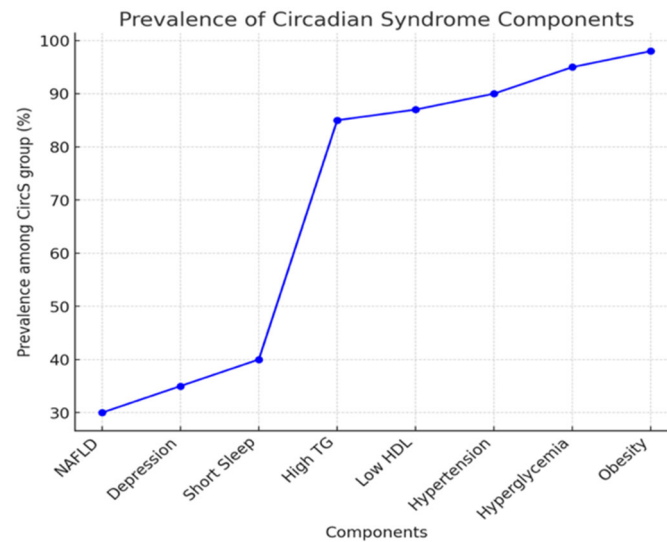


Hyperuricemia as a Biomarker for Circadian syndrome: A Cross-Sectional Study

(Supplementary Material)

Supplementary Figure 1. Circadian Syndrome (CircS) Components Prevalence



Supplementary Table 1. Comparison of Baseline Characteristics Between Included and Excluded Participants

Variable	Included	Excluded	p-value
Age, median (IQR)	44 (32)	52 (31)	<0.001
Sex			<0.001
Male	51.6%	44.4%	
Female	48.4%	55.6%	
Ethnicity			<0.001
Hispanic	25.5%	25.0%	
White	41.0%	39.4%	
Black	21.4%	24.7%	
Others	12.2%	10.8%	
Education			<0.001
Below high school	23.0%	27.1%	
High school	51.7%	53.6%	
Graduate	25.3%	19.3%	
PIR			<0.001
PIR <1	21.7%	23.3%	
PIR ≥5	18.4%	15.6%	

Hyperuricemia			<0.001
Yes	16.7%	45.2%	
CKD			<0.001
Yes	2.8%	4.3%	
Variable	Included	Excluded	p-value
Age, median (IQR)	44 (32)	52 (31)	<0.001
Sex			<0.001
Male	51.6%	44.4%	
Female	48.4%	55.6%	
Ethnicity			<0.001
Hispanic	25.5%	25.0%	
White	41.0%	39.4%	
Black	21.4%	24.7%	
Others	12.2%	10.8%	
Education			<0.001
Below high school	23.0%	27.1%	
High school	51.7%	53.6%	
Graduate	25.3%	19.3%	
PIR			<0.001
PIR <1	21.7%	23.3%	
PIR ≥5	18.4%	15.6%	
Hyperuricemia			<0.001
Yes	16.7%	45.2%	
CKD			<0.001
Yes	2.8%	4.3%	

Supplementary Table 2. Logistic Regression Model for Circadian Syndrome Using Age as a Continuous Covariate (Model Used for Forest Plot Visualization)

Variable	Categories	Odds Ratio	P-value	95% UI
Hyperuricemia		3.16	<0.001	2.71 – 3.67
Age (in years)		1.03	<0.001	1.03 – 1.04
Sex				

	Female	1.48	<0.001	1.28 – 1.72
Race				
	White	0.82	0.038	0.68 – 0.99
	Black	0.51	<0.001	0.41 – 0.64
	Others	0.52	<0.001	0.38 – 0.71
Smoking				
	Smoker	1.36	<0.001	1.17– 1.58
alcohol				
	At risk drinking	0.62	<0.001	0.50 – 0.76
Education				
	High school	1.02	0.814	0.85 – 1.23
	Graduate	0.54	<0.001	0.42 – 0.71
Poverty-to-income ratio (PIR)				
	PIR 1–1.9	0.78	0.016	0.63 – 0.95
	PIR 2–2.9	0.60	<0.001	0.46 – 0.76
	PIR 3–3.9	0.72	0.012	0.55 – 0.93
	PIR 4–4.9	0.58	0.001	0.43 – 0.80
	PIR ≥5	0.54	<0.001	0.42 – 0.70
Chronic kidney disease (CKD)				
	CKD	2.79	<0.001	2.05 – 3.79
Healthy eating index (HEI)				
	Moderate	0.73	0.032	0.55 – 0.98
	Poor	0.76	0.116	0.54 – 1.05
Physical activity		1.00	0.992	0.84 – 1.19

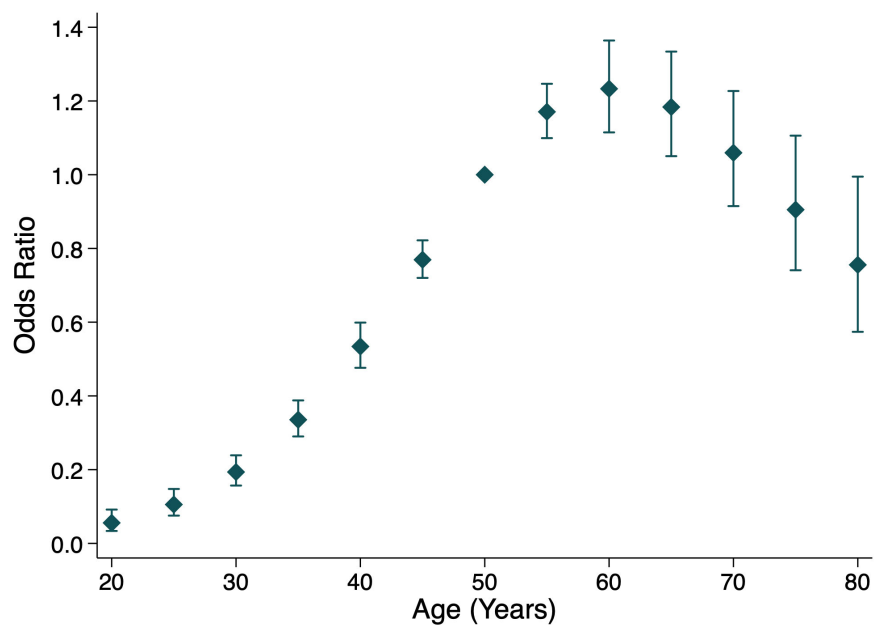
_cons

0.02

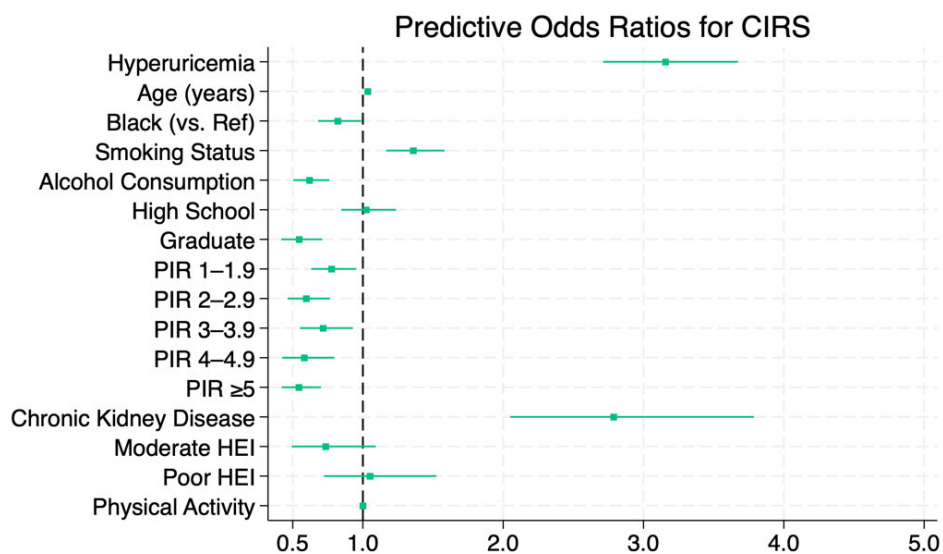
<0.001

0.01 – 0.02

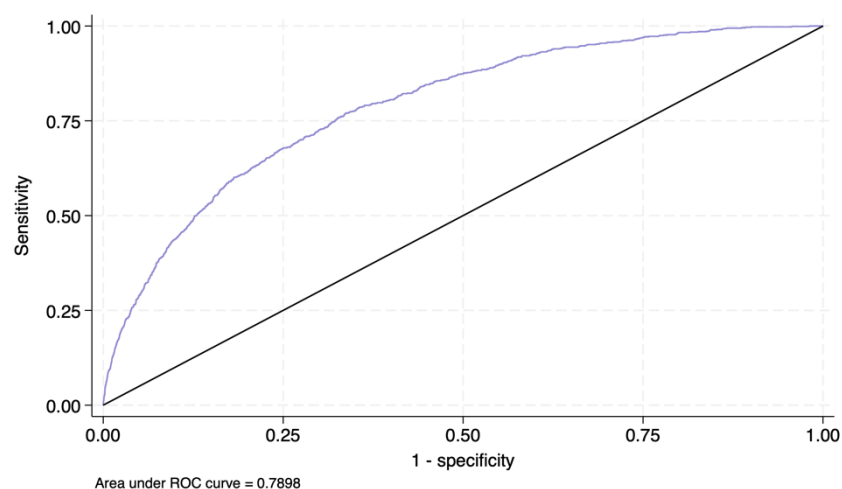
Supplementary figure 2. Impact of Age on the Odds of Circadian Syndrome



Supplementary figure 3. Forest plot



Supplementary figure 4. ROC curve



Supplementary Table 3. Linktest results

Variable	Coefficient	Std. Err.	z	P-Value	95% UI
_hat	1.105	0.115	9.57	<0.001	0.88 – 1.33
_hatsq	0.022	0.023	0.96	0.335	-0.02 – 0.07
_cons	0.102	0.138	0.74	0.459	-0.17 – 0.37

Dose response relationship of uric acid with individual components of CircS:

1. Uric acid as quartiles:

Supplementary Table 4. Uric acid and hypertension

Variable	Odds ratio	P-Value	95% UI
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Uric acid quartiles			
G2 (4.9–5.8 mg/dL)	1.32	<0.001	1.22 – 1.42
G3 (5.9–6.9 mg/dL)	1.73	<0.001	1.59 – 1.87
G4 (≥7.0 mg/dL)	3.03	<0.001	2.78 – 3.30
Age (Splines)			
age_spline1	1.09	<0.001	1.08 – 1.10
age_spline2	1.02	0.282	0.99 – 1.05
age_spline3	0.92	0.042	0.85 – 1.00
Gender			
Female	1.04	0.186	0.98 – 1.11
Ethnicity			
White	1.00	0.909	0.93 – 1.07
Black	2.23	<0.001	2.06 – 2.42
Others/multi-racial	1.05	0.385	0.95– 1.16
_cons	0.02	<0.001	0.01 – 0.10

Supplementary Table 5. Uric acid and Glycemia

Variable	Odds ratio	P-Value	95% UI
Uric acid quartiles			
G2 (4.9–5.8 mg/dL)	1.43	<0.001	1.31 – 1.55
G3 (5.9–6.9 mg/dL)	1.60	<0.001	1.48– 1.75
G4 (≥7.0 mg/dL)	2.32	<0.001	2.12 – 2.54
Age (Splines)			
age_spline1	1.06	<0.001	1.04 – 1.07
age_spline2	1.04	0.014	1.01– 1.07

age_spline3	0.83	<0.001	0.76 – 0.89
Gender			
Female	0.68	<0.001	0.64 – 0.73
Ethnicity			
White	0.57	<0.001	0.53– 0.61
Black	0.65	<0.001	0.59 – 0.70
Others/multi-racial	0.81	<0.001	0.73 – 0.89
_cons	0.10	<0.001	0.08 – 0.13

Supplementary Table 6. Uric acid and dyslipidemia (HDL)

Variable	Odds ratio	P-Value	95% UI
Uric acid quartiles			
G2 (4.9–5.8 mg/dL)	1.42	<0.001	1.33– 1.51
G3 (5.9–6.9 mg/dL)	1.95	<0.001	1.83– 2.08
G4 (≥7.0 mg/dL)	2.56	<0.001	2.39 – 2.74
Age (splines)			
age_spline1	1.02	<0.001	1.01 – 1.03
age_spline2	0.94	<0.001	0.92– 0.93
age_spline3	1.13	<0.001	1.07– 1.20
Gender			
Female	1.79	<0.001	1.71 – 1.88
Ethnicity			
White	0.76	<0.001	0.72– 0.80
Black	0.50	<0.001	0.47 – 0.53
race2: Others/Multi-racial	0.64	<0.001	0.60 – 0.69

_cons	0.17	<0.001	0.14 – 0.21
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Supplementary Table 7. Uric acid and dyslipidemia (TGs)

Variable	Odds ratio	P-value	95% UI
Uric acid quartiles			
G2 (4.9–5.8 mg/dL)	1.22	<0.001	1.11 – 1.36
G3 (5.9–6.9 mg/dL)	1.73	<0.001	1.56 – 1.91
G4 (≥7.0 mg/dL)	2.83	<0.001	2.55 – 3.13
Age (splines)			
age_spline1	1.06	<0.001	1.05 – 1.07
age_spline2	0.92	<0.001	0.89 – 0.95
age_spline3	1.14	0.004	1.043 – 1.25
Gender			
Female	0.94	0.085	0.87 – 1.01
Ethnicity			
White	0.82	<0.001	0.75 – 0.88
Black	0.27	<0.001	0.24 – 0.30
Others/multi-racial	0.68	<0.001	0.61 – 0.76
_cons	0.05	<0.001	0.03– 0.06

Supplementary Table 8. Uric acid and obesity

Variable	Odds ratio	P-Value	95% UI
Uric acid quartiles			
G2 (4.9–5.8 mg/dL)	1.93	<0.001	1.81 – 2.05
G3 (5.9–6.9 mg/dL)	3.12	<0.001	2.91 – 3.34

G4 (≥7.0 mg/dL)	5.50	<0.001	5.10 – 5.93
Age (splines)			
age_spline1	1.07	<0.001	1.06 – 1.07
age_spline2	0.92	<0.001	0.90– 0.94
age_spline3	1.14	<0.001	1.08 – 1.21
Gender			
Female	5.90	<0.001	5.59– 6.24
Ethnicity			
White	0.85	<0.001	0.80 – 0.90
Black	0.91	0.004	0.85 – 0.97
Others/multi-racial	0.29	<0.001	0.27 – 0.32
_cons	0.03	<0.001	0.02 – 0.03

Supplementary Table 9. Uric acid and NAFLD

Variable	Odds ratio	P-value	95% UI
Uric acid quartiles			
G2 (4.9–5.8 mg/dL)	2.60	<0.001	1.76 – 3.83
G3 (5.9–6.9 mg/dL)	3.74	<0.001	2.55 – 5.50
G4 (≥7.0 mg/dL)	7.08	<0.001	4.85 – 10.34
Age (splines)			
age_spline1	1.07	<0.001	1.03 – 1.11
age_spline2	0.94	0.282	0.86 – 1.05
age_spline3	1.04	0.794	0.78 – 1.38
Gender			
Female	1.17	0.156	0.94 – 1.46

Ethnicity			
White	0.91	0.424	0.72 – 1.15
Black	0.39	<0.001	0.29 – 0.54
Others/multi-racial	0.70	0.050	0.50– 1.00
_cons	0.00	<0.001	0.00 – 0.00

Supplementary Table 10. Uric acid and Depression

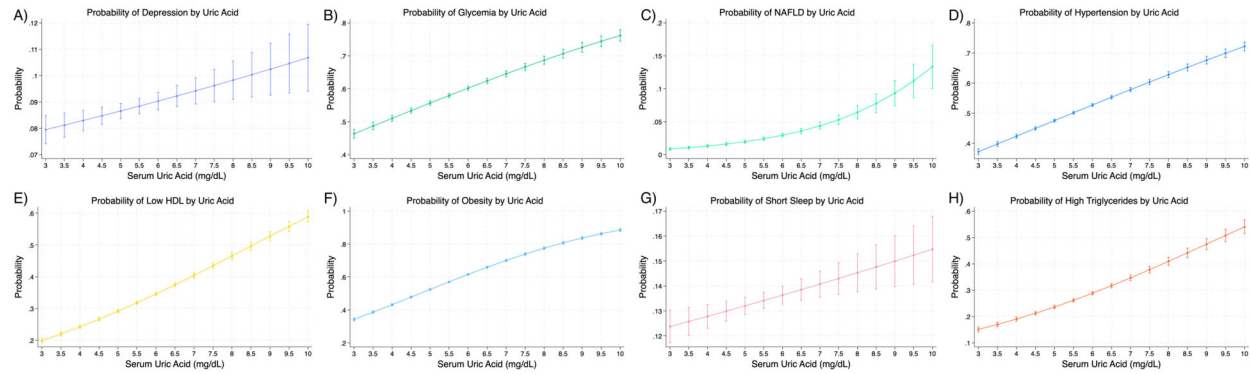
Variable	Odds ratio	P-value	95% UI
Uric acid quartiles			
G2 (4.9–5.8 mg/dL)	1.07	0.158	0.97 – 1.19
G3 (5.9–6.9 mg/dL)	1.05	0.367	0.94 – 1.17
G4 (≥7.0 mg/dL)	1.19	0.002	1.06 – 1.33
Age (splines)			
age_spline1	1.01	0.319	0.99– 1.02
age_spline2	1.04	0.039	1.00 – 1.07
age_spline3	0.83	<0.001	0.75 – 0.91
Gender			
Female	1.84	<0.001	1.69 – 1.99
Ethnicity			
White	0.91	0.046	0.83 – 0.99
Black	0.92	0.107	0.83 – 1.02
Others/multi-racial	0.66	<0.001	0.57 – 0.76
_cons	0.05	<0.001	0.04 – 0.07

Supplementary Table 11. Uric acid and short sleep

Variable	Odds ratio	P-value	95% UI
Uric acid quartiles			
G2 (4.9–5.8 mg/dL)	1.11	0.014	1.02 – 1.21
G3 (5.9–6.9 mg/dL)	1.12	0.004	1.04 – 1.24
G4 (≥7.0 mg/dL)	1.20	<0.001	1.10 – 1.32
Age (splines)			
age_spline1	1.04	<0.001	1.03 – 1.05
age_spline2	0.92	<0.001	0.90 – 0.95
age_spline3	1.18	<0.001	1.09 – 1.27
Gender			
Female	0.98	0.567	0.92 – 1.05
Ethnicity			
White	0.88	0.002	0.82 – 0.96
Black	1.95	<0.001	1.80 – 2.11
Others/multi-racial	0.90	0.071	0.81 – 1.01
_cons	0.04	<0.001	0.03 – 0.05

2. Uric acid as continuous variable:

Supplementary Figure 5. Probability of individual CircS components across uric acid levels (mg/dL)



Supplementary Table 12. Uric acid and hypertension

Variable	Odds ratio	P-Value	95% UI
Uric acid (mg/dL)	1.38	<0.001	1.35 – 1.41
Age (Splines)			
age_spline1	1.09	<0.001	1.08 – 1.10
age_spline2	1.01	0.320	0.99 – 1.04
age_spline3	0.92	0.049	0.85 – 0.99
Gender			
Female	1.09	0.009	1.02 – 1.15
Ethnicity			
White	0.99	0.826	0.93 – 1.06
Black	2.21	<0.001	2.03 – 2.39
Others/multi-racial	1.03	0.512	0.93 – 1.14
_cons	0.00	<0.001	0.00 – 0.00

Supplementary Table 13. Uric acid and glycemia

Variable	Odds ratio	P-Value	[95% conf. interval]
Uric acid (mg/dL)	1.25	<0.001	1.22 – 1.28
Age (splines)			
age_spline1	1.06	<0.001	1.05 – 1.07
age_spline2	1.04	0.013	1.01 – 1.07
age_spline3	0.82	<0.001	0.76 – 0.89
Gender			
Female	0.69	<0.001	0.65 – 0.74
Ethnicity			
White	0.56	<0.001	0.52 – 0.61
Black	0.64	<0.001	0.58 – 0.69
Others/multi-racial	0.80	<0.001	0.72 – 0.89
_cons	0.04	<0.001	0.03 – 0.059

Supplementary Table 14. Uric acid and dyslipidemia (HDL)

Variable	Odds ratio	P-Value	95% UI
Uric acid (mg/dL)	1.30	<0.001	1.28 – 1.32
Age (splines)			
age_spline1	1.02	<0.001	1.01 – 1.03
age_spline2	0.94	<0.001	0.92 – 0.96
age_spline3	1.13	<0.001	1.07– 1.19
Gender			
Female	1.81	<0.001	1.72– 1.90
Ethnicity			

White	0.75	<0.001	0.71 – 0.80
Black	0.49	<0.001	0.46 – 0.52
Others/multi-racial	0.64	<0.001	0.59 – 0.69
_cons	0.07	<0.001	0.06 – 0.08

Supplementary Table 15. Uric acid and dyslipidemia (TGs)

Variable	Odds ratio	P-Value	95% UI
Uric acid (mg/dL)	1.33	<0.001	1.30 – 1.36
Age (splines)			
age_spline1	1.06	<0.001	1.05 – 1.07
age_spline2	0.92	<0.001	0.89 – 0.95
age_spline3	1.14	0.005	1.04 – 1.24
Gender			
Female	0.94	0.111	0.88 – 1.01
Ethnicity			
White	0.81	<0.001	0.75 – 0.88
Black	0.26	<0.001	0.24 – 0.29
Others/multi-racial	0.67	<0.001	0.60 – 0.75
_cons	0.02	<0.001	0.01 – 0.02

Supplementary Table 16. Uric acid and obesity

Variable	Odds ratio	P-Value	95% UI
Uric acid (mg/dL)	1.60	<0.001	1.57 – 1.64

Age (splines)			
age_spline1	1.07	<0.001	1.06 – 1.07
age_spline2	0.92	<0.001	0.90 – 0.94
age_spline3	1.14	<0.001	1.07 – 1.21
Gender			
Female	5.98	<0.001	5.66 – 6.31
Ethnicity			
White	0.84	<0.001	0.80 – 0.90
Black	0.89	0.001	0.84 – 0.95
Others/multi-racial	0.28	<0.001	0.26 – 0.31
_cons	0.01	<0.001	0.00 – 0.01

Supplementary Table 17. Uric acid and NAFLD

Variable	Odds ratio	P-Value	95% UI
Uric acid (mg/dL)	1.52	<0.001	1.42 – 1.63
Age (splines)			
age_spline1	1.07	<0.001	1.03 – 1.11
age_spline2	0.95	0.337	0.85 – 1.06
age_spline3	1.02	0.896	0.77 – 1.35
Gender			
Female	1.13	0.289	0.90 – 1.40
Ethnicity			
White	0.93	0.562	0.74 – 1.18
Black	0.38	<0.001	0.28 – 0.53
Others/multi-racial	0.73	0.076	0.51 – 1.03

_cons	0.00	<0.001	0.00 – 0.00
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Supplementary Table 18. Uric acid and depression

Variable	Odds ratio	P-Value	95% UI
Uric acid (mg/dL)	1.05	0.001	1.02 – 1.08
Age (splines)			
age_spline1	1.01	0.314	0.99 – 1.02
age_spline2	1.04	0.042	1.00 – 1.07
age_spline3	0.83	<0.001	0.75 – 0.91
Gender			
Female	1.85	<0.001	1.71– 2.01
Ethnicity			
White	0.91	0.043	0.83 – 1.00
Black	0.92	0.096	0.83 – 1.02
Others/multi-racial	0.66	<0.001	0.57 – 0.76
_cons	0.05	<0.001	0.03 – 0.06

Supplementary Table 19. Uric acid and short sleep

Variable	Odds ratio	P-Value	95% UI
Uric acid (mg/dL)	1.04	0.001	1.02 – 1.06
Age (splines)			
age_spline1	1.04	<0.001	1.03 – 1.05
age_spline2	0.93	<0.001	0.90 – 0.95

age_spline3	1.17	<0.001	1.09 – 1.27
Gender			
Female	0.97	0.343	0.91 – 1.03
Ethnicity			
White	0.90	0.002	0.82 - 0.96
Black	1.95	<0.001	1.81 - 2.11
Others/multi-racial	0.91	0.075	0.81 - 1.01
_cons	0.04	<0.001	0.03 - 0.05

Sensitivity analysis:

Supplementary Table 20. Model A (>7mg/dL in males, >6mg/dL in females)

Variable	Odds ratio	P-Value	95% UI
Hyperuricemia (Model A)	3.21	<0.001	2.75 – 3.75
Age (Splines)			
age_spline1	1.14	<0.001	1.10 – 1.18
age_spline2	0.87	0.006	0.80 – 0.96
age_spline3	1.16	0.244	0.90 – 1.49
Gender	1.47	<0.001	1.27 – 1.70
Ethnicity	0.76	<0.001	0.70 – 0.83
smoking	1.36	<0.001	1.17 – 1.59
alcohol	0.59	<0.001	0.48 – 0.72
Education	0.78	<0.001	0.69 – 0.88
Poverty- to- income ratio (PIR)	0.88	<0.001	0.84 – 0.92

Chronic kidney disease (CKD)	2.81	<0.001	2.07 – 3.83
Healthy eating index (HEI)	1.23	0.004	1.07 – 1.42
Physical activity	1.00	0.015	1.00 – 1.00
_cons	0.00	<0.001	0.00 – 0.00

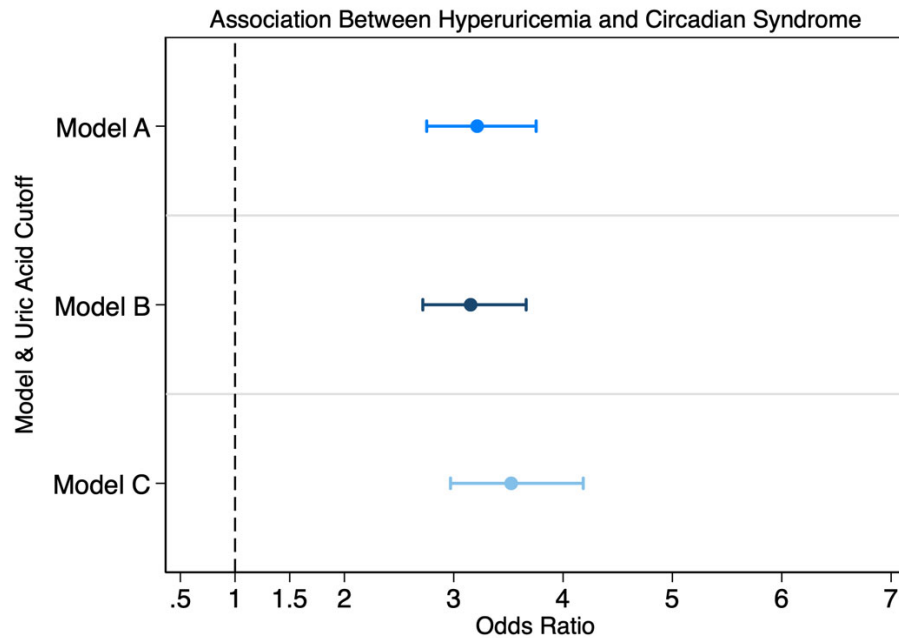
Supplementary Table 21. Model B (>6.8mg/dL in males, >5.7mg/dL in females)

Variable	Odds ratio	P-Value	95% UI
Hyperuricemia (model B)	3.15	<0.001	2.72 – 3.66
age_spline1	1.14	<0.001	1.10 – 1.18
age_spline2	0.87	0.006	0.79 – 0.96
age_spline3	1.16	0.229	0.91 – 1.49
Gender	1.467	<0.001	1.26 – 1.70
Ethnicity	0.76	<0.001	0.69 – 0.82
smoking	1.37	<0.001	1.18 – 1.60
alcohol	0.58	<0.001	0.47 – 0.72
Education	0.78	<0.001	0.69 – 0.89
Poverty- to- income ratio (PIR)	0.87	<0.001	0.83 – 0.91
Chronic kidney disease (CKD)	2.88	<0.001	2.12 – 3.91
Healthy eating index (HEI)	1.24	0.003	1.08 – 1.43
Physical activity	1.00	0.016	1.00 – 1.00
_cons	0.00	<0.001	0.00 – 0.00

Supplementary Table 22. Model C (>7.5mg/dL in males, >6.5mg/dL in females)

Variable	Odds ratio	P-Value	95% UI
Hyperuricemia (Model C)	3.53	<0.001	2.97– 4.18
age_spline1	1.14	<0.001	1.01– 1.18
age_spline2	0.87	0.006	0.79– 0.96
age_spline3	1.16	0.231	0.91– 1.49
Gender	1.46	<0.001	1.26 – 1.69
Ethnicity	0.76	<0.001	0.70 – 0.83
smoking	1.37	<0.001	1.18 – 1.59
alcohol	0.60	<0.001	0.49 – 0.73
Education	0.80	<0.001	0.70 – 0.89
Poverty- to- income ratio (PIR)	0.88	<0.001	0.84 – 0.92
Chronic kidney disease (CKD)	2.83	<0.001	2.08 – 3.85
Healthy eating index (HEI)	1.22	0.005	1.06 – 1.41
Physical activity	1.00	0.016	1.00 – 1.00
_cons	0.00	<0.001	0.00 – 0.00

Supplementary Figure 6. Visualization of sensitivity analysis results



10% Random Subsample Validation Analysis

A 10% random subsample of the study population (n = 2,733) was analyzed using the same multivariable logistic regression model as the primary analysis to assess robustness.

Supplementary Table 23. Baseline distribution in 10% random subsample

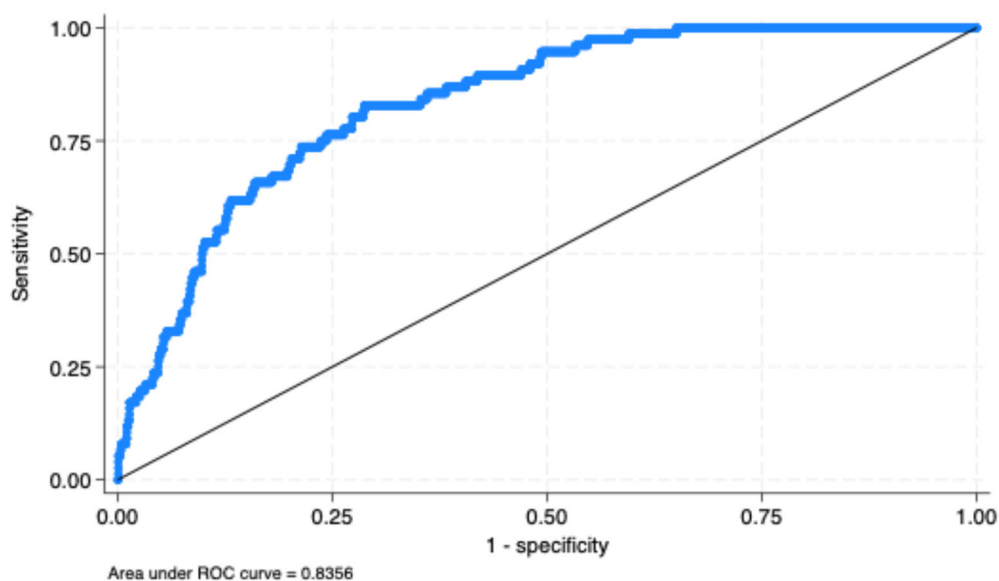
	No Hyperuricemia	Hyperuricemia	Total
No Circadian Syndrome	2,113	416	2,529
Circadian Syndrome	137	67	204
Total	2,250	483	2,733

Supplementary Table 24. Multivariable logistic regression model in 10% subsample

Variable	Odds Ratio (OR)	P-value	95% CI
Hyperuricemia	3.03	<0.001	1.73 – 5.31
Age spline 1	1.11	0.138	0.97 – 1.27

Age spline 2	1.05	0.782	0.73 – 1.51
Age spline 3	0.60	0.280	0.24 – 1.52
Female (vs Male)	1.89	0.016	1.13 – 3.18
White	1.01	0.969	0.54 – 1.88
Black	0.38	0.021	0.17 – 0.86
Others / Multiracial	0.29	0.060	0.08 – 1.06
Smoking	1.95	0.018	1.12 – 3.39
Alcohol	0.73	0.352	0.37 – 1.42
High school education	0.71	0.305	0.37 – 1.36
Graduate education	0.35	0.017	0.15 – 0.83
CKD	5.11	0.015	1.38 – 18.96
HEI – Moderate	1.69	0.540	0.31 – 9.14
HEI – Poor	2.69	0.232	0.53 – 13.67
Physical activity	1.00	0.244	1.00 – 1.00

Supplementary Figure 7. ROC curve for 10% subsample model



Supplementary Table 25. Link test for model specification

Variable	Coefficient	Std. Error	z	P-value	95% CI
_hat	0.6015	0.3588	1.68	0.094	−0.1017 – 1.3047
_hatsq	−0.0848	0.0746	−1.14	0.256	−0.2311 – 0.0614
Constant	−0.3649	0.4140	−0.88	0.378	−1.1763 – 0.4465