

Supplemental Material

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Supplemental Figures S1-S3

Figure S1. Kaplan-Meier cumulative incidence plot with follow-up years as the time axis and mortality as the outcome stratified by fifths of baseline uric acid. A logrank test was performed to assess for a trend across quartiles of uric acid. SUA F represents fifths of uric acid.

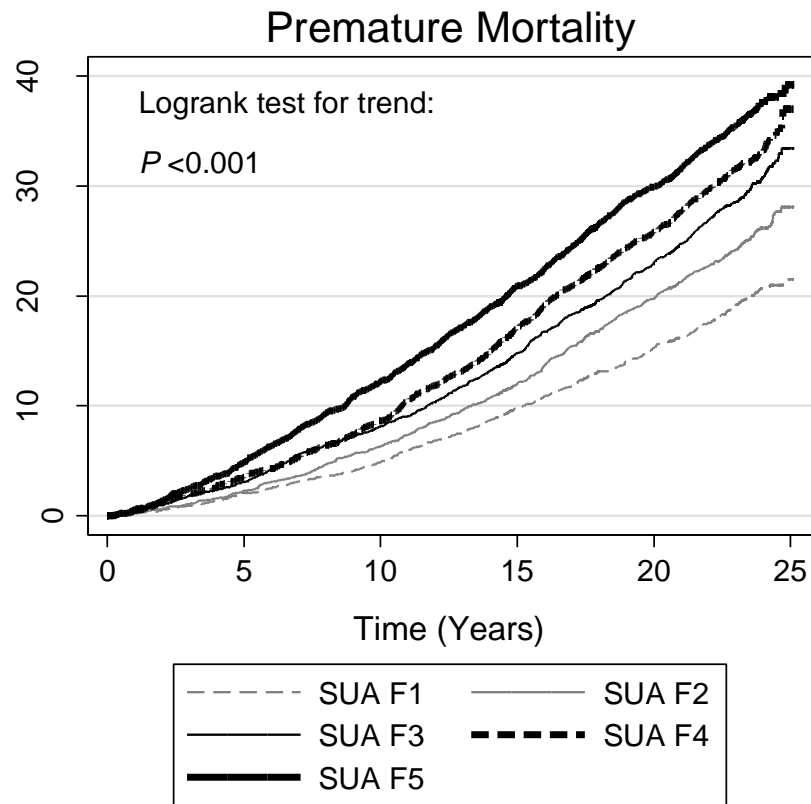


Figure S2. Adjusted hazard ratios (solid line) from restricted cubic spline models for mortality stratified by sex using overall fifths of baseline uric acid (**A**) and sex-specific fifths of uric acid (**B**). Men are depicted in black; women are depicted in gray. Shading and dashed lines are the 95% confidence intervals. The models were expressed relative to the 40th percentile with knots specified at the 20th, 40th, 60th, and 80th percentiles and were adjusted for age, sex, systolic blood pressure, diastolic blood pressure, blood pressure medication use, systolic blood pressure & medication use interaction, smoking status, number of cigarettes per day among smokers, total cholesterol, high density lipoprotein cholesterol, body mass index, baseline diabetes status, daily alcohol use, and the Scottish Index of Multiple Deprivation. The plots were truncated at the 1st and 99th percentiles. The hazard ratios are shown on a natural log scale. Vertical lines depict women (W) and men (M) cutpoints for hyperuricemia.

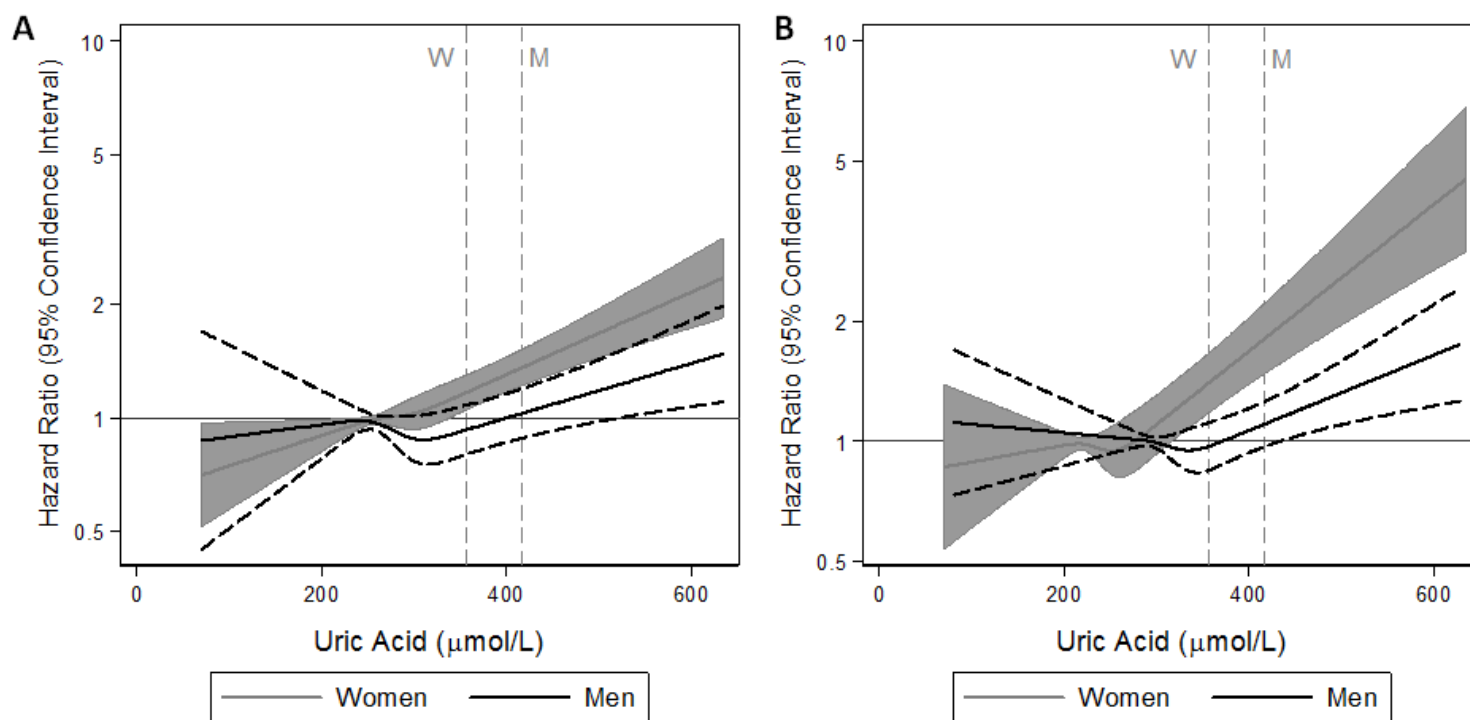
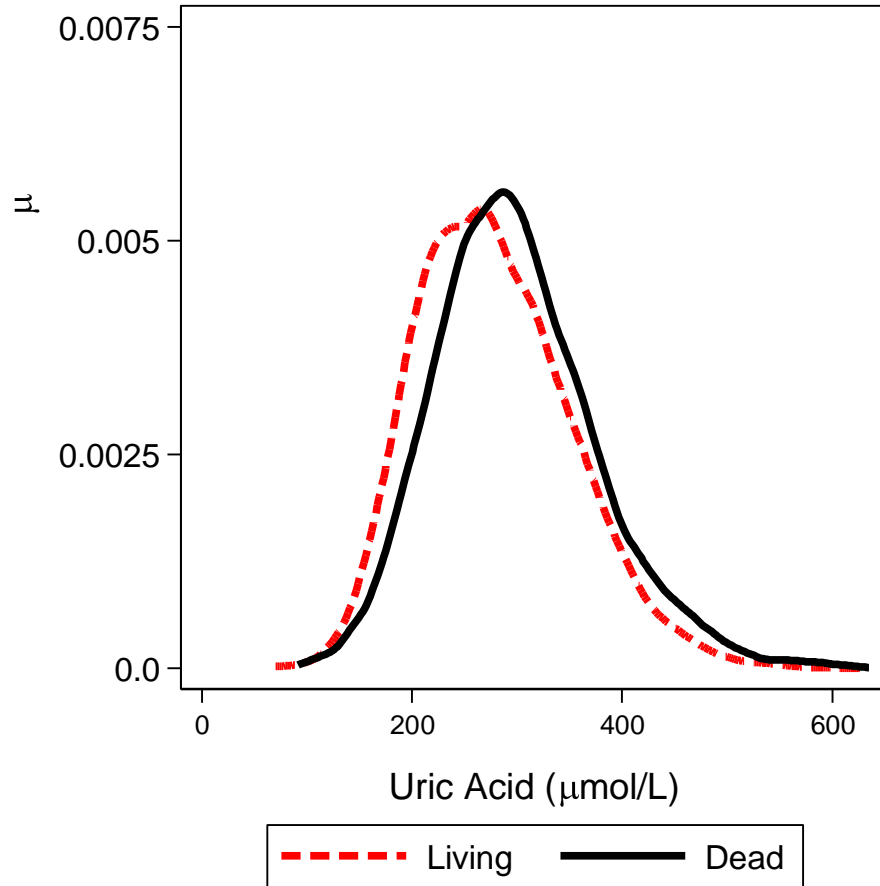


Figure S3. Kernel density plots depicting the distribution uric acid by participants who died (solid) versus those who did not die (dash). The distributions were significantly different by two-sample Kolmogorov-Smirnov equality-of-distributions tests ($P < 0.001$).



Supplemental Tables S1-S8

Supplemental Table S1. Hazard Ratios for all-cause mortality according to categories and continuous uric acid concentrations by strata of participants with baseline hyperuricemia* versus normouricemia

	Hyperuricemia, N = 1,003	Normouricemia, N = 14,080
Uric acid per 100 $\mu\text{mol/L}$	1.51 (1.23, 1.86)	1.02 (0.95, 1.09)
<i>P</i> value	<0.001	<0.001

Both models adjusted for age, sex, systolic blood pressure, diastolic blood pressure, blood pressure medication use, systolic blood pressure & medication use interaction, smoking status, number of cigarettes per day among smokers, total cholesterol, high density lipoprotein cholesterol, body mass index, baseline diabetes status, daily alcohol use, and the Scottish Index of Multiple Deprivation

*Hyperuricemia is defined as a uric acid >416 (7 mg/dL) $\mu\text{mol/L}$ in men and >357 $\mu\text{mol/L}$ (6 mg/dL) in women; normouricemia is defined as a uric acid \leq 416 $\mu\text{mol/L}$ in men and \leq 357 $\mu\text{mol/L}$ in women.

Supplemental Table S2. Hazard Ratios for mortality according to categories and continuous uric acid concentrations with fifth 1 as reference.

	Hazard Ratio (95% CI)		
	Model 1	Model 2	Model 3
Fifths of uric acid, $\mu\text{mol/L}$			
37.88 - 218.53	1 (reference)	1 (reference)	1 (reference)
218.55 - 259.01	0.99 (0.89, 1.11)	0.97 (0.86, 1.08)	0.97 (0.86, 1.08)
259.01 - 296.53	1.02 (0.91, 1.14)	0.98 (0.88, 1.10)	0.99 (0.88, 1.11)
296.55 - 344.35	1.03 (0.92, 1.16)	0.99 (0.88, 1.12)	1.00 (0.89, 1.13)
344.37 - 782.75	1.19 (1.06, 1.34)	1.12 (0.99, 1.27)	1.14 (1.00, 1.29)
<i>P</i> trend across fifths	<0.001	0.02	0.008

Model 1: age, sex

Model 2: Model 1 + systolic blood pressure, diastolic blood pressure, blood pressure medication use, systolic blood pressure & medication use interaction, smoking status, number of cigarettes per day among smokers, total cholesterol, high density lipoprotein cholesterol, body mass index, baseline diabetes status, daily alcohol use

Model 3: Model 2 + Scottish Index of Multiple Deprivation

Supplemental Table S3. Hazard Ratios for mortality according to categories and continuous uric acid concentrations by sex

	Hazard Ratio (95% CI)		<i>P</i> -interaction
	Men, N = 7,559	Women, N = 7,524	
Fifths of uric acid, $\mu\text{mol/L}$			
37.88 - 218.53	1.05 (0.85, 1.30)	1.05 (0.91, 1.21)	
218.55 - 259.01	1 (reference)	1 (reference)	
259.01 - 296.53	0.96 (0.83, 1.10)	1.09 (0.94, 1.27)	0.002
296.55 - 344.35	0.91 (0.79, 1.04)	1.27 (1.08, 1.50)	
344.37 - 782.75	0.99 (0.86, 1.14)	1.69 (1.40, 2.04)	
<i>P</i> trend across fifths	0.82	<0.001	
Hyperuricemia	1.23 (1.07, 1.42)	1.68 (1.41, 2.00)	0.03
<i>P</i> value	0.004	<0.001	
Uric acid per 100 $\mu\text{mol/L}$	1.05 (0.98, 1.12)	1.29 (1.18, 1.40)	0.02
<i>P</i> value	0.14	<0.001	

All models adjusted for age, sex, systolic blood pressure, diastolic blood pressure, blood pressure medication use, systolic blood pressure & medication use interaction, smoking status, number of cigarettes per day among smokers, total cholesterol, high density lipoprotein cholesterol, body mass index, baseline diabetes status, daily alcohol use, and the Scottish Index of Multiple Deprivation

Supplemental Table S4. Hazard Ratios for mortality by sex-specific fifths of uric acid (Hazard ratio, 95% CI)

Fifths of uric acid, $\mu\text{mol/L}$	Men (N=7,599)
53.98 - 267.24	1.03 (0.91, 1.16)
267.26 - 300.89	1 (reference)
300.90 - 332.19	0.93 (0.82, 1.06)
332.20 - 373.37	1.00 (0.88, 1.14)
373.43 - 705.34	1.05 (0.92, 1.20)
<i>P</i> trend across fifths	0.70

Fifths of uric acid, $\mu\text{mol/L}$	Women (N = 7,524)
37.88 - 195.29	0.95 (0.79, 1.14)
195.30 - 223.86	1 (reference)
223.87 - 251.63	1.02 (0.85, 1.21)
251.64 - 290.04	0.98 (0.83, 1.17)
290.06 - 782.75	1.31 (1.10, 1.55)
<i>P</i> trend across fifths	<0.001

Both models adjusted for age, sex, systolic blood pressure, diastolic blood pressure, blood pressure medication use, systolic blood pressure & medication use interaction, smoking status, number of cigarettes per day among smokers, total cholesterol, high density lipoprotein cholesterol, body mass index, baseline diabetes status, daily alcohol use, and the Scottish Index of Multiple Deprivation

Supplemental Table S5. Adjusted hazard ratios (95% CI) for cardiovascular conditions present at the time of death according to fifths of uric acid concentration, hyperuricemia, and continuous uric acid concentrations (N=15,083)

	Congestive heart failure mortality	Coronary heart disease mortality	Cerebrovascular mortality	Peripheral vascular disease mortality	Thromboembolic mortality
Fifths of uric acid					
37.88 - 218.55	1.29 (0.87, 1.93)	1.20 (0.97, 1.50)	1.11 (0.79, 1.55)	2.26 (1.22, 4.20)	0.68 (0.30, 1.56)
218.56 - 258.97	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
259.01 - 296.58	1.17 (0.82, 1.66)	0.94 (0.78, 1.14)	0.96 (0.70, 1.31)	2.06 (1.16, 3.63)	0.61 (0.28, 1.32)
296.59 - 344.41	1.05 (0.74, 1.51)	0.88 (0.73, 1.06)	0.96 (0.70, 1.31)	1.82 (1.01, 3.27)	1.13 (0.57, 2.21)
344.43 - 782.75	1.26 (0.88, 1.80)	0.97 (0.80, 1.17)	1.06 (0.76, 1.47)	1.61 (0.86, 3.00)	1.83 (0.94, 3.60)
<i>P</i> trend across fifths	0.68	0.16	0.99	0.81	0.008
Hyperuricemia	1.72 (1.27, 2.33)	1.21 (1.01, 1.46)	1.17 (0.83, 1.65)	1.25 (0.72, 2.20)	1.81 (0.95, 3.45)
<i>P</i> value	0.001	0.04	0.36	0.43	0.07
Uric acid per 100 µmol/L	1.20 (1.02, 1.41)	0.99 (0.91, 1.09)	1.03 (0.88, 1.21)	1.10 (0.85, 1.41)	1.61 (1.17, 2.23)
<i>P</i> value	0.03	0.87	0.71	0.48	0.004

All models adjusted for age, sex, systolic blood pressure, diastolic blood pressure, blood pressure medication use, systolic blood pressure & medication use interaction, smoking status, number of cigarettes per day among smokers, total cholesterol, high density lipoprotein cholesterol, body mass index, baseline diabetes status, daily alcohol use, and the Scottish Index of Multiple Deprivation

Table S6. Primary cause of death

	All Deaths		Normouricemia		Hyperuricemia		P-value*
	N	% of deaths	N	% of deaths	N	% of deaths	
Mortality from any cause	3,980	100.0	3,580	89.9	400	10.1	<0.001
Acute CHD	597	15.0	536	15.0	61	15.3	0.89
Chronic CHD	315	7.9	275	7.7	40	10.0	0.17
Acute stroke	216	5.4	199	5.6	17	4.3	0.79
Chronic cerebrovascular disease	71	1.8	59	1.7	12	3.0	0.02
Other cardiovascular	238	6.0	199	5.6	39	9.8	<0.001
Respiratory	389	9.8	351	9.8	38	9.5	0.01
Cancer	1,513	38.0	1,397	39.0	116	29.0	0.07
Other causes	641	16.1	564	15.8	77	19.3	<0.001

Abbreviations: CHD, coronary heart disease

*P-value for the hazard ratio comparing hyperuricemia with normouricemia with cause-specific mortality after adjustment for age, sex, systolic blood pressure, diastolic blood pressure, blood pressure medication use, systolic blood pressure & medication use interaction, smoking status, number of cigarettes per day among smokers, total cholesterol, high density lipoprotein cholesterol, body mass index, baseline diabetes status, daily alcohol use, and the Scottish Index of Multiple Deprivation

Table S7. Hazard Ratios (95% CI) for specific causes of mortality according to categories and continuous uric acid concentrations with adjustment for estimated glomerular filtration rate, N = 12,611

	Mortality from Any Cause	Cardiovascular Mortality	Cancer-related Mortality	Kidney-related Mortality
Fifths of uric acid				
37.88 - 218.55	1.07 (0.95, 1.21)	1.14 (0.95, 1.37)	0.97 (0.80, 1.16)	0.76 (0.39, 1.47)
218.56 - 258.97	1.00 (1.00, 1.00)	1.0 (reference)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
259.01 - 296.58	1.06 (0.94, 1.18)	0.93 (0.79, 1.09)	1.04 (0.88, 1.23)	1.28 (0.77, 2.14)
296.59 - 344.41	1.13 (1.00, 1.26)	0.99 (0.84, 1.17)	0.96 (0.80, 1.15)	1.27 (0.75, 2.17)
344.43 - 782.75	1.28 (1.13, 1.45)	1.15 (0.97, 1.36)	1.16 (0.96, 1.40)	1.62 (0.95, 2.77)
<i>P</i> trend across fifths	<0.001	0.32	0.15	0.03
Hyperuricemia	1.48 (1.31, 1.68) <0.001	1.47 (1.25, 1.74) <0.001	1.38 (1.11, 1.70) 0.003	2.52 (1.67, 3.81) <0.001
Uric acid per 100 µmol/L	1.18 (1.11, 1.25) <0.001	1.13 (1.04, 1.23) 0.004	1.12 (1.02, 1.23) 0.02	1.55 (1.21, 1.97) <0.001

All models adjusted for age, sex, systolic blood pressure, diastolic blood pressure, blood pressure medication use, systolic blood pressure & medication use interaction, smoking status, number of cigarettes per day among smokers, total cholesterol, high density lipoprotein cholesterol, body mass index, baseline diabetes status, daily alcohol use, estimated glomerular filtration rate, and the Scottish Index of Multiple Deprivation

Table S8. Cardiovascular conditions present at the time of death (Hazard Ratio,95% CI) with adjustment for estimated glomerular filtration rate, N = 12,611

	Congestive heart failure mortality	Coronary heart disease mortality	Cerebrovascular mortality	Peripheral vascular disease mortality	Thromboembolic mortality
Fifths of uric acid					
37.88 - 218.55	1.35 (0.88, 2.08)	1.26 (0.99, 1.59)	1.28 (0.88, 1.87)	1.84 (0.94, 3.58)	0.63 (0.25, 1.59)
218.56 - 258.97	1.0 (reference)	1.0 (reference)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
259.01 - 296.58	1.09 (0.73, 1.61)	0.96 (0.77, 1.18)	0.96 (0.67, 1.37)	1.81 (0.99, 3.30)	0.48 (0.19, 1.21)
296.59 - 344.41	1.07 (0.72, 1.60)	0.96 (0.78, 1.18)	1.03 (0.72, 1.48)	1.64 (0.87, 3.09)	1.25 (0.59, 2.64)
344.43 - 782.75	1.13 (0.75, 1.72)	1.02 (0.82, 1.27)	1.15 (0.79, 1.68)	1.48 (0.75, 2.93)	1.99 (0.93, 4.26)
<i>P</i> trend across fifths	0.80	0.36	0.99	1.00	0.006
Hyperuricemia	1.63 (1.11, 2.38)	1.25 (1.01, 1.55)	1.32 (0.89, 1.96)	0.96 (0.47, 1.96)	2.10 (1.00, 4.39)
<i>P</i> value	0.01	0.04	0.17	0.91	0.05
Uric acid per 100 µmol/L	1.16 (0.95, 1.42)	1.02 (0.92, 1.14)	1.04 (0.86, 1.26)	0.97 (0.71, 1.32)	1.79 (1.23, 2.62)
<i>P</i> value	0.14	0.66	0.68	0.86	0.003

All models adjusted for age, sex, systolic blood pressure, diastolic blood pressure, blood pressure medication use, systolic blood pressure & medication use interaction, smoking status, number of cigarettes per day among smokers, total cholesterol, high density lipoprotein cholesterol, body mass index, baseline diabetes status, daily alcohol use, estimated glomerular filtration rate, and the Scottish Index of Multiple Deprivation