficient; MMA, methylmalonic acid; PLP, pyridoxal-5-phosphate