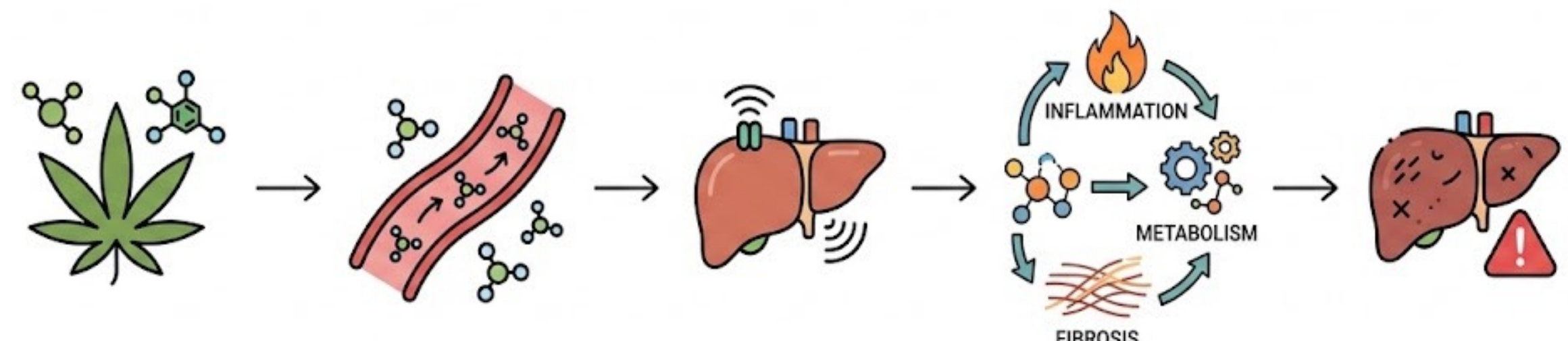




BACKGROUND & AIM

OVERVIEW: CANNABIS EXPOSURE AND LIVER DISEASE PROCESSES



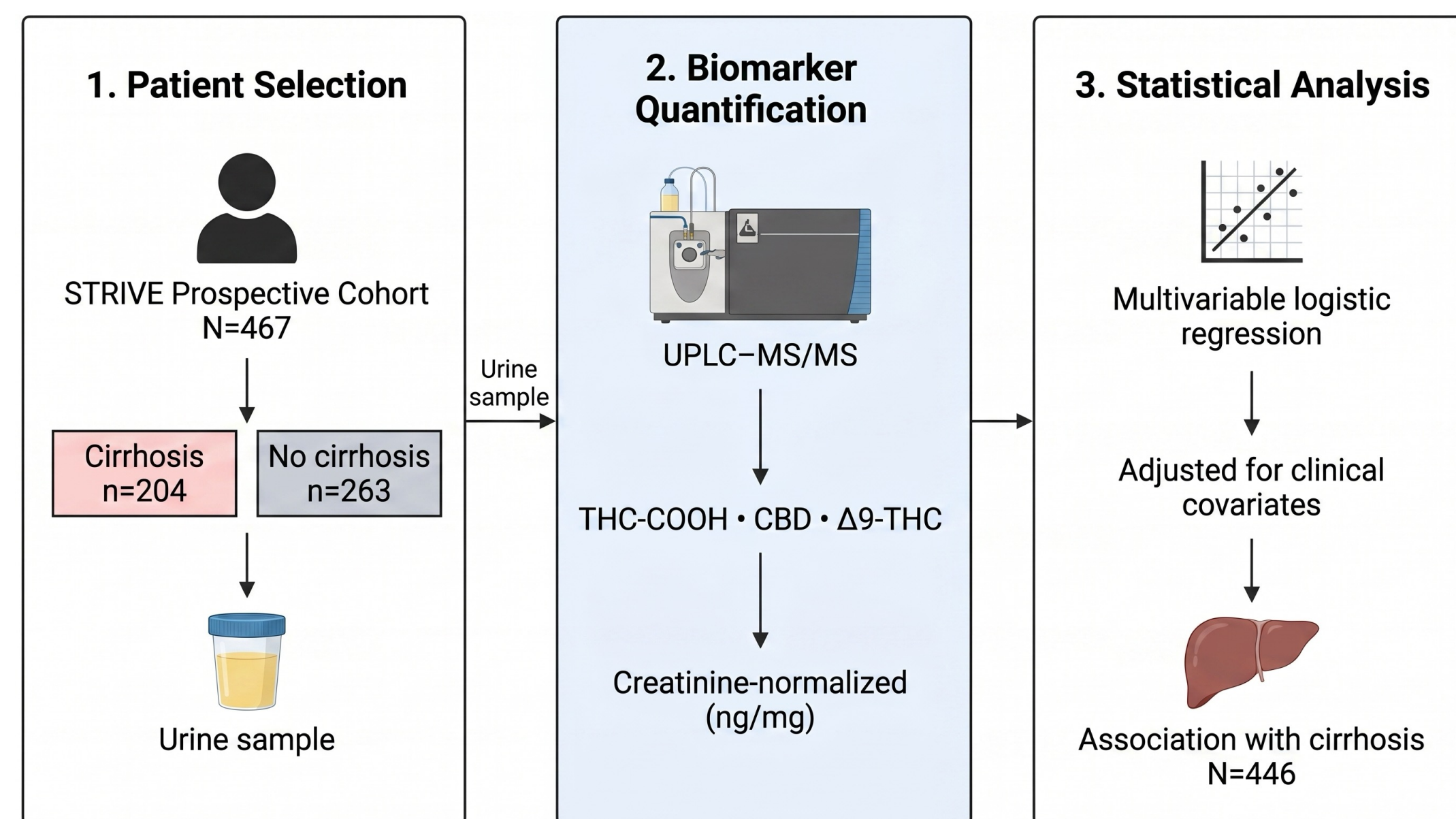
1. CANNABIS EXPOSURE (THC, CBD)
2. CIRCULATING CANNABINOIDS
3. LIVER: CB1 & CB2 RECEPTOR SIGNALING
4. DOWNSTREAM SIGNALING PATHWAYS (INFLAMMATION, METABOLISM, FIBROSIS)
5. LIVER DISEASE DEVELOPMENT

(Endocannabinoid signaling may have complex and context-dependent effects on hepatic inflammation, metabolism, and fibrosis)

- Cannabis use is increasingly prevalent in the U.S., yet its relationship with cirrhosis remains unclear.
- Prior studies rely on self-reported use, limiting accuracy. Objective biomarker-based data are limited
- Hepatic CB1/CB2 receptors are upregulated in cirrhosis and linked to pro- and anti-fibrotic signaling

Aim: To evaluate urinary cannabinoid metabolite detection and concentration, and their association with cirrhosis

MATERIAL & METHODS



Participants: Adults aged 40–75 enrolled in the STRIVE cohort, with and without cirrhosis defined by ICD codes, elastography ≥ 14 kPa, or biopsy. Participants with cirrhosis were enrolled predominantly at Duke, UNC, and Emory; NCSU enrolled primarily otherwise healthy controls.

Design: Cross-sectional analysis at baseline

Biomarkers: Urinary THC-COOH, CBD, and $\Delta 9$ -THC quantified by UPLC-MS/MS (Duke Metabolomics Core Facility) normalized to urinary creatinine

Analysis: Multivariable logistic regression evaluating the association between THC-COOH detection and odds of cirrhosis at baseline, adjusted for age, sex, race/ethnicity, BMI, alcohol use, smoking, diabetes, and site (N=446)

Secondary: Concentration comparisons among detectable levels

RESULTS

Table 1. Baseline Characteristics by Cirrhosis Status

Variable	Cirrhosis n=204	No Cirrhosis n=263
Age, Mean (SD)	60.3 (8.9)	58.6 (10.3)
BMI†, Mean (SD)	31.0 (7.0)	30.4 (7.6)
Sex, Male, n (%)	104 (51.0%)	62 (23.6%)
Race/Ethnicity, n (%)		
White	166 (81.4%)	122 (46.4%)
Black or African American	26 (12.7%)	113 (43.0%)
Hispanic or Latino	6 (2.9%)	15 (5.7%)
Other	6 (2.9%)	13 (4.9%)
Enrollment Site, n (%)		
DUKE	127 (62.3%)	7 (2.7%)
NCSU	3 (1.5%)	207 (78.7%)
EMORY	56 (27.5%)	48 (18.3%)
UNC	18 (8.8%)	1 (0.4%)
Alcohol Use, n (%)		
Never	62 (30.4%)	76 (28.9%)
Current	31 (15.2%)	149 (56.7%)
Former	111 (54.4%)	37 (14.1%)
Ever Smoker (Yes), n (%)	29 (14.2%)	35 (13.3%)
Diabetes (Yes), n (%)	90 (44.1%)	48 (18.3%)
Cannabinoid Detection, n (%)		
THC-COOH	50 (24.5%)	42 (16.0%)
CBD	19 (9.3%)	23 (8.7%)
$\Delta 9$ -THC	18 (8.8%)	15 (5.7%)

†BMI N=447. Missing: Age n=1, Alcohol n=2, others n \leq 1 each. Cirrhosis: self-report/ICD, elastography ≥ 14 kPa, or biopsy.

3.4-Fold Higher Odds of Cirrhosis
THC-COOH detected in **24.5%** of cirrhosis patients vs. **16.0%** of controls *aOR* 3.40
(95% CI 1.17–9.90, *p*=0.025)

CONCLUSIONS and FUTURE DIRECTIONS

- **First large multi-site study** using objective urinary cannabinoid biomarkers in cirrhosis, establishing a methodological foundation for cannabis research in liver disease
- **Nearly 1 in 4** cirrhosis patients had detectable cannabis exposure — even in states where it remains illegal, suggesting exposure may be underrecognized in clinical practice
- As cannabis use rises nationwide, widespread use may be outpacing our understanding of its consequences, much like tobacco before it
- Impact of cannabis on liver disease progression, decompensation, and HCC remains unclear and clinically relevant
- Longitudinal human studies are needed to determine the impact of cannabis exposure on liver-related morbidity and mortality
- Characterizing cannabis use (frequency, route, product type) will better define exposure patterns and inform clinical risk assessment

RESULTS

Cirrhosis patients have lower cannabinoid metabolite concentrations despite higher detection rates

Median THC-COOH: Cirrhosis 138 ng/mg vs. Controls 296 ng/mg (*p* = 0.20 for concentration)

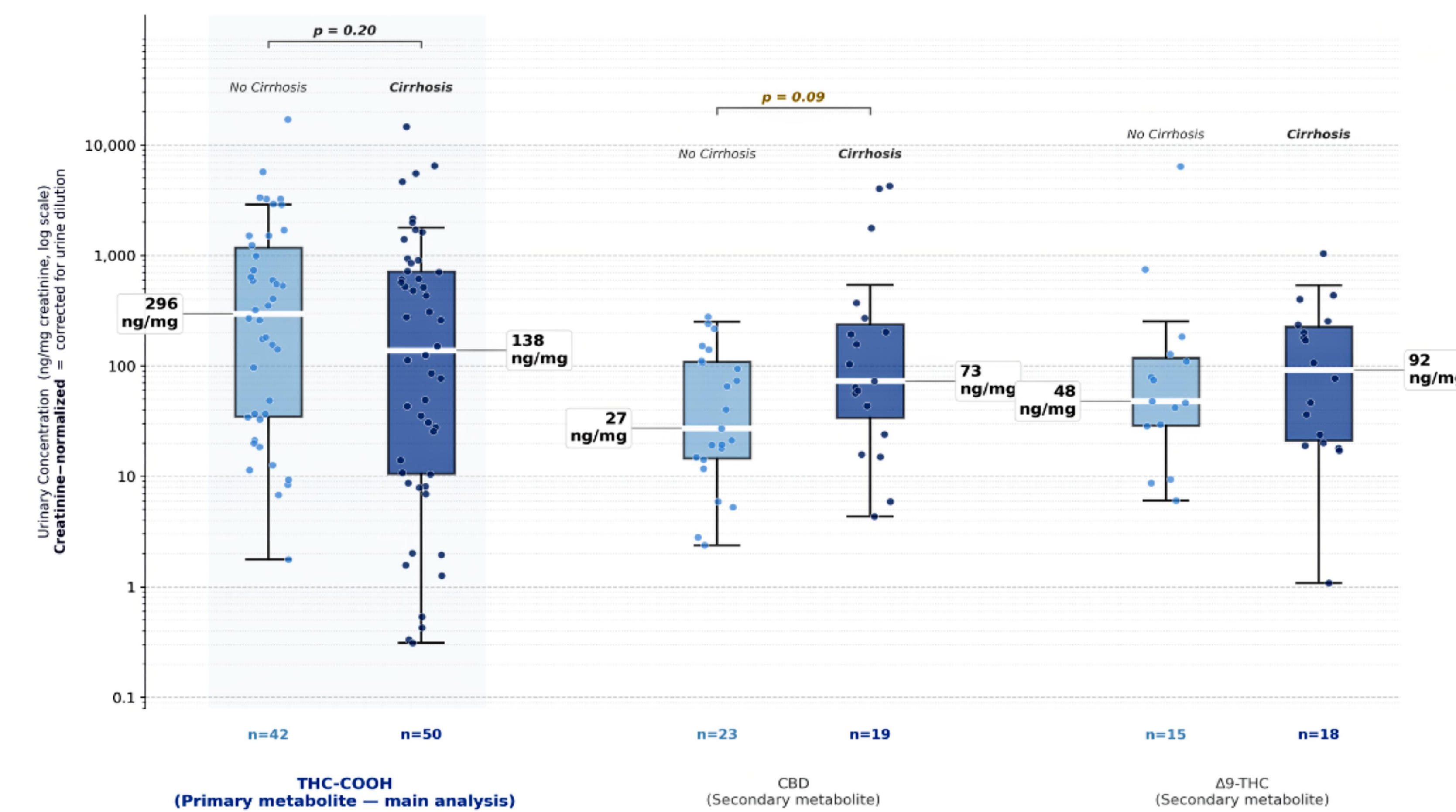


Table 2. Factors Associated with Cirrhosis in Multivariable Analysis (N=446)

Variable	aOR	95% CI	p value
Primary Exposure			
THC-COOH detected	3.40	1.17–9.90	0.025
Demographics			
Age	0.97	0.93–1.02	0.216
Male (vs Female)	1.10	0.48–2.51	0.823
Race/Ethnicity			
Race: White vs Other	5.54	1.03–29.90	0.002
Clinical Factors			
Diabetes (Yes vs No)	3.33	1.37–8.33	0.008
Behavioral Factors			
Alcohol: Current vs Never	3.13	1.14–8.33	0.024
Alcohol: Current vs Former	14.29	4.76–40.00	<0.001
Smoking: Yes vs No	2.12	0.65–6.94	0.214
Study Site			
Site: Emory vs UNC	0.05	0.01–0.46	0.119
Site: NCSU vs UNC	0.001	<0.001–0.014	<0.001

Model adjusted for age, sex, race/ethnicity, BMI, alcohol use, smoking, diabetes, and site (N=446). Significant *p*-values in bold.

