Low AST and ALT Levels Are Associated with Higher Likelihood of Early-Onset Colorectal Cancer in Adults Under 45

Team A: Kersten Bartelt, RN; Eric Barkley
Team B: Dave Little, MD; Joe Deckert, PhD
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Key Findings:

- Among adults aged 18–44 undergoing a first colorectal cancer (CRC) screening, a pre-screening AST below 14 U/L was associated with a 65% higher likelihood of an early-onset CRC diagnosis, and an ALT below 14 U/L with a 68% higher likelihood, each compared with patients whose values fell in the range of 14–29 U/L.
- Higher AST and ALT values ran the opposite way: an AST of 30 U/L or above was associated with a 22% lower likelihood, and an ALT of 30 U/L or above with a 29% lower likelihood.
- A rising AST or ALT over the three years before screening was associated with a lower likelihood of CRC (27% lower for AST, 26% lower for ALT, versus stable values), while a declining AST or ALT showed no significant association in either direction.

Colorectal cancer (CRC) is increasingly a disease of younger adults, even as it remains most common in older ones. While overall CRC rates have continued to fall among older adults, incidence among adults aged 20 to 49 has risen by roughly 3% per year over the past decade.[1] CRC is now the leading cause of cancer death in Americans under 50 for reasons that remain poorly understood.[2] In response to this shift, the U.S. Preventive Services Task Force (USPSTF) lowered the recommended starting age for routine screening from 50 to 45 in 2021.[3] There is growing interest in whether laboratory values collected during ordinary care might help flag elevated risk earlier. We examined a panel of common, routinely collected metabolic laboratory tests, including liver enzymes AST (aspartate aminotransferase) and ALT (alanine aminotransferase) and several lipid measures. We examined whether these values, measured before colorectal cancer screening, were associated with a subsequent diagnosis of early-onset CRC.

We studied 11,469 U.S. adults aged 18 to 44 who underwent a first CRC screening between January 2017 and March 2025 and who had established care. Eligible patients had at least one AST or ALT result in the three years before screening. Those with a prior cancer diagnosis, inflammatory bowel disease, Lynch syndrome, or pregnancy were excluded. Patients who were diagnosed with CRC within a year of screening were matched with up to four patients who were not. Matching was based on the presence and timing of labs, age, sex, and screening year. For each patient, we examined both the level and the three-year trend of several routinely collected labs: AST, ALT, triglycerides, HDL cholesterol, and the triglyceride-to-HDL ratio. We also included serum potassium as a comparison marker that we would not expect to be related to CRC. We accounted for demographic, socioeconomic, and clinical characteristics including BMI category and weight-change trajectory, smoking, alcohol use disorder, diabetes, hypertension, fatty liver disease, malnutrition, and insulin and statin use. Because we studied several markers at once, we applied a Bonferroni correction, a stricter statistical bar that lowers the chance of a false positive when many comparisons are made.

Adults whose AST fell below 14 U/L had a 65% higher likelihood of an early-onset CRC diagnosis, and those whose ALT fell below 14 U/L had a 68% higher likelihood, each compared with patients whose values sat in the range of 14 to 29 U/L. The pattern reversed at the high end: an AST of 30 U/L or above

was associated with a 22% lower likelihood, and an ALT of 30 U/L or above with a 29% lower likelihood, again relative to the central range. Low AST and ALT can be markers of other underlying conditions, such as reduced muscle mass or poor nutritional status. It is therefore possible that an underlying condition, rather than the low enzyme levels themselves, drives the higher likelihood of CRC. Accounting for BMI, weight trajectory, and malnutrition cannot fully rule out this possibility.

Likelihood of Early-Onset Colorectal Cancer by Pre-Screening AST and ALT Level

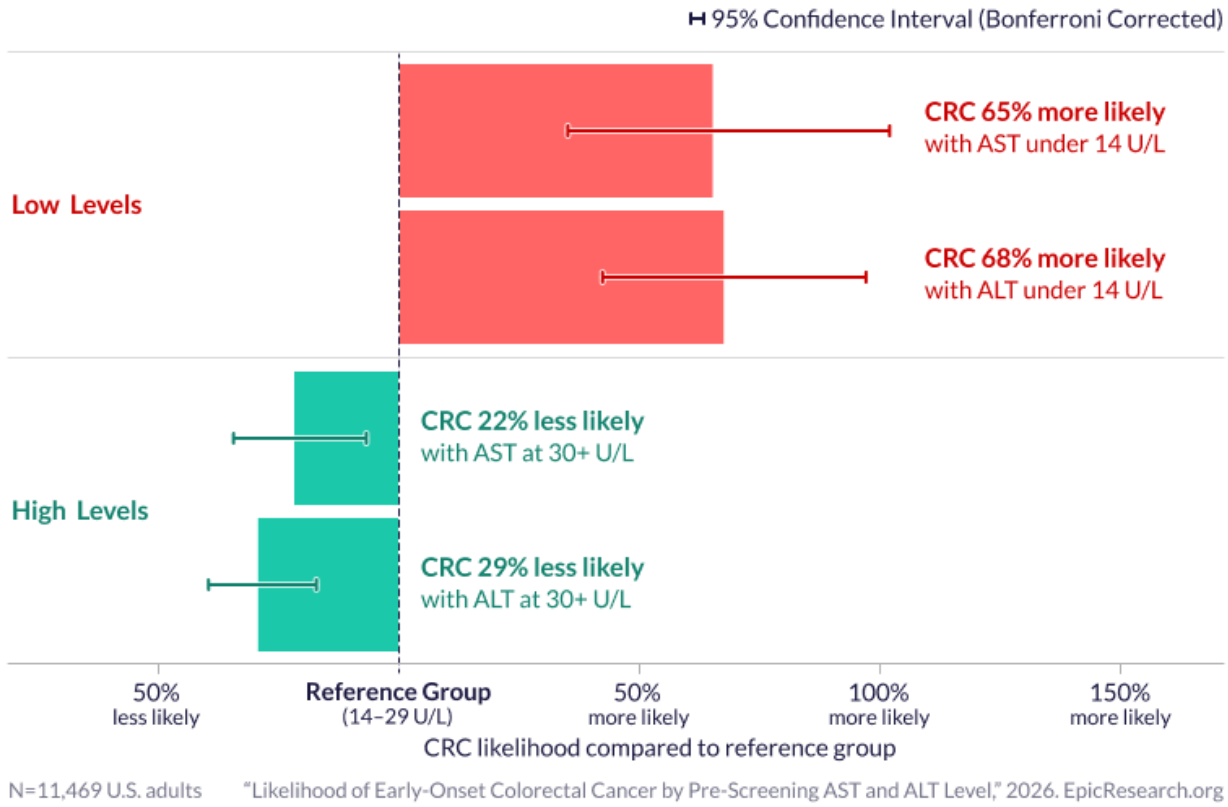

Figure 1. The likelihood of an early-onset colorectal cancer diagnosis among adults with low (below 14 U/L) or high (30 U/L or above) pre-screening AST and ALT values compared with the range of 14–29 U/L.

A rising AST across the three years before screening was associated with a 27% lower likelihood of CRC, and a rising ALT with a 26% lower likelihood, compared with patients whose values held steady. A falling AST or ALT was not associated with CRC.

Likelihood of Early-Onset Colorectal Cancer by AST and ALT Trajectory

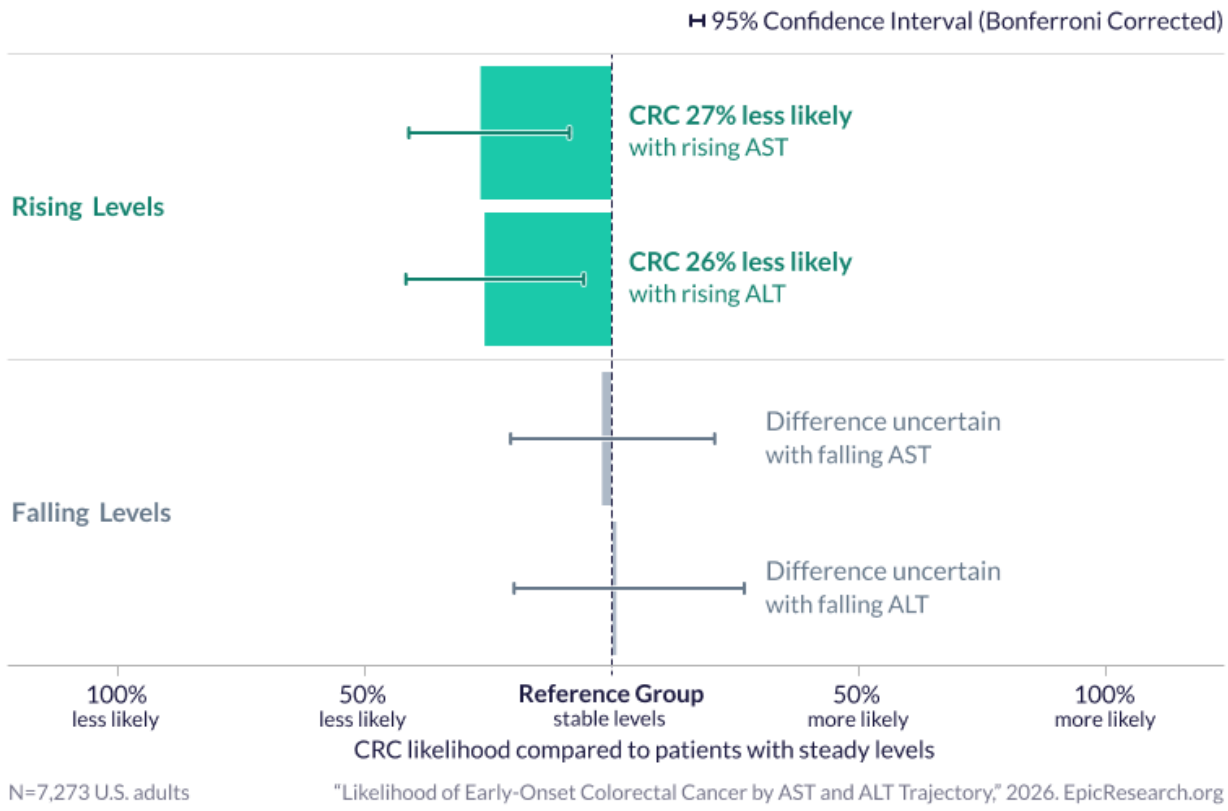

Figure 2. The likelihood of an early-onset colorectal cancer diagnosis among adults whose AST or ALT rose or fell by at least 2.0 U/L over the three years before screening compared with patients whose values remained stable.

None of the other labs we examined were associated with early-onset CRC. Triglycerides, HDL cholesterol, and the triglyceride-to-HDL ratio showed no significant association in either their levels or their trends. Serum potassium also showed no association, as expected.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 310 million patient records from 2,200 hospitals and more than 50,000 clinics from all 50 U.S. states, Canada, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientist. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. Siegel RL, Wagle NS, Star J, Kratzer TB, Smith RA, Jemal A. Colorectal cancer statistics, 2026. CA Cancer J Clin. 2026;76(2):e70067. doi:10.3322/caac.70067
2. Sinicrope FA. Increasing incidence of early-onset colorectal cancer. N Engl J Med. 2022;386(16):1547-1558. doi:10.1056/NEJMra2200869
3. US Preventive Services Task Force; Davidson KW, Barry MJ, Mangione CM, et al. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. JAMA. 2021;325(19):1965-1977. doi:10.1001/jama.2021.6238

Data Definitions

Term	Definition
Study period	1/1/2017 to 3/25/2025
Study population: inclusion	Patients aged 18–44 at their first **CRC screening** during the **study period** with: • At least one AST or ALT result within the three years prior to the screening date • Two or more **outpatient face-to-face encounters** in the three years prior to the screening date and another in the year following
Study population: exclusion	History of any cancer prior to the screening date (ICD-10-CM code C*) Inflammatory bowel disease (ICD-10-CM code K50*, K51*) prior to screening Lynch syndrome (ICD-10-CM code Z15.09) prior to screening Family history of colonic polyps (ICD-10-CM code Z83.71) prior to screening Pregnancy (ICD-10-CM code O*) from three years before through one year after screening
Index date	Date of the first **CRC screening** within the **study period**
Outcome (case)	A colorectal cancer diagnosis (ICD-10-CM C18*, C19, C20, C21*, C26.0) within one year of the **CRC screening**
Control	A patient who underwent **CRC screening** with no subsequent **colorectal cancer diagnosis** within one year of the **CRC screening** (test-negative control)
Exposures	Average values of labs over the lookback window Difference between the earliest and latest lab in the lookback window when multiple values were documented **AST (U/L)**: • <14, 14–29, 30+ • 2.0+ loss, 2.0+ gain, steady **ALT (U/L)**: • <14, 14–29, 30+ • 2.0+ loss, 2.0+ gain, steady **Triglycerides (mg/dL)**: • 0–54, 55–149, 150+ • 10.0+ loss, 10.0+ gain, steady **HDL (mg/dL)**: • 0–39, 40–69, 70+ • 5.0+ loss, 5.0+ gain, steady **Triglycerides:HDL ratio**: • 0–0.7, 0.8–4.9, 5.0+ • 0.2+ loss, 0.2+ gain, steady **Serum potassium (mEq/L)**: • 0–3.5, 3.6–4.3, 4.4+ • 0.5+ loss, 0.5+ gain, steady
AST	LOINC codes 88112-8, 30239-8, 1920-8
ALT	LOINC codes 77144-4, 76625-3, 1744-2, 1743-4, 1742-6
Triglycerides	LOINC codes 2571-8, 14927-8
HDL	LOINC codes 2085-9, 18263-4, 49130-8
Triglycerides:HDL ratio	Triglycerides and HDL resulted on the same day; combined-panel results included via LOINC 44733-4 and 55607-6

Serum potassium	LOINC codes 32713-0, 77142-8, 6298-4, 39789-3, 2823-3
CRC screening	Colonoscopy: HCPCS codes G2204, G0105, or G0121 or CPT code 44388, 44389, 44390, 44391, 44394, 44401–44408, 45378– 45382, 45384–45386, 45391, or 45392 sDNA-FIT: CPT code 81528, SNOMED code 457591000124105, or LOINC code 77353-1 or 77354-9 FIT/gFOBT: LOINC code 14563-1, 14564-9, 14565-6, 2335-8, 27396-1, 29771-3, 50196-5, 57803-9, 58453-2, 57905-2, 56490-6, 56491-4, 80372-6, 12504-7, 27926-5, 27401-9, 12503-9, or 27925-7, HCPCS code G0328, or CPT codes 82270, 82272, or 82274 Flexible sigmoidoscopy: CPT code 45330–45335, 45337, 45338, or 45340–45342 or HCPCS code G0104 or G0106 CT colonography: CPT code 74261, 74262, or 74263
Outpatient face-to-face encounters	An encounter of type Emergency, Office Visit, Well Child, Follow-up, Telemedicine, Urgent Care, Walk-In, Routine Prenatal, Postpartum Visit, or Fetal Care Consult
Insulin use	History of insulin use prior to the **index date** (simple-generic name string match: insulin)
Statin use	History of statin use prior to the **index date** (simple-generic name string match: atorvastatin, simvastatin, rosuvastatin, pravastatin, lovastatin, fluvastatin, pitavastatin)
Matching	Cases matched to controls 1:4 on presence and timing of the most recent lab (<6 months, 6–12 months, or 1–3 years before **index date**), age, evaluated sex, and year of **index date**
Confounders	Age at **index date** Evaluated sex Screening year BMI category (closest to screening) Weight-change trajectory Social Vulnerability Index quintile Smoking status Insurance used as the primary coverage in the three years prior to the index date through a year after: Medicaid, Medicare, Self-pay, or Miscellaneous/Other Diabetes: ICD-10-CM code E08*–E13* Hypertension: ICD-10-CM code I10*–I13* NAFLD/NASH: ICD-10-CM code K75.81 or K76.0* Alcohol use disorder: ICD-10-CM code F10* Malnutrition: ICD-10-CM code E40*–E46* **Insulin use** **Statin use** **Race and ethnicity:** Hispanic; non-Hispanic White, Black, Asian, Multiracial, or Other
Model specifications	Primary analysis: Unconditional logistic regression on the matched 1:4 case-control cohort Sensitivity analysis: Unconditional logistic regression on the pre-matched populations; results were consistent with the primary analysis Confidence intervals applied a Bonferroni correction to adjust for repeating significance tests across five different lab categories.
Limitations	Colorectal cancer screening age recommendations changed during the reporting period.

	AST and ALT values might be influenced by medications (e.g., statins), acute illness, or timing relative to meals, so residual confounding is possible despite adjustment. The test-negative control design assumes screen-negative patients represent the non-CRC population; screening selection bias may limit generalizability. The requirement for available lab results might bias the cohort toward patients with more frequent healthcare use.

Table 1. Likelihood of Early-Onset Colorectal Cancer by Pre-Screening AST and ALT Level

Marker and category	Comparison group	Change in likelihood	95% CI (Bonferroni corrected)	Significant	Analysis N
AST < 14 U/L	AST 14–29 U/L	+65%	1.35–2.02	Yes	11,327
AST ≥ 30 U/L	AST 14–29 U/L	−22%	0.66–0.93	Yes	11,327
ALT < 14 U/L	ALT 14–29 U/L	+68%	1.42–1.97	Yes	11,392
ALT ≥ 30 U/L	ALT 14–29 U/L	−29%	0.60–0.83	Yes	11,392

Table 2. Likelihood of Early-Onset Colorectal Cancer by AST and ALT Trajectory

Marker and category	Comparison group	Change in likelihood	95% CI (Bonferroni corrected)	Significant	Analysis N
AST rising (≥ 2.0 U/L)	AST stable	−27%	0.59–0.91	Yes	7,130
AST falling (≥ 2.0 U/L)	AST stable	−2%	0.80–1.21	No	7,130
ALT rising (≥ 2.0 U/L)	ALT stable	−26%	0.58–0.94	Yes	7,180
ALT falling (≥ 2.0 U/L)	ALT stable	+1%	0.80–1.27	No	7,180

Table 3. Likelihood of Early-Onset Colorectal Cancer by Each Metabolic Marker Examined

Marker	Category	Comparison group	Change in likelihood	95% CI (Bonferroni corrected)	Significant	Analysis N
AST	< 14 U/L	14–29 U/L	+65%	1.35–2.02	Yes	11,327
	≥ 30 U/L	14–29 U/L	−22%	0.66–0.93	Yes	11,327
	Rising (≥ 2.0 U/L)	Stable	−27%	0.59–0.91	Yes	7,130
	Falling (≥ 2.0 U/L)	Stable	−2%	0.80–1.21	No	7,130
ALT	< 14 U/L	14–29 U/L	+68%	1.42–1.97	Yes	11,392
	≥ 30 U/L	14–29 U/L	−29%	0.60–0.83	Yes	11,392
	Rising (≥ 2.0 U/L)	Stable	−26%	0.58–0.94	Yes	7,180

	Falling (≥ 2.0 U/L)	Stable	+1%	0.80–1.27	No	7,180
Triglycerides	< 55 mg/dL	55–149 mg/dL	+5%	0.81–1.37	No	7,906
	≥ 150 mg/dL	55–149 mg/dL	−16%	0.69–1.02	No	7,906
	Rising (≥ 10 mg/dL)	Stable	+15%	0.81–1.65	No	3,339
	Falling (≥ 10 mg/dL)	Stable	+27%	0.89–1.81	No	3,339
HDL cholesterol	< 40 mg/dL	40–69 mg/dL	+19%	0.98–1.45	No	7,923
	≥ 70 mg/dL	40–69 mg/dL	−2%	0.77–1.26	No	7,923
	Rising (≥ 5 mg/dL)	Stable	−17%	0.61–1.13	No	3,353
	Falling (≥ 5 mg/dL)	Stable	−3%	0.72–1.31	No	3,353
Triglyceride-to-HDL ratio	< 0.8	0.8–4.9	+15%	0.87–1.52	No	7,765
	≥ 5.0	0.8–4.9	−18%	0.64–1.06	No	7,765
	Rising (≥ 0.2)	Stable	−20%	0.57–1.13	No	3,246
	Falling (≥ 0.2)	Stable	−21%	0.56–1.11	No	3,246
Serum potassium	< 3.6 mEq/L	3.6–4.3 mEq/L	+8%	0.78–1.52	No	11,499
	≥ 4.4 mEq/L	3.6–4.3 mEq/L	−4%	0.82–1.11	No	11,499
	Rising (≥ 0.5 mEq/L)	Stable	−1%	0.80–1.24	No	7,854
	Falling (≥ 0.5 mEq/L)	Stable	+16%	0.94–1.42	No	7,854