

Supplemental table 1. Baseline characteristics and cardiovascular disease events <sup>a</sup> of the participants with baPWV values  $\geq 1800$  cm/sec at baseline survey in 2011, 2012 (N = 374).

| Baseline characteristics (n = 374)                     |                    |
|--|--------------------|
| Age (years)  | 75.9 $\pm$ 8.4     |
| Height (cm)  | 147.4 $\pm$ 6.4    |
| Weight (kg)  | 49.6 $\pm$ 8.5     |
| BMI ( $\text{kg}/\text{m}^2$ )                         | 22.8 $\pm$ 3.6     |
| aBMD at the spine ( $\text{g}/\text{cm}^2$ )           | 0.821 $\pm$ 0.160  |
| aBMD at the femoral neck ( $\text{g}/\text{cm}^2$ )    | 0.582 $\pm$ 0.111  |
| aBMD at the total hip ( $\text{g}/\text{cm}^2$ )       | 0.698 $\pm$ 0.138  |
| BMC at whole body (g)                                  | 1278.4 $\pm$ 288.7 |
| Osteoporosis, n (%)                                    | 171 (45.7%)        |
| Systolic blood pressure (mmHg)                         | 144.3 $\pm$ 19.8   |
| Diastolic blood pressure (mmHg)                        | 77.1 $\pm$ 10.4    |
| Total cholesterol (mg/dL)                              | 209.6 $\pm$ 34.5   |
| Triglyceride (mg/dL)                                   | 110.6 $\pm$ 61.2   |
| HDL-cholesterol (mg/dL)                                | 60.2 $\pm$ 15.3    |
| LDL-cholesterol (mg/dL)                                | 122.4 $\pm$ 30.3   |
| Fasting blood glucose (mg/dL)                          | 96.0 $\pm$ 17.8    |
| HbA1c (%)  | 5.3 $\pm$ 0.6      |
| Hypertension, n (%)                                    | 317 (84.8%)        |
| Hyperlipidemia, n (%)                                  | 236 (63.1%)        |
| Diabetes mellitus n (%)                                | 46 (12.3%)         |
| Medication for hypertension, n (%)                     | 224 (59.9%)        |
| Medication for hyperlipidaemia, n (%)                  | 126 (33.7%)        |
| Medication for diabetes mellitus, n (%)                | 36 (9.6%)          |
| Current smokers, n (%)                                 | 4 (1.1%)           |
| Habitual drinkers, n (%)                               | 19 (5.1%)          |
| History of fragility fractures, n (%)                  | 28 (7.5%)          |
| Histoy of cardiovascular diseases <sup>a</sup> , n (%) | 35 (9.4%)          |
| eGFR (ml/min/1.73m <sup>2</sup> )                      | 70.6 $\pm$ 16.9    |
| Osteocalcin <sup>b</sup> (nmol/L)                      | 7.51               |
| ucOC <sup>b</sup> (nmol/L)                             | 4.81               |
| BAP <sup>b</sup> (ng/mL)                               | 15.38              |
| Sclerostin <sup>b</sup> (pmol/L)                       | 36.18              |
| baPWV (cm/sec) <sup>c</sup>                            | 2105 (1954, 2369)  |
| During follow-up period (n=242)                        |                    |
| CVD events <sup>a</sup> , n (%)                        | 10 (4.1%)          |
| MI events <sup>a</sup> , n (%)                         | 3 (1.2%)           |
| stroke events <sup>a</sup> , n (%)                     | 5 (2.1%)           |
| angina events <sup>a</sup> , n (%)                     | 6 (2.5%)           |

baPWV: brachial-ankle pulse wave velocity n: number of participants BMI: body mass index aBMD: areal bone mineral density eGFR: estimated glomerular filtration rate ucOC: undercarboxylated osteocalcin BAP: bone-specific alkaline phosphatase baPWV: brachial-ankle pulse wave velocity

The values denote mean  $\pm$  SD or prevalence rate (%).

<sup>a</sup> The informations of cardiovascular events were obtained by ansers to a quetionnaire.

<sup>b</sup> The values indicate the geometric means.

<sup>c</sup> The values indicate the median and interquartile ranges in parentheses.

Supplemental table 2 . Baseline characteristics of the participants with no history of cardiovascular disease, categorized according to serum sclerostin level, of the Japanese Population-based Osteoporosis Cohort Study (N = 538)

|   | Total (N = 538)   | Low tertile       | Middle tertile    | High tertile      | P-value <sup>b</sup><br>(Unadjusted) | P-value<br>(Adjusted for<br>age) | P-value<br>(Adjusted for<br>age and BMI) |
|---|-------------------|-------------------|-------------------|-------------------|--------------------------------------|----------------------------------|--|
| Range of sclerostin values (pmol/L)           | 8.12-32.49        | 32.50-44.78       | 44.79-109.22      |                   |                                      |                                  |  |
| Age (years)                                   | 62.2 ± 8.0        | 64.1 ± 7.4        | 62.1 ± 8.0        | 60.3 ± 8.1        | <0.001                               | -                                | -  |
| Height (cm)                                   | 153.5 ± 5.6       | 152.6 ± 5.6       | 153.9 ± 5.7       | 154.0 ± 5.4       | 0.015                                | 0.716                            | -  |
| Weight (kg)                                   | 53.5 ± 8.6        | 52.2 ± 8.3        | 54.0 ± 8.5        | 54.4 ± 8.8        | 0.015                                | 0.036                            | -  |
| BMI (kg/m <sup>2</sup> )                      | 22.7 ± 3.5        | 22.4 ± 3.2        | 22.8 ± 3.3        | 23.0 ± 3.9        | 0.110                                | 0.021                            | -  |
| aBMD at the spine (g/cm <sup>2</sup> )        | 0.896 ± 0.154     | 0.832 ± 0.150     | 0.891 ± 0.135     | 0.964 ± 0.148     | <0.001                               | <0.001                           | <0.001                                   |
| aBMD at the femoral neck (g/cm <sup>2</sup> ) | 0.663 ± 0.106     | 0.626 ± 0.100     | 0.664 ± 0.098     | 0.698 ± 0.109     | <0.001                               | <0.001                           | <0.001                                   |
| aBMD at the total hip (g/cm <sup>2</sup> )    | 0.785 ± 0.116     | 0.738 ± 0.107     | 0.787 ± 0.106     | 0.830 ± 0.116     | <0.001                               | <0.001                           | <0.001                                   |
| BMC at whole body (g)                         | 1550.2 ± 282.5    | 1421.4 ± 254.9    | 1559.3 ± 262.5    | 1670.0 ± 274.2    | <0.001                               | <0.001                           | <0.001                                   |
| Osteoporosis, n (%)                           | 127 (23.6%)       | 74 (41.3%)        | 34 (18.9%)        | 19 (10.6%)        | <0.001                               | <0.001                           | <0.001                                   |
| Systolic blood pressure (mmHg)                | 126.3 ± 16.0      | 126.7 ± 14.5      | 125.0 ± 15.9      | 127.1 ± 17.4      | 0.813                                | -                                | -  |
| Diastolic blood pressure (mmHg)               | 72.6 ± 9.4        | 72.3 ± 9.0        | 72.4 ± 9.4        | 73.1 ± 9.9        | 0.409                                | -                                | -  |
| Total cholesterol (mg/dL)                     | 214.5 ± 31.4      | 213.7 ± 30.3      | 216.8 ± 32.2      | 212.8 ± 31.8      | 0.787                                | -                                | -  |
| Triglyceride (mg/dL)                          | 103.5 ± 78.5      | 92.3 ± 49.3       | 112.4 ± 97.7      | 105.7 ± 79.8      | 0.105                                | -                                | -  |
| HDL-cholesterol (mg/dL)                       | 64.4 ± 15.7       | 65.7 ± 15.1       | 64.4 ± 16.3       | 63.0 ± 15.8       | 0.104                                | -                                | -  |
| LDL-cholesterol (mg/dL)                       | 125.4 ± 28.3      | 125.1 ± 27.4      | 126.0 ± 29.0      | 125.3 ± 28.6      | 0.944                                | -                                | -  |
| Fasting blood glucose (mg/dL)                 | 90.7 ± 17.9       | 91.3 ± 14.0       | 88.9 ± 9.8        | 91.9 ± 25.9       | 0.746                                | -                                | -  |
| HbA1c (%)                                     | 5.6 ± 0.6         | 5.5 ± 0.4         | 5.6 ± 0.5         | 5.6 ± 0.7         | 0.274                                | -                                | -  |
| Hypertension, n (%)                           | 192 (35.7%)       | 70 (39.1%)        | 56 (31.1%)        | 66 (36.9%)        | 0.659                                | -                                | -  |
| Hyperlipidemia, n (%)                         | 272 (50.6%)       | 89 (49.7%)        | 98 (54.4%)        | 85 (47.5%)        | 0.673                                | -                                | -  |
| Diabetes mellitus n (%)                       | 31(5.8%)          | 9 (5.0%)          | 7 (3.9%)          | 15 (8.4%)         | 0.174                                | -                                | -  |
| Medication for hypertension, n (%)            | 123 (22.9%)       | 47 (26.3%)        | 33 (18.3%)        | 43 (24.0%)        | 0.615                                | -                                | -  |
| Medication for hyperlipidaemia, n (%)         | 110 (20.4%)       | 39 (21.8%)        | 43 (23.9%)        | 28 (15.6%)        | 0.150                                | -                                | -  |
| Medication for diabetes mellitus, n (%)       | 21 (3.9%)         | 4 (2.2%)          | 7 (3.9%)          | 10 (5.6%)         | 0.102                                | -                                | -  |
| Current smokers, n (%)                        | 20 (3.7%)         | 7 (3.9%)          | 6 (3.3%)          | 7 (3.9%)          | 0.999                                | -                                | -  |
| Habitual drinkers (≥6 times/week), n (%)      | 48 (8.9%)         | 17 (9.5%)         | 13 (7.2%)         | 18 (10.1%)        | 0.853                                | -                                | -  |
| History of fragility fractures, n (%)         | 42 (7.8%)         | 15 (8.4%)         | 16 (8.9%)         | 11 (6.1%)         | 0.432                                | -                                | -  |
| eGFR (ml/min/1.73m <sup>2</sup> )             | 78.6 ± 13.7       | 80.0 ± 13.2       | 78.1 ± 12.6       | 77.6 ± 15.2       | 0.091                                | -                                | -  |
| Osteocalcin <sup>a</sup> (nmol/L)             | 7.54              | 7.77              | 7.60              | 7.24              | 0.032                                | 0.022                            | -  |
| ucOC <sup>a</sup> (nmol/L)                    | 5.10              | 5.36              | 5.34              | 4.62              | 0.015                                | 0.002                            | -  |
| BAP <sup>a</sup> (ng/mL)                      | 14.85             | 15.55             | 14.67             | 14.37             | 0.025                                | 0.052                            | -  |
| baPWV (cm/sec) <sup>c</sup>                   | 1451 (1306, 1623) | 1481 (1347, 1622) | 1447 (1301, 1602) | 1422 (1279, 1637) | 0.016                                | 0.813                            | -  |

n: number of participants BMI: body mass index aBMD: areal bone mineral density eGFR: estimated glomerular filtration rate ucOC: undercarboxylated osteocalcin BAP: bone-specific alkaline phosphatase baPWV: brachial-ankle pulse wave velocity

The values denote the mean ± SD or prevalence rate (%).

<sup>a</sup>The values indicate the geometric means.

<sup>b</sup>The values indicate the median and interquartile ranges in parentheses.

<sup>c</sup>The P -value was obtained by test for linearity or Cochran-Armitage trend test.

Supplemental table 3 . Baseline characteristics of the participants without past history of cardiovascular diseases categorized by developed or not developed increased arterial stiffness <sup>a</sup> during the follow-up period of the Japanese Population-based Osteoporosis Cohort Study (N = 538).

|   | Increased arterial stiffness <sup>a</sup> |                         | <i>P</i> -value |
|---|---|-------------------------|-----------------|
|   | Developed (n = 89)                        | Not developed (n = 449) |                 |
| Age (years)                                   | 67.6 ± 7.4                                | 61.1 ± 7.6              | <0.001          |
| Height (cm)                                   | 151.9 ± 6.1                               | 153.8 ± 5.5             | 0.003           |
| Weight (kg)                                   | 52.4 ± 7.7                                | 53.7 ± 8.7              | 0.196           |
| BMI (kg/m <sup>2</sup> )                      | 22.8 ± 3.4                                | 22.7 ± 3.5              | 0.868           |
| aBMD at the spine (g/cm <sup>2</sup> )        | 0.853 ± 0.148                             | 0.904 ± 0.154           | 0.004           |
| aBMD at the femoral neck (g/cm <sup>2</sup> ) | 0.625 ± 0.094                             | 0.670 ± 0.107           | <0.001          |
| aBMD at the total hip (g/cm <sup>2</sup> )    | 0.746 ± 0.113                             | 0.793 ± 0.115           | <0.001          |
| BMC at whole body (g)                         | 1438.9 ± 260.3                            | 1572.3 ± 281.7          | <0.001          |
| Osteoporosis, n (%)                           | 33 (37.1%)                                | 94 (20.9%)              | 0.002           |
| Systolic blood pressure (mmHg)                | 133.0 ± 15.4                              | 124.9 ± 15.8            | <0.001          |
| Diastolic blood pressure (mmHg)               | 75.3 ± 9.2                                | 72.1 ± 9.4              | 0.003           |
| Total cholesterol (mg/dL)                     | 214.7 ± 30.2                              | 214.4 ± 31.7            | 0.947           |
| Triglyceride (mg/dL)                          | 106.3 ± 75.3                              | 102.9 ± 79.2            | 0.708           |
| HDL-cholesterol (mg/dL)                       | 63.2 ± 15.1                               | 64.6 ± 15.8             | 0.434           |
| LDL-cholesterol (mg/dL)                       | 124.3 ± 26.9                              | 125.7 ± 28.6            | 0.678           |
| Fasting blood glucose (mg/dL)                 | 92.7 ± 20.5                               | 90.3 ± 17.4             | 0.252           |
| HbA1c (%)                                     | 5.7 ± 0.8                                 | 5.5 ± 0.5               | 0.071           |
| Hypertension, n (%)                           | 48 (53.9%)                                | 144 (32.1%)             | <0.001          |
| Hyperlipidemia, n (%)                         | 51 (57.3%)                                | 221 (49.2%)             | 0.166           |
| Diabetes mellitus n (%)                       | 10 (11.2%)                                | 21 (4.7%)               | 0.023           |
| Medication for hypertension, n (%)            | 33 (37.1%)                                | 90 (20.0%)              | 0.001           |
| Medication for hyperlipidaemia, n (%)         | 27 (30.3%)                                | 83 (18.5%)              | 0.014           |
| Medication for diabetes mellitus, n (%)       | 7 (7.9%)                                  | 14 (3.1%)               | 0.064           |
| Current smokers, n (%)                        | 2 (2.2%)                                  | 18 (4.0%)               | 0.553           |
| Habitual drinkers, n (%)                      | 8 (9.0%)                                  | 40 (8.9%)               | 0.999           |
| History of fragility fractures, n (%)         | 11 (12.4%)                                | 31 (6.9%)               | 0.086           |
| eGFR (ml/min/1.73m <sup>2</sup> )             | 75.2 ± 14.2                               | 79.2 ± 13.6             | 0.012           |
| Osteocalcin <sup>b</sup> (nmol/L)             | 7.59                                      | 7.53                    | 0.816           |
| ucOC <sup>b</sup> (nmol/L)                    | 4.77                                      | 5.16                    | 0.247           |
| BAP <sup>b</sup> (ng/mL)                      | 14.84                                     | 14.85                   | 0.987           |
| Sclerostin <sup>b</sup> (pmol/L)              | 34.43                                     | 37.63                   | 0.043           |
| baPWV (cm/sec) <sup>c</sup>                   | 1686 (1620, 1759)                         | 1407 (1280, 1551)       | <0.001          |

n: number of participants BMI: body mass index aBMD: areal bone mineral density eGFR: estimated glomerular filtration rate ucOC: undercarboxylated osteocalcin BAP: bone-specific alkaline phosphatase baPWV: brachial-ankle pulse wave velocity

The values denote mean ± SD or prevalence rate (%).

<sup>a</sup> Increased arterial stiffness was defined as baPWV values equal or more than 1800 cm/sec at the follow-up survey.

<sup>b</sup> The values indicate the geometric means.

<sup>c</sup> The values indicate the median and interquartile ranges in parentheses.