

# Low Uric Acid Levels Associated with Increased Risk of Degenerative Neurologic Conditions

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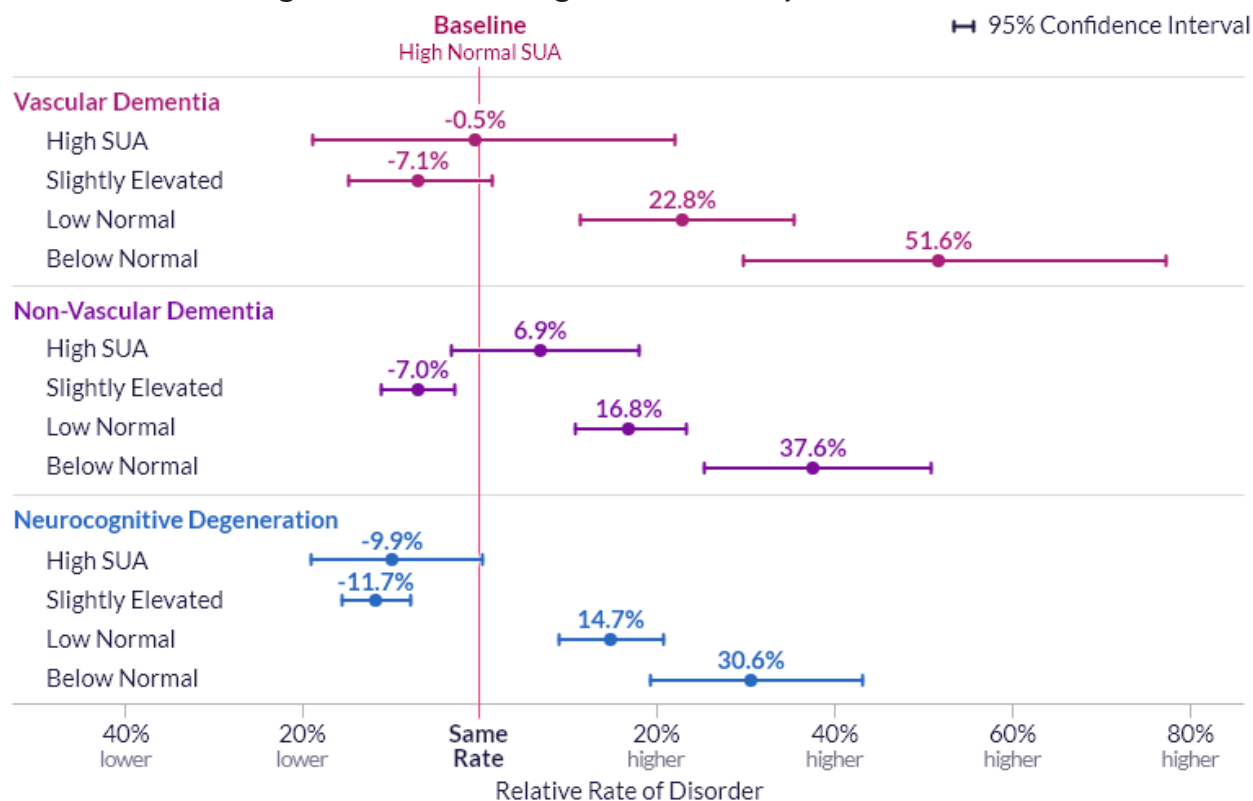
## Key Findings:

- Uric acid levels below 3.5 mg/dL are correlated with increased rates of being diagnosed with non-vascular and vascular dementia, as well as other degenerative neurologic conditions.
- Uric acid levels above 7.5 mg/dL are correlated with marginally decreased rates of being diagnosed with non-vascular dementia and other degenerative neurologic conditions.

Uric acid levels are measured through a lab test of a patient's blood or urine and are commonly used to diagnose conditions such as gout or to monitor patients undergoing chemotherapy.<sup>1</sup> While some studies have found no correlation between uric acid levels and increased risk of dementia, others have suggested that uric acid has antioxidant properties and may offer protective benefits against neurologic conditions.<sup>2,3</sup>

To better understand the relationship between uric acid levels and degenerative neurologic conditions, we studied 131,552 patients over the age of 50 who had at least one serum uric acid lab result between January 1, 2017, and November 1, 2021. We adjusted for various factors, including obesity, sex, age, ethnicity, and comorbidities. We calculated the risk of being diagnosed with a degenerative neurologic condition within the two years following a patient's randomly selected serum uric acid reading. Our findings indicate that patients with a uric acid level below 3.5 mg/dL have increased rates of vascular and non-vascular dementia and other degenerative neurologic conditions compared to those with a high normal uric acid level (at 3.5-7.5 mg/dL), as seen in Figure 1. Conversely, those with a uric acid level above normal range (at 7.5-10 mg/dL) have a slightly decreased rates of non-vascular dementia and other degenerative neurologic conditions. We did not find consistent evidence of a correlation between Alzheimer's disease and uric acid levels.

## Relative Rate of Degenerative Neurologic Conditions by Serum Uric Acid Level



N=131,452 patients

"Relative Rate of Degenerative Neurologic Conditions by Serum Uric Acid Level," 2023. EpicResearch.org

Figure 1. The relative likelihood of being diagnosed with a degenerative neurologic condition by serum uric acid (SUA) level. High SUA is defined as greater than 10 mg/dL, slightly elevated is defined as 7.5 - 10 mg/dL, high normal is defined as 3.5 - 7.5 mg/dL, low normal is defined as 2.5 - 3.5 mg/dL, and below normal is defined as less than 2.5 mg/dL.

A sensitivity analysis using a Cox proportional hazards model that adjusted for obesity, sex, age, social vulnerability, race, ethnicity, and comorbidities showed similar results for the relationship between uric acid levels and degenerative neurologic conditions.

These data come from Cosmos, a collaboration of 236 Epic health systems representing over 227 million patient records from 1,301 hospitals and more than 28,600 clinics from all 50 states and Lebanon. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

## References

1. Uric Acid Test. *MedlinePlus*. Published December 15, 2022. <https://medlineplus.gov/lab-tests/uric-acid-test/>. Accessed November 30, 2023.
2. Alam AB, Wu A, Power MC, West NA, Alonso A. Associations of serum uric acid with incident dementia and cognitive decline in the ARIC-NCS cohort. *J Neurol Sci*. 2020;414:116866. doi:10.1016/j.jns.2020.116866
3. Tana C, Ticinesi A, Prati B, Nouvenne A, Meschi T. Uric Acid and Cognitive Function in Older Individuals. *Nutrients*. 2018; 10(8):975. <https://doi.org/10.3390/nu10080975>

## Data Definitions

Term	Definition
Study period	1/1/2017 to 11/1/2023
Study population	<p>Patients aged 50 and older with a serum <b>uric acid lab</b> between 1/1/2017 and 11/1/2021.</p> <p>These patients must also:</p> <ol style="list-style-type: none"> <li>1. Have had at least one encounter in the last year.</li> <li>2. Have legal sex of male or female.</li> <li>3. Have documented <b>social vulnerability index</b> value.</li> <li>4. Not have a diagnosis suggesting <b>end stage renal disease</b> or <b>CKD 4 or 5</b>.</li> <li>5. Have at least two years' worth of encounters following the date of their selected <b>uric acid lab</b>.</li> </ol> <p>Patients were observed until the first of either:</p> <ol style="list-style-type: none"> <li>1. The date of the associated condition, if available.</li> <li>2. The last outpatient face-to-face encounter in the <b>study period</b>.</li> </ol>
Uric acid lab	<p>A randomly selected lab associated with LOINC code 3084-1 that occurred before the onset of an <b>outcome</b>.</p> <p>Numeric readings must be between 0 and 100 mg/dL.</p>
Vascular dementia	A diagnosis with ICD-10-CM code F01*.
Non-vascular dementia	A diagnosis with ICD-10-CM code F02.* or F03.*.
Other degenerative neurological conditions	A diagnosis with ICD-10-CM code G31*.
CKD 4 or 5	A diagnosis with ICD-10-CM code N18.4 or N18.5.
End stage renal disease	A diagnosis with ICD-10-CM code N18.6.
Cox proportional hazards model for sensitivity analysis	<p>Model definitions:</p> <ul style="list-style-type: none"> <li>• Patients were censored at the date of their most recent outpatient face-to-face visit.</li> <li>• Outcomes were measured for each condition as the date of the patient's first diagnosis for the respective condition.</li> </ul> <p>Model covariates:</p> <ul style="list-style-type: none"> <li>• <b>Obesity class</b></li> <li>• <b>Uric acid level</b></li> <li>• Sex</li> <li>• Age</li> <li>• <b>Social vulnerability index</b></li> <li>• Race and ethnicity</li> <li>• <b>Comorbidities</b></li> </ul>
Obesity class	<p>Under Weight: BMI &lt; 17.5</p> <p>Healthy Weight: BMI between 17.5 and 25</p> <p>Overweight: BMI between 25 and 30</p> <p>Stage 1 Obesity: BMI between 30 and 35</p> <p>Stage 2 Obesity: BMI between 35 and 40</p> <p>Stage 3 Obesity: BMI of 40 or above</p>
Uric acid level	High SUA is defined as greater than 10 mg/dL, slightly elevated is defined as 7.5 up to 10 mg/dL, high normal is defined as 3.5 up to 7.5 mg/dL, low

	normal is defined as 2.5 up to 3.5 mg/dL, and below normal is defined as less than 2.5 mg/dL.
<b>Comorbidities</b>	<b>Cardiovascular disease</b> <b>CKD 1, 2, or 3</b> <b>Essential hypertension</b> <b>Diabetes</b> <b>Cancer</b> <b>Psychiatric condition</b>
<b>Social vulnerability index (SVI)</b>	The SVI quartile for the ZIP Code of the patient's most recent address.
<b>Cardiovascular disease</b>	A diagnosis with ICD-10-CM code I20.*, I21.*, I22.*, I23.*, I24.*, I25.*, I26.*, I27.*, I28.*, I7*, I50.*, I3*, or I4*.
<b>CKD 1, 2, or 3</b>	A diagnosis with ICD-10-CM code N18.1*, N18.2*, or N18.3*.
<b>Essential hypertension</b>	A diagnosis with ICD-10-CM code I10.
<b>Diabetes</b>	A diagnosis with ICD-10-CM code E11.* or E10.*.
<b>Cancer</b>	A diagnosis with ICD-10-CM code C00-C96.
<b>Psychiatric conditions</b>	A diagnosis with ICD-10-CM code F31.*, F33.*, F34.*, or F39.*.

**Table 1: Relative Rate of Degenerative Neurologic Conditions by Serum Uric Acid Level**

Condition	Urate Level (mg/dL)	Number of Patients	Number of Cases	Case Rate	Case Ratio	Lower CI	Upper CI
Dementia Vascular	[0,2.5)	276	103	0.4	1.5	1.3	1.8
Dementia Vascular	[2.5,3.5)	1,039	314	0.3	1.2	1.1	1.4
Dementia Vascular	[7.5,10.0)	1,989	455	0.2	0.9	0.9	1.0
Dementia Vascular	10.0+	294	72	0.2	1.0	0.8	1.2
Dementia Other	10.0+	1,137	301	0.3	1.1	1.0	1.2
Dementia Other	[0,2.5)	892	304	0.3	1.4	1.3	1.5
Dementia Other	[2.5,3.5)	3,652	1,057	0.3	1.2	1.1	1.2
Dementia Other	[7.5,10.0)	7,434	1,712	0.2	0.9	0.9	1.0
Neurocognitive Degeneration	10.0+	1,155	261	0.2	0.9	0.8	1.0
Neurocognitive Degeneration	[0,2.5)	968	317	0.3	1.3	1.2	1.4
Neurocognitive Degeneration	[2.5,3.5)	3,985	1,146	0.3	1.1	1.1	1.2
Neurocognitive Degeneration	[7.5,10.0)	8,188	1,813	0.2	0.9	0.8	0.9

**Table 2: Cox Proportional Hazards Model - Degenerative Neurologic Conditions and Serum Uric Acid**

Condition	Sex	Age	Count	[0,2.5)	[2.5,5.0)	[7.5,10.0)	10.0+	
Vascular Dementia	Any	Any	15,056	1.516	1.228	0.929	0.995	
		[50,65)	1,568	1.421	1.294	0.987	1.181	
		[65,75)	3,880	1.624	1.301	0.940	1.280	
		75+	9,608	1.491	1.188	0.916	0.838	
	Female	Any	7,804	1.493	1.187	0.997	0.947	
		[50,65)	756	0.864	1.475	1.564	0.508	
		[65,75)	1,968	1.597	1.191	0.840	1.283	
		75+	5,080	1.545	1.138	0.996	0.887	
	Male	Any	7,252	1.614	1.336	0.878	1.026	
		[50,65)	812	2.314	0.962	0.749	1.587	
		[65,75)	1,912	1.663	1.540	1.014	1.279	
		75+	4,528	1.356	1.318	0.851	0.798	
	Other Dementia	Any	Any	55,468	1.376	1.168	0.930	1.069
			[50,65)	4,836	1.425	1.180	0.881	1.362
			[65,75)	14,212	1.625	1.252	0.944	1.168
			75+	36,420	1.264	1.136	0.931	0.980
Female		Any	28,868	1.398	1.147	0.989	1.130	
		[50,65)	2,304	1.149	1.120	1.043	1.045	
		[65,75)	7,024	1.599	1.186	1.004	1.394	
		75+	19,540	1.361	1.136	0.979	1.041	
Male		Any	26,600	1.347	1.241	0.884	1.014	
		[50,65)	2,532	2.085	1.341	0.816	1.535	
		[65,75)	7,188	1.704	1.422	0.902	0.989	
		75+	16,880	1.022	1.158	0.890	0.920	
Neurocognitive Degeneration		Any	Any	60,928	1.306	1.147	0.883	0.901
			[50,65)	11,028	1.577	1.152	0.909	1.037
			[65,75)	19,876	1.264	1.233	0.867	0.844
			75+	30,024	1.221	1.089	0.884	0.884
	Female	Any	29,364	1.217	1.135	0.909	0.951	
		[50,65)	5,300	1.476	1.107	0.930	1.383	
		[65,75)	9,156	1.068	1.260	0.896	0.834	
		75+	14,908	1.201	1.073	0.909	0.886	
	Male	Any	31,564	1.524	1.182	0.865	0.864	
		[50,65)	5,728	1.811	1.278	0.894	0.860	
		[65,75)	10,720	1.690	1.200	0.848	0.848	
		75+	15,116	1.285	1.132	0.865	0.882	