

**Table 1. Characteristics of male participants in the Japanese Specific Health Checkups and Guidance System (n=90,710)**

	Serum Uric Acid Category (mg/dl)						
	≤2	2.1 – 3.0	3.1 – 4.0	4.1 – 5.0	5.1 – 6.0	6.1 – 7.0	>7.0
	(n = 193 [0.2%])	(n = 774 [0.9%])	(n = 4,565 [5.0%])	(n = 14,310 [15.8%])	(n = 27,252 [30.0%])	(n = 25,192 [27.8%])	(n = 18,424 [20.3%])
Serum uric acid, mg/dl	1.1 (0.5) <sup>a</sup>	2.7 (0.2) <sup>a</sup>	3.7 (0.3) <sup>a</sup>	4.6 (0.3)	5.6 (0.3) <sup>a</sup>	6.5 (0.3) <sup>a</sup>	7.9 (0.8) <sup>a</sup>
Age, years	63.3 (9.3)	64.9 (7.9)	65.1 (7.8) <sup>a</sup>	64.6 (8.0)	64.1 (8.4) <sup>a</sup>	63.5 (8.7) <sup>a</sup>	62.7 (9.1) <sup>a</sup>
BMI, kg/m <sup>2</sup>	23.7 (2.9) <sup>a</sup>	22.5 (3.0) <sup>a</sup>	22.9 (3.0)	22.9 (2.9)	23.4 (2.9) <sup>a</sup>	24.0 (2.9) <sup>a</sup>	24.6 (3.1) <sup>a</sup>
History of stroke, %	4.1	6.3	5.2	4.7	4.4	5.0	5.0
History of heart disease, %	7.8	10.1	7.7	7.7	7.6	8.1	8.3
History of renal failure, %	1.0	0.3	0.6	0.4	0.6	0.7 <sup>a</sup>	1.0 <sup>a</sup>
Current smoker, %	20.7	25.8	26.1	26.3	25.6	25.5	26.1
Daily drinker, %	34.7	35.0	38.6	38.7	41.4 <sup>a</sup>	45.7 <sup>a</sup>	50.4 <sup>a</sup>
Hypertension, %	47.7	41.6	44.8	44.2	47.3 <sup>a</sup>	53.0 <sup>a</sup>	57.5 <sup>a</sup>
Diabetes, %	14.0	20.5	19.8*	17.0	13.6 <sup>a</sup>	12.2 <sup>a</sup>	11.4 <sup>a</sup>
Hypercholesterolemia, %	30.1	28.0	31.1	30.6	33.6 <sup>a</sup>	35.6 <sup>a</sup>	37.0 <sup>a</sup>
Systolic BP, mm Hg	129 (17)	128 (17)	129 (17)	129 (17)	130 (17) <sup>a</sup>	132 (17) <sup>a</sup>	133 (17) <sup>a</sup>
Diastolic BP, mm Hg	77 (10)	76 (10)	77 (10)	77 (11)	78 (10) <sup>a</sup>	79 (11) <sup>a</sup>	80 (11) <sup>a</sup>
LDL cholesterol, mg/dl	116 (30)	115 (29) <sup>a</sup>	118 (29)	118 (29)	121 (29) <sup>a</sup>	122 (30) <sup>a</sup>	123 (32) <sup>a</sup>
HDL cholesterol, mg/dl	59 (16)	60 (16)	59 (16)	59 (15)	58 (15) <sup>a</sup>	57 (15) <sup>a</sup>	55 (15) <sup>a</sup>
Triglycerides, mg/dl	96 [75, 134]	87 [65, 122] <sup>a</sup>	91 [67, 130]	93 [68, 131]	101 [73, 141] <sup>a</sup>	112 [80, 158] <sup>a</sup>	129 [90, 189] <sup>a</sup>
Glucose, mg/dl	100 (24)	103 (26) <sup>a</sup>	103 (24) <sup>a</sup>	101 (21)	100 (19) <sup>a</sup>	100 (18) <sup>a</sup>	100 (17) <sup>a</sup>
Hemoglobin A <sub>1c</sub> , %	5.7 (1.0)	5.9 (0.9)	5.9 (0.8) <sup>a</sup>	5.8 (0.7)	5.7 (0.7) <sup>a</sup>	5.7 (0.6) <sup>a</sup>	5.7 (0.5) <sup>a</sup>
AST, IU/l	22 [19, 28]	22 [19, 26] <sup>a</sup>	22 [19, 26]	22 [19, 26]	22 [19, 27] <sup>a</sup>	23 [20, 28] <sup>a</sup>	24 [20, 30] <sup>a</sup>
ALT, IU/l	21 [15, 29]	18 [14, 24] <sup>a</sup>	19 [15, 25]	19 [15, 25]	20 [16, 27] <sup>a</sup>	21 [16, 29] <sup>a</sup>	23 [17, 32] <sup>a</sup>
γ-GTP, IU/l	31 [21, 52]	27 [19, 43]	28 [20, 44]	28 [20, 44]	30 [21, 47] <sup>a</sup>	35 [23, 56] <sup>a</sup>	42 [27, 74] <sup>a</sup>
S Cr, mg/dl	0.81 (0.20)	0.76 (0.14) <sup>a</sup>	0.78 (0.21) <sup>a</sup>	0.80 (0.16)	0.83 (0.20) <sup>a</sup>	0.87 (0.19) <sup>a</sup>	0.94 (0.29) <sup>a</sup>
Proteinuria, %	5.2	5.9	6.5	6.6	6.6	7.7 <sup>a</sup>	10.4 <sup>a</sup>
eGFR, ml/min/1.73 m <sup>2</sup>	79.7 (22.9)	82.2 (17.3) <sup>a</sup>	79.7 (16.4) <sup>a</sup>	77.7 (15.1)	74.9 (14.6) <sup>a</sup>	71.5 (14.7) <sup>a</sup>	67.5 (15.4) <sup>a</sup>
Reduced kidney function, %	16.1	7.0 <sup>a</sup>	9.0	10.0	14.3 <sup>a</sup>	21.5 <sup>a</sup>	33.1 <sup>a</sup>

Data are shown as % for categorical variables, and mean (standard deviation) or median [interquartile range] for continuous variables.

BMI = body mass index; BP = blood pressure; S Cr = serum creatinine; LDL = low-density lipoprotein; HDL = high-density lipoprotein; AST = aspartate transaminase; ALT = alanine transaminase; γ-GTP = gamma glutamyl transpeptidase; eGFR = estimated glomerular filtration rate.

\* Indicates statistical significance ( $P<0.05$ ) compared to the reference category (i.e., serum uric acid levels of 4.1 - 5.0 mg/dl).

**Table 2. Characteristics of female participants in the Japanese Specific Health Checkups and Guidance System (n=136,935)**

	Serum Uric Acid Category (mg/dl)						
	≤2	2.1 – 3.0	3.1 – 4.0	4.1 – 5.0	5.1 – 6.0	6.1 – 7.0	>7.0
	(n = 540 [0.4%])	(n = 6,331 [4.6%])	(n = 32,223 [23.5%])	(n = 52,579 [38.4%])	(n = 31,892 [23.3%])	(n = 10,339 [7.6%])	(n = 3,031 [2.2%])
Serum uric acid, mg/dl	1.5 (0.6) <sup>a</sup>	2.7 (0.2) <sup>a</sup>	3.6 (0.3) <sup>a</sup>	4.5 (0.3)	5.5 (0.3) <sup>a</sup>	6.4 (0.3) <sup>a</sup>	7.7 (0.7) <sup>a</sup>
Age, years	62.5 (9.0) <sup>a</sup>	62.4 (9.0) <sup>a</sup>	62.7 (8.7) <sup>a</sup>	63.6 (7.9)	64.5 (7.3) <sup>a</sup>	65.1 (7.0) <sup>a</sup>	65.3 (7.0) <sup>a</sup>
BMI, kg/m <sup>2</sup>	21.7 (3.3) <sup>a</sup>	21.5 (3.0) <sup>a</sup>	21.8 (3.0) <sup>a</sup>	22.5 (3.2)	23.6 (3.5) <sup>a</sup>	24.7 (3.8) <sup>a</sup>	25.4 (4.2) <sup>a</sup>
History of stroke, %	1.7	2.1	2.2	2.3	2.9 <sup>a</sup>	3.4 <sup>a</sup>	4.8 <sup>a</sup>
History of heart disease, %	4.4	4.5	4.3	4.6	5.5 <sup>a</sup>	6.8 <sup>a</sup>	8.9 <sup>a</sup>
History of renal failure, %	0.6	0.5	0.4	0.4	0.6 <sup>a</sup>	0.9 <sup>a</sup>	2.3 <sup>a</sup>
Current smoker, %	7.2	6.3	6.3	6.0	6.8 <sup>a</sup>	8.1 <sup>a</sup>	9.7 <sup>a</sup>
Daily drinker, %	4.8	5.3 <sup>a</sup>	5.6 <sup>a</sup>	7.0	8.7 <sup>a</sup>	10.3 <sup>a</sup>	12.5 <sup>a</sup>
Hypertension, %	38.1	31.8 <sup>a</sup>	33.5 <sup>a</sup>	39.4	49.4 <sup>a</sup>	59.0 <sup>a</sup>	70.0 <sup>a</sup>
Diabetes, %	7.4	7.0	6.4	6.7	8.6 <sup>a</sup>	11.8 <sup>a</sup>	17.0 <sup>a</sup>
Hypercholesterolemia, %	41.1 <sup>a</sup>	40.9 <sup>a</sup>	44.0 <sup>a</sup>	50.8	55.5 <sup>a</sup>	59.9 <sup>a</sup>	60.8 <sup>a</sup>
Systolic BP, mm Hg	127 (18)	125 (18) <sup>a</sup>	126 (18) <sup>a</sup>	128 (18)	131 (18) <sup>a</sup>	133 (17) <sup>a</sup>	135 (18) <sup>a</sup>
Diastolic BP, mm Hg	74 (10)	73 (11) <sup>a</sup>	74 (10) <sup>a</sup>	75 (10)	76 (10) <sup>a</sup>	78 (10) <sup>a</sup>	78 (11) <sup>a</sup>
LDL cholesterol, mg/dl	122 (30) <sup>a</sup>	124 (29) <sup>a</sup>	127 (29) <sup>a</sup>	130 (30)	133 (31) <sup>a</sup>	135 (32) <sup>a</sup>	133 (33) <sup>a</sup>
HDL cholesterol, mg/dl	69 (17) <sup>a</sup>	69 (16) <sup>a</sup>	68 (16) <sup>a</sup>	66 (16)	64 (16) <sup>a</sup>	61 (15) <sup>a</sup>	59 (16) <sup>a</sup>
Triglycerides, mg/dl	83 [61, 111] <sup>a</sup>	78 [59, 104] <sup>a</sup>	82 [62, 111] <sup>a</sup>	90 [68, 123]	102 [75, 140] <sup>a</sup>	115 [84, 158] <sup>a</sup>	128 [95, 180] <sup>a</sup>
Glucose, mg/dl	91 (20)	94 (18)	93 (16) <sup>a</sup>	94 (15)	96 (15) <sup>a</sup>	98 (16) <sup>a</sup>	101 (19) <sup>a</sup>
Hemoglobin A <sub>1c</sub> , %	5.6 (0.7)	5.7 (0.6) <sup>a</sup>	5.6 (0.6) <sup>a</sup>	5.7 (0.5)	5.7 (0.5) <sup>a</sup>	5.8 (0.6) <sup>a</sup>	5.9 (0.6) <sup>a</sup>
AST, IU/l	21 [18, 25]	21 [18, 24] <sup>a</sup>	21 [18, 25] <sup>a</sup>	21 [19, 25]	22 [19, 26] <sup>a</sup>	23 [20, 27] <sup>a</sup>	24 [20, 29] <sup>a</sup>
ALT, IU/l	16 [13, 20] <sup>a</sup>	15 [13, 20] <sup>a</sup>	16 [13, 20] <sup>a</sup>	17 [14, 22]	18 [14, 24] <sup>a</sup>	20 [15, 27] <sup>a</sup>	21 [16, 29] <sup>a</sup>
γ-GTP, IU/l	18 [13, 26] <sup>a</sup>	17 [13, 23] <sup>a</sup>	18 [14, 24] <sup>a</sup>	19 [15, 27]	21 [16, 31] <sup>a</sup>	24 [18, 37] <sup>a</sup>	28 [20, 44] <sup>a</sup>
S Cr, mg/dl	0.58 (0.17) <sup>a</sup>	0.58 (0.10) <sup>a</sup>	0.60 (0.11) <sup>a</sup>	0.63 (0.11)	0.66 (0.14) <sup>a</sup>	0.70 (0.22) <sup>a</sup>	0.80 (0.41) <sup>a</sup>
Proteinuria, %	3.9	2.8	2.9	3.0	4.7 <sup>a</sup>	7.4 <sup>a</sup>	13.8 <sup>a</sup>
eGFR, ml/min per 1.73 m <sup>2</sup>	83.5 (19.6) <sup>a</sup>	83.3 (16.7) <sup>a</sup>	79.9 (15.4) <sup>a</sup>	75.3 (14.4)	71.2 (14.4) <sup>a</sup>	67.2 (14.7) <sup>a</sup>	61.6 (17.0) <sup>a</sup>
Reduced kidney function, %	6.1 <sup>a</sup>	3.8 <sup>a</sup>	5.4 <sup>a</sup>	9.8	17.9 <sup>a</sup>	28.6 <sup>a</sup>	43.7 <sup>a</sup>

Data are shown as % for categorical variables, and mean (standard deviation) or median [interquartile range] for continuous variables.

BMI = body mass index; BP = blood pressure; S Cr = serum creatinine; LDL = low-density lipoprotein; HDL = high-density lipoprotein; AST = aspartate transaminase; ALT = alanine transaminase; γ-GTP = gamma glutamyl transpeptidase; eGFR = estimated glomerular filtration rate.

<sup>a</sup> Indicates statistical significance ( $P<0.05$ ) compared to the reference category (i.e., serum uric acid levels of 4.1 - 5.0 mg/dl).

## **Figure legends**

### **Figure 1. Prevalence of hypouricemia by gender and age.**

Trends were significant for women ( $\square$ ;  $P<0.001$ ), but not for men ( $\blacksquare$ ;  $P=0.24$ ).

### **Figure 2. Forest plot showing odds ratios with 95% confidence intervals for the relationship between serum uric acid levels and reduced kidney function.**

All analyses were adjusted for the following covariates: age (per 10-year increase), daily drinker, current smoker, hypertension, hypercholesterolemia, obesity, and history of renal failure.