

**Supplemental Figure1. Flow chart of the participants**

**Supplemental Table 1. The association between plasma magnesium and new-onset hyperuricemia in participants excluding cases (including stroke, cancer and all-cause mortality)**

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| --- | --- | --- | --- |
| Magnesium, μmol/L | Events/N (%) | Model 1 | Model 2 |
| OR (95%CI) | *P* value | OR (95%CI) | *P* value |
|  Per SD increment  | 220/1341 (16.4) | 0.84 (0.71, 0.98) | 0.031 | 0.84 (0.71, 1.00) | 0.045 |
|  Tertiles |  |  |  |  |  |
|  T1 (<819.6) | 80/443 (18.1) | ref. |  | ref. |  |
|  T2 (819.6-<885.0) | 73/456 (16.0) | 0.73 (0.50, 1.06) | 0.099 | 0.68 (0.46, 1.01) | 0.058 |
|  T3 (≥885.0) | 67/442 (15.2) | 0.65 (0.44, 0.95) | 0.026 | 0.64 (0.43, 0.95) | 0.028 |
|  *P* for trend |  | 0.026 |  | 0.028 |  |

**Model 1:** Adjusted for age, sex, and uric acid (UA) at baseline.

**Model 2:** Adjusted for age, sex, body mass index (BMI), UA, fasting glucose, total cholesterol, triglycerides (TG), total homocysteine (tHcy), folate, eGFR, systolic blood pressure (SBP), smoking and drinking status at baseline, treatment group, and mean SBP during the treatment period.

**Supplemental Table 2. The association between plasma magnesium and study outcomes in study 1**

|  |  |  |  |
| --- | --- | --- | --- |
| Magnesium, μmol/L | Events/N (%) | Model 1 | Model 2 |
| OR (95%CI)  | *P* value | OR (95%CI)  | *P* value |
| **New-onset Hyperuricemia** |
| Per SD increment | 179/995 (18.0) | 0.81 (0.68, 0.96) | 0.017 | 0.79 (0.65, 0.95) | 0.015 |
| Tertiles |  |  |  |  |  |
|  T1 (<817.3) | 65/332 (19.6) | ref. |  | ref. |  |
|  T2 (817.3-<881.4) | 57/331 (17.2) | 0.72 (0.47, 1.09) | 0.121 | 0.66 (0.42, 1.04) | 0.071 |
|  T3 (≥881.4) | 57/332 (17.2) | 0.62 (0.41, 0.95) | 0.028 | 0.57 (0.36, 0.90) | 0.016 |
|  *P* for trend |  | 0.028 |  | 0.017 |  |
|  | Mean (SD) | β (95%CI) | *P* value | β (95%CI) | *P* value |
| **Change in UA concentration, μmol/L** |
| Per SD increment | 49.2 (71.2) | -5.71 (-9.97, -1.46) | 0.009 | -4.93 (-9.21, -0.64) | 0.024 |
| Tertiles |  |  |  |  |  |
|  T1 (<817.3) | 57.6 (71.9) | ref. |  | ref. |  |
|  T2 (817.3-<881.4) | 46.9 (75.1) | -8.85 (-19.26, 1.56) | 0.096 | -6.96 (-17.37, 3.45) | 0.190 |
|  T3 (≥881.4) | 43.0 (65.6) | -10.02 (-20.47, 0.43) | 0.060 | -8.66 (-19.18, 1.87) | 0.107 |
|  *P* for trend |  | 0.060 |  | 0.110 |  |

**Model 1:** Adjusted for age, sex, and uric acid (UA) at baseline.

**Model 2:** Adjusted for age, sex, body mass index (BMI), UA, fasting glucose, total cholesterol, triglycerides (TG), total homocysteine (tHcy), folate, eGFR, systolic blood pressure (SBP), smoking and drinking status at baseline, treatment group, and mean SBP during the treatment period.

**Supplemental Table 3. The association between plasma magnesium and study outcomes in study 2**

|  |  |  |  |
| --- | --- | --- | --- |
| Magnesium, μmol/L | Events/N (%) | Model 1 | Model 2 |
| OR (95%CI)  | *P* value | OR (95%CI)  | *P* value |
| **New-onset Hyperuricemia** |
| Per SD increment | 122/775 (15.7) | 0.92 (0.75, 1.13) | 0.440 | 0.90 (0.72, 1.12) | 0.347 |
| Tertiles |  |  |  |  |  |
|  T1(<819.7) | 38/258 (14.7) | ref. |  | ref. |  |
|  T2(819.7-<889.3) | 46/258 (17.8) | 1.13 (0.69, 1.84) | 0.636 | 1.12 (0.67, 1.86) | 0.664 |
|  T3(≥889.3) | 38/259 (14.7) | 0.92 (0.56, 1.53) | 0.757 | 0.87 (0.51, 1.48) | 0.615 |
|  *P* for trend |  | 0.751 |  | 0.610 |  |
|  | Mean (SD) | β (95%CI) | *P* value | β (95%CI) | *P* value |
| **Change in UA concentration, μmol/L** |
| Per SD increment | 37.2 (63.8) | -1.18 (-5.54, 3.18) | 0.596 | -2.93 (-7.47, 1.60) | 0.205 |
| Tertiles |  |  |  |  |  |
|  T1(<819.7) | 40.9 (64.6) | ref. |  | ref. |  |
|  T2(819.7-<889.3) | 34.1 (67.0) | -4.54 (-15.22, 6.13) | 0.405 | -5.80 (-16.71, 5.11) | 0.298 |
|  T3(≥889.3) | 36.6 (59.5) | -2.69 (-13.37, 7.99) | 0.622 | -6.02 (-17.10, 5.07) | 0.288 |
|  *P* for trend |  | 0.622 |  | 0.287 |  |

**Model 1:** Adjusted for age, sex, and uric acid (UA) at baseline.

**Model 2:** Adjusted for age, sex, body mass index (BMI), UA, fasting glucose, total cholesterol, triglycerides (TG), total homocysteine (tHcy), folate, eGFR, systolic blood pressure (SBP), smoking and drinking status at baseline, treatment group, and mean SBP during the treatment period.

**Supplemental Table 4. The association between plasma magnesium and study outcomes in the enalapril alone group**

|  |  |  |  |
| --- | --- | --- | --- |
| Magnesium, μmol/L | Events/N (%) | Model 1 | Model 2 |
| OR (95%CI)  | *P* value | OR (95%CI)  | *P* value |
| **New-onset Hyperuricemia** |
| Per SD increment | 150/885 (16.9) | 0.78 (0.65, 0.94) | 0.011 | 0.77 (0.63, 0.95) | 0.013 |
| Tertiles |  |  |  |  |  |
|  T1 (<813.1) | 65/317 (20.5) | ref. |  | ref. |  |
|  T2 (813.1-<882.8) | 42/285 (14.7) | 0.54 (0.34, 0.84) | 0.007 | 0.50 (0.31, 0.81) | 0.005 |
|  T3 (≥882.8) | 43/283 (15.2) | 0.53 (0.34, 0.84) | 0.006 | 0.50 (0.31, 0.82) | 0.005 |
|  *P* for trend |  | 0.005 |  | 0.004 |  |
|  | Mean (SD) | β (95%CI) | *P* value | β (95%CI) | *P* value |
| **Change in UA concentration, μmol/L** |
| Per SD increment | 46.7 (67.5) | -5.46 (-9.75, -1.16) | 0.013 | -5.52 (-9.93, -1.10) | 0.015 |
| Tertiles |  |  |  |  |  |
|  T1 (<817.3) | 57.1 (71.7) | ref. |  | ref. |  |
|  T2 (817.3-<881.4) | 41.9 (68.4) | -12.41 (-22.78, -2.05) | 0.019 | -12.96 (-23.55, -2.37) | 0.017 |
|  T3 (≥881.4) | 39.9 (60.2) | -12.65 (-23.08, -2.22) | 0.018 | -13.36 (-24.11, -2.61) | 0.015 |
|  *P* for trend |  | 0.016 |  | 0.014 |  |

**Model 1:** Adjusted for age, sex, and uric acid (UA) at baseline.

**Model 2:** Adjusted for age, sex, body mass index (BMI), UA, fasting glucose, total cholesterol, triglycerides (TG), total homocysteine (tHcy), folate, eGFR, systolic blood pressure (SBP), smoking and drinking status at baseline, and mean SBP during the treatment period.

**Supplemental Table 5. A sequential model for** **the association between plasma magnesium and new-onset hyperuricemia \***

|  |  |  |
| --- | --- | --- |
| Adusted Model  | Mg-hyperuricemia adjusted OR (95%CI)  | *P* value |
| Model 1 | 0.86 (0.75, 0.98) | 0.029 |
| + Baseline body mass index | 0.85 (0.74, 0.97) | 0.020 |
| + Baseline smoking status | 0.85 (0.74, 0.98) | 0.023 |
| + Baseline drinking status  | 0.85 (0.74, 0.98) | 0.024 |
| + Baseline SBP | 0.86 (0.75, 0.99) | 0.034 |
| + Time-averaged SBP | 0.86 (0.75, 0.99) | 0.033 |
| + Treatment group | 0.86 (0.75, 0.99) | 0.034 |
| + Baseline total homocysteine | 0.85 (0.74, 0.98) | 0.026 |
| + Baseline folate | 0.86 (0.75, 0.99) | 0.042 |
| + Baseline fasting glucose | 0.86 (0.74, 0.99) | 0.036 |
| + Baseline eGFR | 0.85 (0.74, 0.99) | 0.031 |
| + Baseline total cholesterol | 0.85 (0.74, 0.99) | 0.031 |
| + Baseline triglycerides  | 0.85 (0.74, 0.99)  | 0.032 |

**Model 1:** Adjusted for age, sex, and uric acid (UA) at baseline.

**\*** Body mass index (BMI), fasting glucose, total cholesterol, triglycerides (TG), total homocysteine (tHcy), folate, eGFR, systolic blood pressure (SBP), smoking and drinking status at baseline, treatment group, and mean SBP during the treatment period one by one adding to adjusted model.

**Supplemental Table 6. Concomitant medications during the treatment period by magnesium tertiles\***

|  |  |  |
| --- | --- | --- |
| Medication, No. (%) | Magnesium, μmol/L | *P* value |
| T1 (<818.9) | T2 (818.9-<885.5) | T3 (≥885.5) |
| Anti-hypertension drugs |  |  |  |  |
|  Calcium channel blockers | 461 (82) | 457 (81.5) | 467 (83.1) | 0.768 |
|  Diuretics  | 346 (61.6) | 336 (59.9) | 356 (63.3) | 0.493 |
| Glucose-lowering drugs | 23 (4.1) | 14 (2.5) | 7 (1.2) | 0.011 |
| Antiplatelet drugs | 4 (0.7) | 4 (0.7) | 4 (0.7) | 1.000 |

\* Regular concomitant medication was defined as 180 or more cumulative days of taking the drug of interest.

**Supplemental Table 7. The association between plasma magnesium and study outcomes with further adjustment for the use of** **glucose-lowering drugs during the treatment period**

|  |  |  |  |
| --- | --- | --- | --- |
| Magnesium, μmol/L | Events/N (%) | Model 1 | Model 2 |
| OR (95%CI)  | *P* value | OR (95%CI)  | *P* value |
| **New-onset Hyperuricemia** |
| Per SD increment  | 290/1685 (17.2) | 0.85 (0.74, 0.99) | 0.032  | 0.85 (0.74, 0.99) | 0.032 |
| Tertiles |  |  |  |  |  |
|  T1 (<818.9) | 103/562 (18.3) | ref. |  | ref. |  |
|  T2 (818.9-<885.5) | 96/561 (17.1) | 0.74 (0.53, 1.05) | 0.089  | 0.74 (0.53, 1.05) | 0.089 |
|  T3 (≥885.5) | 91/562 (16.2) | 0.67 (0.48, 0.95) | 0.026 | 0.67 (0.48, 0.96) | 0.027 |
|  *P* for trend |  | 0.027 |  | 0.027 |  |
|  | Mean (SD) | β (95%CI) | *P* value | β (95%CI) | *P* value |
| **Change in UA concentration, μmol/L** |
| Per SD increment  | 44.2 (67.9) | -3.96 (-7.14, -0.79) | 0.014  | -3.96 (-7.14, -0.79) | 0.014 |
| Tertiles |  |  |  |  |  |
|  T1 (<818.9) | 51.0 (69.5) | ref. |  | ref. |  |
|  T2 (818.9-<885.5) | 41.4 (70.7) | -8.09 (-15.76, -0.43) | 0.039 | -8.10 (-15.76, -0.43) | 0.039 |
|  T3 (≥885.5) | 40.1 (62.7) | -8.35 (-16.12, -0.58) | 0.035 | -8.36 (-16.14, -0.59) | 0.035 |
|  *P* for trend |  | 0.036 |  | 0.036 |  |

**Model 1:** Adjusted for age, sex, body mass index (BMI), UA, fasting glucose, total cholesterol, triglycerides (TG), total homocysteine (tHcy), folate, eGFR, systolic blood pressure (SBP), smoking and drinking status at baseline, treatment group, and mean SBP during the treatment period.

**Model 2:** Model 1 + use of glucose-lowering drugs during the treatment period.