

Online-Only Supplements

Supplementary Methods

Supplementary Tables

Table S1. Age-adjusted mean values and proportion (95% confidence interval) of baseline characteristics according to the hematuria change category among women (n = 95 363)

Table S2. Age-adjusted mean values and proportion (95% confidence interval) of baseline characteristics according to the hematuria change category among men (n = 136 857)

Table S3. Development of decreased EGFR (<60 mg/dl) by sex and hematuria change category (n = 232 220)

Table S4. Development of proteinuria by sex and hematuria change category (n = 232 220)

Table S5. Development of chronic kidney disease (CKD) and proteinuria by the menopausal status and hematuria change category (n = 95 363)

Table S6. Hazard ratio (95% CI) of incident all chronic kidney disease (CKD) by the hematuria change category in clinically relevant subgroups

Table S7. Development of persistent chronic kidney disease (CKD) and persistent proteinuria by the hematuria change category among participants with at least two follow-up visits after baseline period (n = 177 024)

Table S8. Development of chronic kidney disease and proteinuria by the hematuria change category when microscopic hematuria was defined as the presence of ≥ 3 red blood cells per high-power field (n = 232 220)

Table S9. Development of chronic kidney disease (CKD) and proteinuria by the hematuria change category, after excluding 328 participants with incident genitourinary cancer or endometrial cancer (n = 231 892)

Table S10. Development of chronic kidney disease (CKD) and proteinuria by the hematuria change category, after excluding 1631 participants with microscopic hematuria of ≥ 20 /HPF (n = 230 589)

Supplementary methods

Alcohol consumption was categorized into none, <20 g of ethanol/day, and ≥ 20 g of ethanol/day. Physical activity level was collected using the validated Korean version of the International Physical Activity Questionnaire short form ¹ and the participants were categorized into one of three categories: inactive, minimally active, or health-enhancing physical activity which meets either of the two criteria: (i) vigorous-intensity activity on ≥ 3 days per week totaling $\geq 1,500$ MET min/week, or (ii) 7 days with any combination of walking, moderate-intensity, or vigorous-intensity activities achieving at least 3,000 MET min/week ¹. Obesity was defined as BMI ≥ 25 kg/m² according to Asian-specific criteria.² Hypertension was defined as systolic BP ≥ 140 mmHg, diastolic BP ≥ 90 mmHg, or self-reported history of hypertension or antihypertensive medication use.

Fasting (at least 10 h) measurements included serum glucose, creatinine, insulin, and high-sensitivity C-reactive protein (hsCRP) levels and lipid profiles. Fresh and midstream spot urine samples were collected without preservatives; all tests were completed within 1 h of urine collection. Insulin resistance was assessed using the homeostatic model assessment-insulin resistance (HOMA-IR) equation: fasting blood insulin (uU/ml) \times fasting blood glucose (mmol/l) / 22.5. Diabetes was defined as fasting glucose ≥ 126 mg/dL, glycated hemoglobin $\geq 6.5\%$, or self-reported history of diabetes or antidiabetic medication use.

Serum creatinine was measured using the Jaffe method with automated chemistry analyzers: the Modular DPP (Roche Diagnostics, Tokyo, Japan) until 2015 and Cobas 8000 c702 (Roche Diagnostics) thereafter. The within-batch and total coefficients of variation were 1.2–3.9% for low-level and 0.9–2.1% for high-level quality control specimens for the duration of the study.

Urinalysis of protein and red blood cells was performed using a URiSCAN strip (YD Diagnostics, Yong-In, Korea) on the URiSCAN Pro II urine chemistry analyzer (YD

Diagnostics) until 2014 and the URiSCAN Super Plus (YD Diagnostics) thereafter (further details in the Supplement). Upon reaction with a urine specimen, the degree of color development of the reagent strip was measured by a charge-coupled device (CCD) color image sensor under illumination with a light-emitting diode. The CCD read each red (630 nm), green (540 nm), and blue (460 nm) light wavelength. The reflectance rate difference before and after the reaction was then converted to a change in the reflectance rate value, from which an ordinal scale grade was generated according to a predefined range by the manufacturer.³ Urine protein was reported in six grades: absent, trace, 1+, 2+, 3+, and 4+ (corresponding to the following protein levels: undetectable, 10, 30, 100, 300, and 1000 mg/dL, respectively). Proteinuria was defined as a grade $\geq 1+$. Microscopic examination was performed on the urine specimens by centrifugation at 1800 rpm for 3 min and reported in eight grades: 0–1, 1–3, 3–5, 5–10, 10–20, 20–30, many and numerous cells per high-power field (HPF). Microscopic hematuria was defined as the presence of ≥ 5 red blood cells per HPF under $400\times$ magnification (DMLS2; Leica, Lockbourne, OH, USA).⁴ In sensitivity analyses, the presence of ≥ 3 red blood cells per HPF was used for definition of microscopic hematuria.⁵

Supplementary statistical analyses

To examine the robustness of our findings, we performed several sensitivity analyses as follows: 1) we examined the association between hematuria status and persistent CKD when incident CKD was observed repeatedly in at least one subsequent follow-up visit; 2) analyses were performed using the different definition for microscopic hematuria as presence of ≥ 3 red blood cells per HPF⁵; 3) Finally, sensitivity analyses were performed after excluding participants who developed incident genitourinary cancer during follow-up, or after

excluding participants with microscopic hematuria with RBC count ≥ 20 /HPF which may indicate undiagnosed genitourinary disease.⁶

Supplementary References

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Table S1. Baseline characteristics according to hematuria category among women (n = 95 363)

Characteristics	Overall	Hematuria change category			
		None (G1)	Regressed (G2)	Developed (G3)	Persistent (G4)
Number of participants	95,363	90,785	1,600	1,926	1,052
Age (years)	37.7 (7.7)	37.6 (7.7)	39.4 (8.6)	39.3 (8.3)	41.4 (8.8)
Seoul center (%)	56.9	56.3	68.7	64.3	76.2
Alcohol intake (%) ^a	6.1	6.1	6.0	5.5	3.7
Current smoker (%)	2.1	2.1	2.1	2.3	2.0
HEPA (%)	14.0	14.0	13.6	14.6	14.5
Education level (%) ^b	78.9	79.0	78.3	77.4	77.2
History of diabetes (%)	0.9	0.9	0.6	0.7	0.6
History of hypertension (%)	3.1	3.0	3.4	4.2	5.8
History of CVD (%)	0.6	0.6	0.8	0.4	0.7
Anti-lipid medication use (%)	1.3	1.2	1.7	2.0	2.3
Obesity (%) ^c	11.9	11.9	11.1	11.6	11.8
Body mass index (kg/m ²) ^d	21.6 (3.0)	21.6 (3.0)	21.7 (3.0)	21.6 (3.1)	21.6 (2.7)
SBP (mmHg) ^d	102.3 (11.4)	102.3 (11.4)	102 (11.7)	101.9 (11.3)	102.5 (12.3)
eGFR (mg/dl) ^d	107.8 (12.5)	107.9 (12.5)	106.3 (12.8)	107 (12.8)	104.6 (12.9)
DBP (mmHg) ^d	65.2 (8.3)	65.2 (8.3)	65.1 (8.6)	64.8 (8.4)	65.2 (8.7)
Glucose (mg/dl) ^d	91.5 (10.9)	91.5 (11.0)	91 (9.7)	91.2 (11.2)	91.6 (8.3)
Total cholesterol (mg/dl) ^d	186.4 (32.0)	186.4 (31.9)	186.2 (31.9)	186.5 (32.3)	187.9 (31.9)
LDL-C (mg/dL) ^d	109.8 (29.1)	109.7 (29.1)	109.9 (29.7)	110.8 (29.3)	111.4 (29.0)
HDL-C (mg/dL) ^d	65.9 (15.0)	66.0 (15.0)	65.8 (14.5)	65.5 (15.2)	65.4 (14.7)
Triglycerides (mg/dL) ^e	70 (54-95)	70 (54-95)	68 (52-92)	71 (55-94)	69.5 (55-97)
GGT (U/L) ^e	13 (10-17)	13 (10-17)	13 (10-17)	13 (10-18)	13 (11-17)
ALT (U/L) ^e	13 (10-17)	13 (10-17)	13 (10-17)	13 (10-17)	13 (10-17)
HOMA-IR ^e	1.08 (0.72-1.57)	1.08 (0.72-1.58)	1.00 (0.69-1.47)	1.04 (0.70-1.53)	1.05 (0.71-1.53)
hsCRP ^e	0.3 (0.2-0.7)	0.3 (0.2-0.6)	0.4 (0.2-0.9)	0.3 (0.2-0.7)	0.3 (0.2-0.7)

^a≥20 g/day; ^b≥ college graduate; ^c BMI ≥25 kg/m².

Data are ^d the mean (standard deviation), ^emedian (interquartile range), or percentage.

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; G1, no hematuria at baseline and no hematuria at 2nd visit (reference group); G2, hematuria at baseline and no hematuria at 2nd visit (hematuria regressed group); G3, no hematuria at baseline and hematuria at 2nd visit (hematuria developed group); G4, hematuria at baseline and hematuria at 2nd visit (persistent hematuria group); GGT, gamma-glutamyltransferase; HDL-C, high-density lipoprotein cholesterol; HEPA, health-enhancing physical activity; HOMA-IR, homeostasis model assessment of insulin resistance; hs-CRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

Table S2. Baseline characteristics according to hematuria category among men (n = 136 857)

Characteristics	Overall	Hematuria change category			
		None (G1)	Regressed (G2)	Developed (G3)	Persistent (G4)
Number of participants	136,857	134,972	682	827	376
Age (years)	38.6 (7.6)	38.6 (7.5)	39.7 (8.5)	39.8 (8)	40.9 (8.2)
Seoul center (%)	59.1	58.9	71.7	69.8	79.5
Alcohol intake (%) ^a	35.2	35.2	32.2	36.8	36.0
Current smoker (%)	36.5	36.5	38.1	39.5	45.7
HEPA (%)	17.1	17.1	13.6	18.0	12.7
Education level (%) ^b	89.2	89.2	90.4	89.2	89.9
History of diabetes (%)	2.5	2.5	2.1	3.0	2.1
History of hypertension (%)	9.9	9.9	11.7	9.3	12.2
History of CVD (%)	1.0	1.0	0.9	1.8	0.8
Anti-lipid medication use (%)	2.3	2.3	1.3	1.5	3.2
Obesity (%) ^c	39.9	40.0	38.3	38.7	36.4
Body mass index (kg/m ²) ^d	24.5 (3.0)	24.5 (3.0)	24.3 (3.1)	24.4 (3.3)	24.3 (3.0)
SBP (mmHg) ^d	114.7 (11.4)	114.8 (11.4)	114.7 (12.4)	114.1 (11.7)	113.8 (11.7)
eGFR (mg/dl) ^d	98.0 (12.8)	98.0 (12.8)	96.8 (13.1)	97.6 (12.6)	96.2 (13.8)
DBP (mmHg) ^d	73.7 (9.3)	73.7 (9.3)	74.4 (9.8)	73.2 (9.4)	73.5 (9.7)
Glucose (mg/dl) ^d	97.3 (14.8)	97.3 (14.8)	96 (11.5)	97.2 (14.9)	96.8 (12.3)
Total cholesterol (mg/dl) ^d	198.9 (34.3)	198.9 (34.3)	197.9 (34.1)	196.9 (33.5)	198.3 (33.6)
LDL-C (mg/dL) ^d	128.3 (31.5)	128.3 (31.5)	127.1 (30.9)	125.8 (31.7)	128.1 (31.3)
HDL-C (mg/dL) ^d	53.2 (12.9)	53.2 (12.9)	53.3 (13.0)	53.2 (13.3)	52.5 (12.8)
Triglycerides (mg/dL) ^e	112 (80-162)	112 (80-162)	109 (76-159)	113 (80-162)	111.5 (80-161)
GGT (U/L) ^e	30 (20-48)	30 (20-48)	30 (20-49)	30 (20-48)	30 (20-45)
ALT (U/L) ^e	24 (17-35)	24 (17-35)	23 (17-35)	22 (16-33)	22 (16-33.5)
HOMA-IR ^e	1.29 (0.85-1.94)	1.3 (0.85-1.94)	1.29 (0.85-1.90)	1.23 (0.84-1.92)	1.29 (0.83-1.97)
hsCRP ^e	0.5 (0.3-1.0)	0.5 (0.3-1.0)	0.6 (0.3-1.4)	0.5 (0.3-1.0)	0.6 (0.3-1.0)

^a≥20 g/day; ^b≥ college graduate; ^c BMI ≥25 kg/m².

Data are ^d the mean (standard deviation), ^emedian (interquartile range), or percentage.

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; G1, no hematuria at baseline and no hematuria at 2nd visit (reference group); G2, hematuria at baseline and no hematuria at 2nd visit (hematuria regressed group); G3, no hematuria at baseline and hematuria at 2nd visit (hematuria developed group); G4, hematuria at baseline and hematuria at 2nd visit (persistent hematuria group); GGT, gamma-glutamyltransferase; HDL-C, high-density lipoprotein cholesterol; HEPA, health-enhancing physical activity; HOMA-IR, homeostasis model assessment of insulin resistance; hs-CRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure.

Table S3. Development of decreased eGFR (<60 mg/dl) by sex and hematuria change category (n = 232 220)

Hematuria change category	Hematuria status at 1st and 2nd visits		Person-years	Incident cases	Incidence density (/ 10 ³ PY)	Age-adjusted HR (95% CI)	Multivariable-adjusted HR ^a (95% CI)		HR (95% CI) ^b in a model with time-dependent variables
	1 st test	2 nd test					Model 1	Model 2	
Total (n = 232 220)									
None (G1)	none	none	1,032,045	716	0.7	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	9,961	11	1.1	1.24 (0.69-2.26)	1.68 (0.92-3.05)	1.82 (1.00-3.32)	1.84 (1.01-3.35)
Developed (G3)	none	hematuria	12,722	17	1.3	1.49 (0.92-2.41)	2.25 (1.38-3.65)	2.35 (1.44-3.81)	2.25 (1.38-3.66)
Persistent (G4)	hematuria	hematuria	6,558	14	2.1	1.84 (1.08-3.13)	3.09 (1.81-5.28)	2.15 (1.26-3.68)	2.28 (1.33-3.89)
Women (n = 95 363)									
None (G1)	none	none	408,917	132	0.3	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	6,958	6	0.9	2.00 (0.88-4.53)	2.06 (0.91-4.68)	2.31 (1.01-5.25)	2.38 (1.05-5.40)
Developed (G3)	none	hematuria	8,825	7	0.8	1.74 (0.82-3.73)	1.83 (0.86-3.93)	2.08 (0.97-4.47)	1.97 (0.92-4.23)
Persistent (G4)	hematuria	hematuria	4,862	7	1.4	2.39 (1.12-5.12)	2.55 (1.19-5.48)	2.20 (1.02-4.74)	2.06 (0.96-4.43)
Men (n = 136 857)									
None (G1)	none	none	623,128	584	0.9	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	3,003	5	1.7	1.39 (0.58-3.35)	1.36 (0.56-3.28)	1.46 (0.60-3.53)	1.44 (0.60-3.48)
Developed (G3)	none	hematuria	3,897	10	2.6	2.34 (1.25-4.37)	2.65 (1.41-4.95)	2.58 (1.38-4.84)	2.49 (1.33-4.66)

Persistent (G4)	hematuri a	hematuri a	1,697	7	4.1	3.23 (1.53- 6.80)	3.83 (1.82- 8.09)	2.11 (1.00- 4.49)	2.54 (1.20-5.37)
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The P-value for the interaction of sex and hematuria change category in the risk of CKD was 0.859 (Model 2).

^aEstimated from Cox proportional hazards models. Multivariable Model 1 was adjusted for age; sex (only for total subjects); center; year of screening; alcohol intake; smoking status; physical activity level; BMI; education level; anti-lipid medication use; and history of diabetes, hypertension, and cardiovascular disease. Model 2: Model 1 plus adjustment for eGFR; total cholesterol, HDL-C, triglyceride, and glucose levels; and SBP.

^bEstimated from Cox proportional hazards models with hematuria change category; smoking status; alcohol consumption; physical activity level; BMI; anti-lipid medication use; history of diabetes, hypertension, and cardiovascular disease; total cholesterol, HDL-C, triglyceride, and glucose levels; and SBP as time-dependent categorical variables and baseline sex, center, year of screening, education level, and eGFR as time-fixed variables.

Abbreviations: BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; G1, no hematuria at baseline and no hematuria at 2nd visit (reference group); G2, hematuria at baseline and no hematuria at 2nd visit (hematuria regressed group); G3, no hematuria at baseline and hematuria at 2nd visit (hematuria developed group); G4, hematuria at baseline and hematuria at 2nd visit (persistent hematuria group); HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; PY, person-years; SBP, systolic blood pressure.

Table S4. Development of proteinuria by sex and hematuria change category (n = 232 220)

Hematuria change category	Hematuria status at 1st and 2nd visits		Person-years	Incident cases	Incidence density (/10 ³ PY)	Age-adjusted HR (95% CI)	Multivariable-adjusted HR ^a (95% CI)		HR (95% CI) ^b in a model with time-dependent variables
	1 st test	2 nd test					Model 1	Model 2	
Total (n = 232 220)									
None (G1)	none	none	1,029,825	1,530	1.5	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	9,904	29	2.9	2.00 (1.39-2.89)	1.84 (1.27-2.66)	1.87 (1.3-2.71)	1.85 (1.28-2.68)
Developed (G3)	none	hematuria	12,599	64	5.1	3.43 (2.67-4.41)	3.32 (2.58-4.27)	3.41 (2.65-4.39)	3.36 (2.61-4.32)
Persistent (G4)	hematuria	hematuria	6,403	66	10.3	7.01 (5.48-8.98)	6.88 (5.36-8.84)	7.03 (5.47-9.03)	6.74 (5.25-8.66)
Women (n = 95 363)									
None (G1)	none	none	407,717	694	1.7	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	6,937	15	2.2	1.29 (0.77-2.15)	1.25 (0.75-2.09)	1.28 (0.77-2.14)	1.29 (0.77-2.14)
Developed (G3)	none	hematuria	8,761	37	4.2	2.48 (1.78-3.46)	2.57 (1.84-3.57)	2.63 (1.89-3.66)	2.63 (1.89-3.67)
Persistent (G4)	hematuria	hematuria	4,778	37	7.7	4.56 (3.28-6.36)	4.76 (3.42-6.64)	4.88 (3.50-6.80)	4.75 (3.41-6.62)
Men (n = 136 857)									
None (G1)	none	none	622,108	836	1.3	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	2,968	14	4.7	3.56 (2.10-6.04)	3.39 (2.00-5.75)	3.41 (2.01-5.79)	3.26 (1.92-5.53)
Developed (G3)	none	hematuria	3,839	27	7.0	5.23 (3.57-7.68)	5.11 (3.48-7.50)	5.28 (3.59-7.75)	5.01 (3.42-7.36)

Persistent (G4)	hematuri a	hematuri a	1,626	29	17.8	13.41 (9.26- 19.42)	13.88 (9.57- 20.13)	14.09 (9.72- 20.44)	12.86 (8.87- 18.66)
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The P-value for the interaction of sex and hematuria change category in the risk of proteinuria was < 0.001 (Model 2).

^aEstimated from Cox proportional hazards models. Multivariable model 1 was adjusted for age; sex (only for total subjects); center; year of screening; alcohol intake; smoking status; physical activity level; BMI, education level; anti-lipid medication use; and history of diabetes, hypertension, and cardiovascular disease. Model 2: Model 1 plus adjustment for eGFR; total cholesterol, HDL-C, triglyceride, and glucose levels; and SBP.

^bEstimated from Cox proportional hazards models with hematuria change category; smoking status; alcohol consumption; physical activity level; BMI; anti-lipid medication use; history of diabetes, hypertension, and cardiovascular disease; total cholesterol, HDL-C, triglyceride, and glucose levels; and SBP as time-dependent categorical variables and baseline sex, center, year of screening, education level, and eGFR as time-fixed variables.

Abbreviations: BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; G1, no hematuria at baseline and no hematuria at 2nd visit (reference group); G2, hematuria at baseline and no hematuria at 2nd visit (hematuria regressed group); G3, no hematuria at baseline and hematuria at 2nd visit (hematuria developed group); G4, hematuria at baseline and hematuria at 2nd visit (persistent hematuria group); HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; PY, person-years; SBP, systolic blood pressure.

Table S5. Development of chronic kidney disease and proteinuria by the menopausal status and hematuria change category (n = 95 363)

Hematuria change category	Hematuria status at 1st and 2nd visits		Multivariable-adjusted HR ^a (95% CI)		
	1 st test	2 nd test	<i>eGFR</i> <60 mg/dl	<i>Proteinuria</i>	<i>CKD</i> (<i>eGFR</i> <60 mg/dl or <i>proteinuria</i>)
Premenopausal women (n = 90 132)					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	3.85 (1.64-9.05)	1.26 (0.75-2.10)	1.55 (1.00-2.39)
Developed (G3)	none	hematuria	1.78 (0.56-5.67)	2.56 (1.83-3.58)	2.51 (1.82-3.47)
Persistent (G4)	hematuria	hematuria	2.04 (0.50-8.36)	4.74 (3.38-6.65)	4.24 (3.04-5.91)
Postmenopausal women (n = 5 222)					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	-	-	-
Developed (G3)	none	hematuria	2.71 (0.96-7.66)	3.62 (0.46-28.62)	2.85 (1.14-7.12)
Persistent (G4)	hematuria	hematuria	2.68 (1.02-6.99)	4.10 (0.52-32.46)	3.82 (1.64-8.91)
<i>P for interaction</i>			0.8	0.9	0.9

^aEstimated from Cox proportional hazards models. Multivariable model 1 was adjusted for age; sex; center; year of screening; alcohol intake; smoking status; physical activity level; BMI; education level; anti-lipid medication use; and history of diabetes, hypertension, cardiovascular disease, eGFR; total cholesterol, HDL-C, triglyceride, and glucose levels; and SBP.

Abbreviations: BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease (*either eGFR*<60 mg/dl or *proteinuria*); eGFR, estimated glomerular filtration rate; G1, no hematuria at baseline and no hematuria at 2nd visit (reference group); G2, hematuria at baseline and no

hematuria at 2nd visit (hematuria regressed group); G3, no hematuria at baseline and hematuria at 2nd visit (hematuria developed group); G4, hematuria at baseline and hematuria at 2nd visit (persistent hematuria group); HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; SBP, systolic blood pressure.

Table S6. Hazard ratio (95% CI) of incident chronic kidney disease by the hematuria change category in clinically relevant subgroups

Subgroup	Hematuria change category				<i>P</i> for interaction
	None (G1)	Regressed (G2)	Developed (G3)	Persistent (G4)	
Age					0.001
<40 years (n = 148 309)	1.00 (reference)	2.16 (1.40-3.32)	4.63 (3.51-6.12)	6.81 (4.78-9.70)	
≥40 years (n = 83 911)	1.00 (reference)	1.61 (1.02-2.53)	1.98 (1.35-2.90)	4.48 (3.32-6.06)	
Current smoking					0.04
No (n = 161 637)	1.00 (reference)	1.76 (1.20-2.58)	3.07 (2.34-4.03)	4.42 (3.30-5.92)	
Yes (n = 49 259)	1.00 (reference)	3.46 (1.90-6.28)	4.66 (2.87-7.55)	7.53 (4.50-12.60)	
Alcohol intake					0.9
<20 g/day (n = 165 392)	1.00 (reference)	1.96 (1.37-2.80)	3.57 (2.78-4.57)	5.47 (4.20-7.12)	
≥20 g/day (n = 51 924)	1.00 (reference)	2.13 (1.06-4.29)	2.91 (1.64-5.15)	5.96 (3.27-10.83)	
HEPA					0.3
No (n = 189 191)	1.00 (reference)	1.98 (1.42-2.78)	3.25 (2.52-4.19)	5.90 (4.59-7.59)	
Yes (n = 35 614)	1.00 (reference)	1.28 (0.48-3.43)	3.14 (1.84-5.36)	2.80 (1.32-5.92)	
BMI					0.9
<25 kg/m ² (n = 166 224)	1.00 (reference)	1.87 (1.28-2.74)	3.06 (2.33-4.02)	4.96 (3.73-6.60)	
≥25 kg/m ² (n = 65 996)	1.00 (reference)	1.83 (1.06-3.17)	3.54 (2.39-5.23)	5.57 (3.79-8.20)	
HOMA-IR					0.6
<2.5 (n = 206 097)	1.00 (reference)	1.77 (1.24-2.51)	3.10 (2.41-3.98)	5.47 (4.27-7.01)	
≥2.5 (n = 25 119)	1.00 (reference)	2.17 (1.03-4.59)	3.88 (2.32-6.51)	3.78 (1.87-7.61)	
hsCRP					0.5
<1.0 mg/L (n = 169 556)	1.00 (reference)	1.88 (1.27-2.80)	3.52 (2.72-4.56)	5.06 (3.82-6.72)	
≥1.0 mg/L (n = 53 466)	1.00 (reference)	1.74 (1.02-2.95)	2.32 (1.44-3.76)	5.22 (3.43-7.92)	
Hypertension					0.3
No (n = 209 325)	1.00 (reference)	1.85 (1.29-2.64)	3.40 (2.67-4.33)	5.73 (4.44-7.39)	
Yes (n = 22 542)	1.00 (reference)	1.83 (0.95-3.55)	2.28 (1.26-4.15)	3.65 (2.14-6.23)	
Diabetes					0.2
No (n = 224 772)	1.00 (reference)	1.97 (1.43-2.71)	3.26 (2.58-4.13)	5.48 (4.32-6.95)	
Yes (n = 7448)	1.00 (reference)	0.53 (0.07-3.76)	2.04 (0.91-4.60)	2.42 (0.90-6.51)	

^aEstimated from Cox proportional hazards models. Multivariable model 1 was adjusted for age; sex; center; year of screening; alcohol intake; smoking status; physical activity level; BMI; education level; anti-lipid medication use; and history of diabetes, hypertension, cardiovascular disease, eGFR; total cholesterol, HDL-C, triglyceride, and glucose levels; and SBP.

Chronic kidney disease was defined as either *eGFR*<60 mg/dl or proteinuria.

Abbreviations: BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; G1, no hematuria at baseline and no hematuria at 2nd visit (reference group); G2, hematuria at baseline and no hematuria at 2nd visit (hematuria regressed group); G3, no hematuria at baseline and hematuria at 2nd visit (hematuria developed group); G4, hematuria at baseline and hematuria at 2nd visit (persistent hematuria group); HDL-C, high-density lipoprotein cholesterol; HEPA, health-enhancing physical activity; HOMA-IR, homeostasis model assessment of insulin resistance; hsCRP, high-sensitivity C-reactive protein; SBP, systolic blood pressure.

Table S7. Development of persistent chronic kidney disease and persistent proteinuria by the hematuria change category among participants with at least two follow-up visits after baseline period (n = 177 024)

Hematuria change category	Hematuria status at 1st and 2nd visits		Multivariable-adjusted HR ^a (95% CI)		
	1 st test	2 nd test	Persistent eGFR<60 mg/dl	Persistent proteinuria	Persistent CKD (eGFR<60 mg/dl or proteinuria)
Total (n = 177 024)					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	1.49 (0.21-10.78)	5.67 (2.25-14.26)	3.18 (1.38-7.31)
Developed (G3)	none	hematuria	4.49 (1.81-11.16)	8.05 (3.88-16.68)	5.72 (3.17-10.33)
Persistent (G4)	hematuria	hematuria	5.22 (2.03-13.41)	47.98 (28.15-81.78)	18.59 (11.66-29.62)
Women (n = 70 071)					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	5.25 (0.69-40.11)	3.25 (0.44-24.24)	3.10 (0.75-12.86)
Developed (G3)	none	hematuria	3.06 (0.40-23.23)	10.25 (3.50-29.97)	5.40 (2.11-13.81)
Persistent (G4)	hematuria	hematuria	10.46 (3.23-33.90)	65.81 (31.95-135.58)	24.42 (13.27-44.92)
Men (n = 106 953)					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	-	7.35 (2.59-20.91)	3.28 (1.18-9.15)
Developed (G3)	none	hematuria	5.24 (1.89-14.50)	6.90 (2.51-18.94)	6.14 (2.87-13.13)
Persistent (G4)	hematuria	hematuria	1.92 (0.26-13.99)	33.19 (14.27-77.16)	12.80 (5.95-27.57)
<i>P for interaction</i>			0.5	0.5	0.6

^aEstimated from Cox proportional hazards models. Multivariable model 1 was adjusted for age; sex; center; year of screening; alcohol intake; smoking status; physical activity level; BMI; education level; anti-lipid medication use; and history of diabetes, hypertension, cardiovascular disease, eGFR; total cholesterol, HDL-C, triglyceride, and glucose levels; and SBP.

Abbreviations: BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; G1, no hematuria at baseline and no hematuria at 2nd visit (reference group); G2, hematuria at baseline and no hematuria at 2nd visit (hematuria regressed group); G3, no hematuria at baseline and hematuria at 2nd visit (hematuria developed group); G4, hematuria at baseline and hematuria at 2nd visit (persistent hematuria group); HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; SBP, systolic blood pressure

Table S8. Development of chronic kidney disease and proteinuria by the hematuria change category when microscopic hematuria was defined as the presence of ≥ 3 red blood cells per high-power field (n = 232 220)

Hematuria change category	Hematuria status at 1st and 2nd visits		Multivariable-adjusted HR ^a (95% CI)		
	1 st test	2 nd test	<i>eGFR</i> < 60 mg/dl	<i>Proteinuria</i>	<i>CKD</i> (<i>eGFR</i> < 60 mg/dl or <i>proteinuria</i>)
Total (n = 232 220)					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	1.64 (1.12-2.41)	1.43 (1.11-1.84)	1.44 (1.16-1.78)
Developed (G3)	none	hematuria	1.59 (1.15-2.20)	2.06 (1.72-2.47)	2.00 (1.71-2.34)
Persistent (G4)	hematuria	hematuria	1.97 (1.42-2.72)	2.99 (2.49-3.59)	2.59 (2.20-3.04)
Women (n = 95 363)					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	1.30 (0.69-2.42)	1.19 (0.87-1.63)	1.15 (0.87-1.53)
Developed (G3)	none	hematuria	1.21 (0.68-2.15)	1.58 (1.25-1.99)	1.53 (1.23-1.89)
Persistent (G4)	hematuria	hematuria	1.64 (0.99-2.70)	2.11 (1.66-2.68)	1.87 (1.51-2.32)
Men (n = 136 857)					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	1.89 (1.16-3.06)	1.92 (1.26-2.94)	1.90 (1.37-2.63)
Developed (G3)	none	hematuria	1.81 (1.22-2.69)	3.15 (2.39-4.15)	2.77 (2.21-3.49)
Persistent (G4)	hematuria	hematuria	2.21 (1.45-3.37)	5.55 (4.22-7.31)	4.15 (3.28-5.25)
<i>P for interaction</i>			0.5	<0.001	<0.001

^aEstimated from Cox proportional hazards models. Multivariable model 1 was adjusted for age; sex; center; year of screening; alcohol intake; smoking status; physical activity level; BMI; education level; anti-lipid medication use; and history of diabetes, hypertension, cardiovascular disease, eGFR; total cholesterol, HDL-C, triglyceride, and glucose levels; and SBP.

Abbreviations: BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; G1, no hematuria at baseline and no hematuria at 2nd visit (reference group); G2, hematuria at baseline and no hematuria at 2nd visit (hematuria regressed group); G3, no hematuria at baseline and hematuria at 2nd visit (hematuria developed group); G4, hematuria at baseline and hematuria at 2nd visit (persistent hematuria group); HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; HPF, high-power field; SBP, systolic blood pressure.

Table S9. Development of chronic kidney disease and proteinuria by the hematuria change category, after excluding 328 participants with incident genitourinary cancer (n = 231 892)

Hematuria change category	Hematuria status at 1st and 2nd visits		Multivariable-adjusted HR ^a (95% CI)		
	1 st test	2 nd test	<i>eGFR</i> < 60 mg/dl	<i>Proteinuria</i>	<i>CKD</i> (<i>eGFR</i> < 60 mg/dl or <i>proteinuria</i>)
Total					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	1.87 (1.03-3.41)	1.88 (1.30-2.72)	1.86 (1.36-2.55)
Developed (G3)	none	hematuria	2.37 (1.46-3.86)	3.43 (2.66-4.41)	3.20 (2.56-4.01)
Persistent (G4)	hematuria	hematuria	2.23 (1.30-3.83)	7.07 (5.50-9.08)	5.28 (4.19-6.65)
Women					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed	hematuria	none	2.33 (1.03-5.30)	1.28 (0.77-2.14)	1.38 (0.89-2.14)

(G2) Developed (G3)	none	hematuria	2.07 (0.97-4.45)	2.65 (1.90-3.68)	2.53 (1.87-3.43)
Persistent (G4)	hematuria	hematuria	2.37 (1.10-5.12)	4.91 (3.52-6.85)	3.97 (2.91-5.40)
Men					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	1.51 (0.63-3.66)	3.42 (2.02-5.80)	2.83 (1.80-4.45)
Developed (G3)	none	hematuria	2.65 (1.41-4.97)	5.29 (3.61-7.77)	4.48 (3.22-6.24)
Persistent (G4)	hematuria	hematuria	2.12 (1.00-4.49)	14.13 (9.74-20.50)	8.39 (5.96-11.82)
<i>P for interaction</i>			0.9	<0.001	<0.001

^aEstimated from Cox proportional hazards models. Multivariable model 1 was adjusted for age; sex; center; year of screening; alcohol intake; smoking status; physical activity level; BMI; education level; anti-lipid medication use; and history of diabetes, hypertension, cardiovascular disease, eGFR; total cholesterol, HDL-C, triglyceride, and glucose levels; and SBP.

Abbreviations: BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; G1, no hematuria at baseline and no hematuria at 2nd visit (reference group); G2, hematuria at baseline and no hematuria at 2nd visit (hematuria regressed group); G3, no hematuria at baseline and hematuria at 2nd visit (hematuria developed group); G4, hematuria at baseline and hematuria at 2nd visit (persistent hematuria group); HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; SBP, systolic blood pressure.

Table S10. Development of chronic kidney disease and proteinuria by the hematuria change category, after excluding 1631 participants with high level microscopic hematuria defined as ≥ 20 /high-power field (n = 230 589)

Hematuria change category	Hematuria status at 1st and 2nd visits		Multivariable-adjusted HR ^a (95% CI)		
	1 st test	2 nd test	<i>eGFR</i> < 60 mg/dl	<i>Proteinuria</i>	<i>CKD</i> (<i>eGFR</i> < 60 mg/dl or <i>proteinuria</i>)
Total					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	2.52 (1.30-4.88)	2.05 (1.30-3.22)	2.11 (1.45-3.07)
Developed (G3)	none	hematuria	2.34 (1.44-3.81)	3.37 (2.62-4.34)	3.15 (2.52-3.95)
Persistent (G4)	hematuria	hematuria	1.94 (0.80-4.73)	3.69 (2.28-5.96)	2.80 (1.80-4.36)
Women					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	3.05 (1.25-7.48)	1.43 (0.77-2.68)	1.59 (0.96-2.66)
Developed (G3)	none	hematuria	2.09 (0.97-4.48)	2.62 (1.88-3.65)	2.51 (1.85-3.40)
Persistent (G4)	hematuria	hematuria	2.29 (0.57-9.30)	2.42 (1.25-4.68)	1.90 (1.02-3.54)
Men					
None (G1)	none	none	1.00 (reference)	1.00 (reference)	1.00 (reference)
Regressed (G2)	hematuria	none	2.06 (0.77-5.54)	3.68 (1.91-7.11)	3.24 (1.87-5.59)
Developed (G3)	none	hematuria	2.57 (1.37-4.81)	5.27 (3.59-7.74)	4.44 (3.19-6.19)
Persistent (G4)	hematuria	hematuria	1.76 (0.56-5.57)	8.18 (4.07-16.43)	5.06 (2.71-9.44)
<i>P</i> for interaction			0.9	<0.001	0.003

^aEstimated from Cox proportional hazards models. Multivariable model 1 was adjusted for age; sex; center; year of screening; alcohol intake; smoking status; physical activity level; BMI; education level; anti-lipid medication use; and history of diabetes, hypertension, cardiovascular disease, eGFR; total cholesterol, HDL-C, triglyceride, and glucose levels; and SBP.

Abbreviations: BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; G1, no hematuria at baseline and no hematuria at 2nd visit (reference group); G2, hematuria at baseline and no hematuria at 2nd visit (hematuria regressed group); G3, no hematuria at baseline and hematuria at 2nd visit (hematuria developed group); G4, hematuria at baseline and hematuria at 2nd visit (persistent hematuria group); HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; HPF, high-power field; SBP, systolic blood pressure.