Urology xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Urology

journal homepage: www.sciencedirect.com/journal/urology

Health Services Research

Association Between Cannabis Use Disorder and Lower Urinary Tract Symptoms in Young Adults: A Nationwide Claims Database Study

Devin M. Dishong[1,*], Emma Giarracco[1], Aurora J. Grutman, Jack A. Campbell, Andrew T. Gabrielson, Andrew J. Cohen

Johns Hopkins Brady Urological Institute, Johns Hopkins University School of Medicine, Baltimore, MD

A B S T R A C T

Objective: To investigate the association of Cannabis Use Disorder (CUD) with new diagnoses of lower urinary tract symptoms (LUTS) in a young adult cohort.
Methods: Using the TriNetX database, we identified patients aged 18-34 and stratified by sex and CUD diagnosis into cohorts. Propensity score matching was utilized on demographics and variables potentially affecting LUTS. The primary outcomes were 5-year risks of new onset lower urinary tract diagnoses, including all-cause LUTS, dysuria, pelvic/perineal pain, overactive bladder, and urinary tract infection, among patients with CUD compared to controls.
Results: We identified 101,761 and 67,110 matched pairs of males and females, respectively. At 5-year follow-up, CUD was associated with a higher risk of new onset of all-cause LUTS in males (RR 1.69, 95% CI 1.60-1.80, $P < .01$) and females (RR 1.81, 95% CI 1.73-1.89, $P < .01$) compared to controls. Increased risks of dysuria, pelvic/perineal pain, and urinary tract infection were observed in both male and female CUD patients compared to controls (all $P < .01$). CUD was not associated with overactive bladder in either males or females.
Conclusion: In a cohort of young adults, CUD was associated with a greater risk of developing LUTS in both men and women. Further research is needed to define the impact of cannabinoids on lower urinary tract function.

The rapid expansion of cannabis legalization has altered the public health landscape in the United States. As of 2025, 24 U.S. states, 3 U.S. territories, and Washington D.C. have legalized recreational marijuana use, and another 7 states have decriminalized its use. Cannabis use disorder (CUD), defined as continued cannabis use despite clinically significant impairment (eg, failure to fulfill major role obligations, physical hazard, and interpersonal problems) or distress, is most prevalent among young adults, with a median age at onset of 22 years.[1,2] The risk of developing CUD increases with the frequency and duration of use.[2,3] Given the high prevalence of cannabis use among young adults, the long-term health consequences of cannabis use are important to assess.

The impact of CUD on the urological system is not clear. Cannabinoid receptors are G-protein coupled receptors located throughout the lower urinary tract, including the urothelium, sub-urothelial nerve plexus, bladder, prostate, and urethra.[3] Chronic cannabis usage promotes increased receptor stimulation affecting host inflammatory response and defense against infection through increased expression of IL-1α, IL-1β, and TNF- α.[3,4] Cannabinoids also mediate pain perception, urgency, and autonomic nerve function mediated through capsaicin-sensitive mucosal afferents.[5,6] This may manifest as symptoms of dysuria or chronic pelvis pain with receptor dysfunction.[3,7,8] While some evidence suggests cannabinoids may have therapeutic potential in neurogenic bladder dysfunction and pain, there is a lack of robust randomized controlled trials to determine causality.[9,10] Conversely, other studies suggest a dose-response relationship between cannabis use and risk of stress, urge, and mixed urinary incontinence in females.[11] Interestingly, CUD has been shown to potentially have a protective effect on the development of lower urinary tract symptoms (LUTS) in adult males; however, evidence is conflicting.[12,13] For both male and female pediatric patients, CUD has been associated with increased risk of developing LUTS.[14] Further, proteomic analyses suggest exogenous cannabinoids may activate or inhibit signaling pathways in the lower urinary tract.[8] These pathways can be altered through chronic exposure, potentially leading to increased immune response activation and resulting in chronic inflammatory processes and voiding dysfunction.[15,16]

The inconclusive evidence between cannabis use and its impact on the development of LUTS highlights the necessity for large-scale, population-based investigation to clarify these associations and help focus the scope of future investigations. The young adult population is particularly interesting in elucidating the association between LUTS and

* Address correspondence to: Devin M. Dishong, BS, Johns Hopkins Brady Urological Institute, 600 N Wolfe Street, Baltimore, MD 21287.
E-mail address: ddishon1@jh.edu (D.M. Dishong).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.urology.2026.06.022
Received 22 April 2026; Accepted 14 June 2026

CUD. Reduced confounding from age-related LUTS etiologies allows any potential observed associations to be more confidently attributed to the exposure of CUD itself rather than benign prostatic hyperplasia, age-related detrusor changes, or other accumulated comorbidities such as diabetes and obesity.[17,18] Additionally, young adults have baseline low LUTS prevalence, which allows any increase in LUTS attributable to cannabis to become more detectable.[13] The combination of high exposure prevalence of cannabis use in young adults and low outcome prevalence allows for assessment of whether or not CUD increases LUTS.[19]

To address this knowledge gap, we investigated the longitudinal relationship between CUD and new-onset LUTS diagnoses in previously healthy young adults using a large global claims database. We hypothesized that CUD would be associated with a higher likelihood of subsequent LUTS among young adults compared to patients without a diagnosis of CUD.

METHODS

Data Source and Study Design

We conducted a retrospective cohort study using the TriNetX research network, which provides access to de-identified electronic medical records (diagnoses, procedures, medications, and demographics) from patients across healthcare organizations nationwide. Data used in this study was collected and analyzed as of December 19, 2025. The TriNetX research network operates in compliance with the Health Insurance Portability and Accountability Act. Data within the platform are deidentified in accordance with a formal determination by a qualified expert, consistent with Section §164.514(b)(1) of the Health Insurance Portability and Accountability Act Privacy Rule. Because this analysis relied exclusively on deidentified records and did not involve access to individually identifiable patient information, it qualified for exemption from Institutional Review Board oversight. Accordingly, results are reported only as aggregate counts and summary statistics to ensure the continued protection of patient privacy.

Cohorts and Outcome Measures

We identified young adult patients aged 18-34 years. This age range was selected in accordance with the United States Census Bureau's definition of young adults.[16] The study population was stratified by sex to create distinct male and female cohorts, which were analyzed independently to account for physiological differences. The exposure group consisted of patients with a diagnosis of CUD. The CUD diagnosis served as a point-in-time index event; patients were not required to have persistent CUD diagnostic codes at subsequent follow-up intervals to remain in the exposure cohort. The control group included patients seeking medical care without a diagnosis of CUD. To isolate new-onset LUTS specifically associated with CUD, we excluded patients with congenital malformations of the urinary or neurological system, a history of urologic surgery, prior urologic malignancy, history of renal calculus, or prior use of medications that may affect urinary function (eg, diuretics, anticholinergics, and 5-alpha reductase inhibitors) and a previous history of LUTS diagnosis prior to CUD diagnosis. The comprehensive list of billing codes used is displayed in Supplementary Table 1. The index event was defined as the first documentation of CUD or medical encounter within the study time frame for our experimental and control groups, respectively.

The primary outcomes were the 5-year rates of new lower urinary tract disorder diagnoses, including all-cause LUTS as a composite measure (defined as polyuria, painful micturition, or other difficulties with micturition), dysuria, pelvic and perineal pain, overactive bladder (OAB), and urinary tract infection (UTI). Secondary outcomes included incident LUTS diagnoses at 1 and 3 years. In both female and male cohort, rates were compared between patients with CUD and matched controls. Incident LUTS diagnoses at 1-, 3-, and 5-years were analyzed as independent intervals. These specific time points were selected to align with recent literature investigating cannabis-related urologic outcomes.[14]

Statistical Analysis

Rates of lower urinary tract diagnoses were evaluated using the analytic tools available within the TriNetX platform. To improve comparability between exposure groups, patients with CUD were matched 1:1 to controls using propensity scores. TriNetX implements a nearest-neighbor matching approach, pairing each exposed patient with a control subject who has the closest estimated propensity score. This matching process proceeds sequentially and does not reconsider previously assigned matches. A caliper width of 0.1 pooled standard deviations was applied to restrict matches to individuals with sufficiently similar propensity scores, thereby reducing imbalance between cohorts. Propensity score matching was performed using the following covariates: demographics (age at index event, race, and ethnicity) and relevant comorbidities including mental, behavioral, and neurodevelopmental disorders, nicotine dependence, alcohol-related disorders, body mass index, and diabetes mellitus. For the female cohort, pregnancy, childbirth, and the puerperium were included as additional matching covariates, as pregnancy and potential complications have previously been associated with the development of LUTS.[20] Cohort balance was assessed using the standardized difference, with a value of < 0.1 considered indicative of adequate matching. We calculated risk ratios (RR) with 95% confidence intervals (CI) to compare outcomes, and statistical significance was assessed using a Z test. A P value $< .05$ was considered statistically significant.

RESULTS

Prior to matching, we identified 68,600 females and 106,330 males with CUD, alongside 4514,616 female and 4017,406 male controls without CUD. Following propensity score matching, we had a final study population of 67,110 female matched pairs and 101,761 male matched pairs. Post-matching analysis confirmed that all baseline characteristics were well-balanced between groups across demographic and comorbid covariates (Tables 1 and 2).

Figure 1 displays the results of our primary outcomes. For both males and females, CUD was significantly associated with higher risk of all-cause LUTS, dysuria, pelvic pain, and UTI 5 years after CUD diagnosis (all $P < .01$) (Fig. 1A and B). No relationship was observed for OAB at this time point for males or females ($P = .30$ and .92, respectively) (Fig. 1A and B).

Females diagnosed with CUD demonstrated a significantly increased risk of developing LUTS compared to matched controls at 1 and 3 years of follow-up. At the 1-year follow-up, the risk of all-cause LUTS was significantly elevated among patients with CUD compared to controls (RR 2.65; 95% CI 2.41-2.91). While the RR decreased over time, it remained significantly elevated at 5 years (RR 1.81; 95% CI 1.73-1.89). Among specific subtypes, UTIs showed the highest initial risk association (RR 3.97; 95% CI 3.57-4.43) at 1 year. There was not enough data for analysis of OAB at the 1-year interval, and OAB diagnoses did not show a statistically significant association with CUD at the 3-year time point (Table 3).

Males with CUD exhibited similar trends, showing a significantly elevated risk for LUTS compared to controls at all time points. The risk for all-cause LUTS was highest at the 1-year follow-up (RR 2.52; 95% CI 2.21-2.88) and remained significant at 5 years (RR 1.69; 95% CI 1.60-1.80). Dysuria, pelvic/perineal pain, and UTI were consistently associated with CUD, with pelvic pain showing a sustained elevation in risk from 1 year to 5 years. Similar to the female cohort, OAB did not demonstrate a significant association with CUD at the 3-year ($P = .53$) or 5-year mark ($P = .30$), and data were insufficient for analysis at the 1-year time point (Table 3).

Table 1
Baseline characteristics of the female cohort before and after propensity score matching.

Characteristic	Before Matching				After Matching			
	CUD	Control	*P* value	Std. Diff.	CUD	Control	*P* value	Std. Diff.
Total Patients (N)	68,600	4,514,616			67,110	67,110		
Age at Index, Mean ± SD	20.1 ± 3.85	16.2 ± 6.34	< .001	0.74	20.0 ± 3.83	20.2 ± 3.95	< .001	0.05
BMI (kg/m²), Mean ± SD	26.5 ± 7.42	24.3 ± 7.09	< .001	0.31	26.5 ± 7.43	26.7 ± 7.38	.01	0.02
Race, n (%)								
White	38,896 (56.7%)	2,529,364 (59.2%)	< .001	0.05	38,212 (56.9%)	38,342 (57.1%)	.47	0.00
Black or African American	19,601 (28.6%)	702,618 (16.4%)	< .001	0.29	18,931 (28.2%)	18,830 (28.1%)	.54	0.00
Asian	1157 (1.7%)	171,366 (4.0%)	< .001	0.14	1154 (1.7%)	1157 (1.7%)	.95	0.00
American Indian or Alaska Native	543 (0.8%)	20,709 (0.5%)	< .001	0.04	519 (0.8%)	526 (0.8%)	.83	0.00
Native Hawaiian or Other Pacific Islander	636 (0.9%)	33,452 (0.8%)	< .001	0.02	613 (0.9%)	601 (0.9%)	.73	0.00
Other Race	3459 (5.0%)	234,496 (5.5%)	< .001	0.02	3406 (5.1%)	3433 (5.1%)	.74	0.00
Unknown Race	4298 (6.3%)	581,262 (13.6%)	< .001	0.25	4275 (6.4%)	4221 (6.3%)	.55	0.00
Ethnicity, n (%)								
Not Hispanic or Latino	49,255 (71.8%)	2,657,988 (62.2%)	< .001	0.21	48,062 (71.6%)	48,314 (72.0%)	.13	0.01
Hispanic or Latino	9645 (14.1%)	647,533 (15.2%)	< .001	0.03	9500 (14.2%)	9747 (14.5%)	.05	0.01
Comorbidities, n (%)								
Mental, Behavioral and Neurodevelopmental disorders	34,657 (50.5%)	181,917 (4.3%)	< .001	1.21	33,177 (49.4%)	33,186 (49.5%)	.96	0.00
Nicotine dependence	9209 (13.4%)	8928 (0.2%)	< .001	0.54	7924 (11.8%)	7069 (10.5%)	< .001	0.04
Alcohol related disorders	3352 (4.9%)	3782 (0.1%)	< .001	0.31	2820 (4.2%)	2634 (3.9%)	.01	0.01
Diabetes mellitus	894 (1.3%)	11,322 (0.3%)	< .001	0.12	827 (1.2%)	851 (1.3%)	.56	0.00

*Std-Diff.: Standardized Difference. *P values < .05 are considered statistically significant.*

Table 2
Baseline characteristics of the male cohort before and after propensity score matching.

Characteristic	Before Matching				After Matching			
	CUD	Control	*P* value	Std. Diff.	CUD	Control	*P* value	Std. Diff.
Total Patients (N)	106,330	4017,406			101,761	101,761		
Age at Index, Mean ± SD	20.4 ± 3.8	15.4 ± 6.5	< .001	0.96	20.3 ± 3.7	20.5 ± 3.9	< .001	0.06
BMI (kg/m²), Mean ± SD	24.5 ± 5.7	22.9 ± 6.3	< .001	0.27	24.5 ± 5.8	24.9 ± 6.0	< .001	0.07
Race, n (%)								
White	62,541 (58.8%)	2340,318 (60.9%)	< .001	0.04	60,209 (59.2%)	60,288 (59.2%)	.72	0.00
Black or African American	27,278 (25.7%)	597,062 (15.6%)	< .001	0.25	25,510 (25.1%)	25,236 (24.8%)	.16	0.01
Asian	1933 (1.8%)	148,356 (3.9%)	< .001	0.12	1902 (1.9%)	1899 (1.9%)	.96	0.00
American Indian or Alaska Native	689 (0.6%)	18,214 (0.5%)	< .001	0.02	649 (0.6%)	732 (0.7%)	.03	0.01
Native Hawaiian or Other Pacific Islander	1113 (1.0%)	37,375 (1.0%)	.02	0.01	1044 (1.0%)	963 (0.9%)	.07	0.01
Other Race	6128 (5.8%)	230,690 (6.0%)	< .001	0.01	5936 (5.8%)	5939 (5.8%)	.98	0.00
Unknown Race	6644 (6.2%)	466,471 (12.2%)	< .001	0.21	6511 (6.4%)	6704 (6.6%)	.08	0.01
Ethnicity, n (%)								
Not Hispanic or Latino	76,812 (72.2%)	2443,790 (63.7%)	< .001	0.18	73,015 (71.8%)	73,015 (71.8%)	1.00	0.01
Hispanic or Latino	16,389 (15.4%)	559,274 (14.6%)	< .001	0.02	15,815 (15.5%)	16,252 (16.0%)	.01	0.01
Comorbidities, n (%)								
Mental, Behavioral and Neurodevelopmental disorders	51,207 (48.2%)	203,416 (5.3%)	< .001	1.11	46,642 (45.8%)	46,463 (45.7%)	.43	0.01
Nicotine dependence	16,615 (15.6%)	11,317 (0.3%)	< .001	0.59	12,686 (12.5%)	10,733 (10.5%)	< .001	0.06
Alcohol related disorders	6971 (6.6%)	5739 (0.2%)	< .001	0.36	5288 (5.2%)	4829 (4.7%)	< .001	0.02
Diabetes mellitus	1215 (1.1%)	11,027 (0.3%)	< .001	0.10	1081 (1.1%)	1072 (1.1%)	.85	0.01

*Std- Diff., Standardized Difference. *P values < .05 are considered statistically significant.*

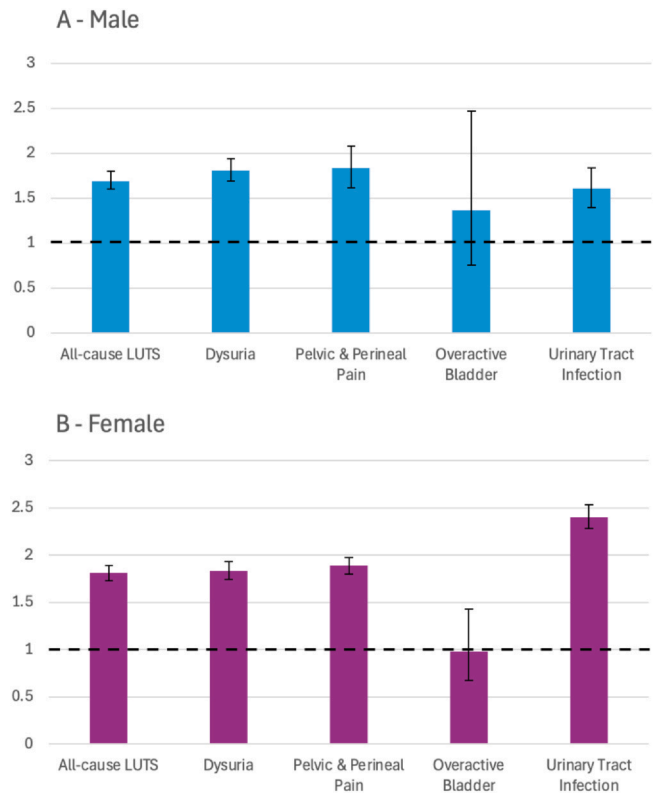

Figure 1. 5-year risk of LUTS in young adults with Cannabis use disorder. Bar graphs displaying the risk ratios (RR) for incident LUTS diagnoses at 5 years post-CUD diagnosis in matched (A) male and (B) female cohorts (aged 18-34 years). Error bars represent 95% confidence intervals. The dashed black line represents the null value (RR = 1.0), indicating no difference in risk. In both panels, statistically significant increased risks ($P < .01$) were observed for all-cause LUTS, dysuria, pelvic and perineal pain, and urinary tract infections. Overactive bladder did not reach statistical significance in either sex ($P = .30$ for males; $P = .92$ for females), as visually demonstrated by the error bars crossing the null line.

DISCUSSION

This large, propensity score-matched retrospective cohort study found that CUD was associated with an increased risk of new onset LUTS among previously healthy young adults. This association was observed in both male and female cohorts and persisted across 1-, 3-, and 5-year follow-up intervals, remaining robust even after adjustment for relevant demographic and clinical confounders. Notably, the risk of developing LUTS was highest in the period immediately following a CUD diagnosis, with the magnitude of the RR remaining significant but attenuating over time. This temporal pattern suggests that CUD may be associated with both acute and chronic-term urinary health outcomes, with the strongest associations observed immediately following diagnosis. This attenuation of risk over time may reflect the natural history of CUD, where the index diagnosis triggers behavioral changes that successfully reduce cannabis consumption. Alternatively, this temporal trend may be driven by the initiation of standard medical therapies (eg, alpha-blockers, anticholinergics, or pelvic floor physical therapy) following an initial LUTS diagnosis.

While the overall trend of increased risk was consistent across sexes, females displayed higher risk magnitude across all LUTS variables, likely reflecting anatomical variations in lower urinary tract function and/or differences in healthcare-seeking behaviors.[16,21] In particular, CUD was most strongly associated with an increased risk of UTIs. This finding may result from the interaction between female anatomy, specifically the shorter urethra, and localized immune system alterations secondary to chronic cannabis exposure.[15] Males with CUD exhibited

Table 3
Longitudinal risk of LUTS outcomes in males and females (1, 3, and 5-year follow-up).

Outcome	Male % CUD	Male % Control	Male RR	Male 95% CI	Male *P* Value	Female % CUD	Female % Control	Female RR	Female 95% CI	Female *P* Value
1-y follow up										
All-cause LUTS	0.75	0.30	2.52	(2.21, 2.88)	< .0001	2.34	0.88	2.65	(2.41, 2.91)	< .0001
Dysuria	0.60	0.23	2.66	(2.28, 3.09)	< .0001	1.71	0.67	2.55	(2.29, 2.84)	< .0001
Pelvic Pain	0.21	0.07	3.17	(2.41, 4.16)	< .0001	2.29	0.96	2.38	(2.18, 2.61)	< .0001
OAB	—	—	Insufficient Data*	—	—	—	—	Insufficient Data*	—	—
UTI	0.14	0.06	2.30	(1.70, 3.10)	< .0001	2.40	0.60	3.97	(3.57, 4.43)	< .0001
3-y follow-up										
All-cause LUTS	1.98	1.02	1.95	(1.81, 2.10)	< .0001	5.76	2.72	2.12	(2.01, 2.24)	< .0001
Dysuria	1.51	0.74	2.04	(1.87, 2.22)	< .0001	4.19	2.02	2.07	(1.94, 2.21)	< .0001
Pelvic Pain	0.44	0.21	2.10	(1.79, 2.47)	< .0001	5.46	2.61	2.09	(1.98, 2.22)	< .0001
OAB	0.01	0.01	1.30	(0.57, 2.97)	.53	0.04	0.05	0.81	(0.48, 1.37)	.42
UTI	0.34	0.18	1.93	(0.34, 2.31)	< .0001	5.12	1.78	2.88	(2.70, 3.07)	< .0001
5-y follow-up										
All-cause LUTS	2.91	1.72	1.69	(1.60, 1.80)	< .0001	8.23	4.56	1.81	(1.73, 1.89)	< .0001
Dysuria	2.17	1.20	1.81	(1.69, 1.94)	< .0001	6.03	3.29	1.83	(1.74, 1.93)	< .0001
Pelvic Pain	0.67	0.37	1.84	(1.62, 2.08)	< .0001	8.09	4.29	1.89	(1.80, 1.97)	< .0001
OAB	0.03	0.02	1.37	(0.76, 2.47)	.30	0.08	0.08	0.98	(0.67, 1.43)	.92
UTI	0.53	0.33	1.61	(1.40, 1.84)	< .0001	7.08	2.94	2.40	(2.28, 2.53)	< .0001

*Patient count was too small to calculate detailed results for Overactive Bladder at 1 year. *P values < .05 are considered statistically significant.*

the highest risk for pelvic and perineal pain, suggesting a potential chronic inflammatory effect or pelvic floor dysfunction unique to male physiology. Interestingly, OAB was not significantly associated with CUD in either sex. This result is contradictory to prior work, which showed an association of cannabis use and increased risk of OAB across various frequencies of cannabis use.[12] However, this data relied on survey design and self-reported cannabis use. Furthermore, their cohort was older with a median age of 39, nearly double the median age of our cohort. Overall, our results suggest that cannabis-related LUTS may be linked to pain pathways, inflammatory processes, or voiding dysfunction rather than detrusor overactivity, although further mechanistic studies are needed.

Several pathophysiological mechanisms may explain these findings. Cannabinoid receptors are present throughout the bladder and urethra and are known to influence sensation, inflammation, and the local immune response.[22–24] Chronic exposure to cannabinoids can induce immunomodulation, potentially altering the host defense against infection.[25] Additionally, cannabinoids have neurogenic effects that can alter pain perception and autonomic nerve function, which may manifest clinically as dysuria or chronic pelvic pain.[23,26,27] Despite these known effects, the null effect observed in OAB deserves special consideration. While cannabinoid receptors are expressed in the bladder urothelium and nerve endings, preclinical evidence indicates that cannabinoid agonizts do not have a direct myorelaxant or stimulatory effect on agonist-induced detrusor smooth muscle contractions.[3] In fact, the endocannabinoid system constitutively downregulates sensory bladder function, with early preclinical evidence showing that receptor activation may affect bladder afferent sensitivity and counteracting bladder overactivity.[8] Consequently, the chronic cannabinoid exposure characteristic of a CUD diagnosis lacks a clear biological mechanism to induce the detrusor hyperactivity or sensory urgency that defines OAB. This neurobiological framework strongly supports our epidemiological findings, reinforcing the concept that cannabis-related urologic dysfunction in a young adult cohort is primarily driven by localized inflammatory responses and altered pain perception, rather than motor dysfunction.

Beyond biological mechanisms, behavioral factors common among those with CUD, such as delayed medical care, may also contribute to symptom development.[28] Furthermore, despite matching for mental health diagnoses, we could not account for the varied severity of these conditions, which are known to influence lower urinary tract function.

These results contribute to a complex body of literature characterized by conflicting findings, where cannabinoids have been investigated for both therapeutic potential and adverse effects.[12,13] Our findings contrast with previous studies that suggest a protective effect of cannabis on male LUTS.[13] However, this work included patients aged 20-59, was cross-sectional in design, and relied on self-report of LUTS symptoms.[7] Our findings build upon Grutman et al's recent pediatric study.[14] Unlike their findings, where no association with all-cause LUTS was observed, our cohort demonstrated a robust, statistically significant increase in risk for both sexes. This suggests that the clinical presentation of urologic dysfunction in young adults may be distinct from adolescents, as evidenced by a significant association with the composite LUTS outcome that was absent in the pediatric study. However, consistent with the pediatric data, we confirmed elevated risks for dysuria, pelvic pain, and UTIs in both males and females. The consistency of these findings across developmental stages may suggest shared underlying biological or behavioral factors, potentially involving inflammatory pathways or altered pain perception, although dedicated mechanistic studies are needed.

This study has several strengths. Its use of a large, multi-institutional claims database allows for a robust sample size and is able to capture long-term follow-up. The use of a sex-stratified analyses investigates potential sex-related differences in how cannabis influences the urinary system given the unique anatomical considerations. Throughout the analysis, propensity score matching achieved excellent covariate balance in the cohorts. By restricting the analysis to new-onset LUTS, we reinforce temporal ordering between CUD diagnosis and LUTS onset, thereby reducing the likelihood that preexisting urinary symptoms influenced CUD diagnosis.

This study is not without limitations. A critical limitation of this study is the inherent reliance on administrative claims data, which introduces significant potential for ascertainment bias and diagnostic misclassification. Furthermore, individuals who receive a CUD diagnosis are, by definition, actively engaging with the healthcare system. This differential healthcare utilization inherently raises the probability of capturing subsequent medical encounters, including new LUTS diagnoses, compared to a potentially less-engaged control cohort. While we attempted to mitigate this by robustly matching for comorbidities that drive healthcare utilization, a scenario in which a portion of the observed associations is driven by ascertainment bias cannot be entirely ruled out. Our selected ICD-10 codes do not capture the complete spectrum of urological phenotypes that fall under the broader umbrella of lower urinary tract dysfunction, such as prostatitis, which may restrict the comprehensiveness of our findings. Reliance on a specifically defined set of ICD-10 codes to identify LUTS maximizes diagnostic specificity but may not fully capture the natural variability in clinical coding practices. It is possible that relevant urologic symptoms were documented under alternative, broader diagnostic labels not included in our analysis. Furthermore, binary ICD-10 codes lack the granularity to capture CUD's dynamic clinical course, including variations in consumption severity, frequency, or remission over time. Consequently, our inability to track these temporal shifts or stratify urologic risk by CUD severity remains a notable limitation.

In addition, there are a variety of clinical factors that influence who receive a CUD diagnosis that TriNetX is unable to robustly capture. For example, individuals who use cannabis more frequently and for longer durations are more likely to receive a CUD diagnosis, and sociodemographic factors that increase risk include adverse childhood experiences, stressful life events, and parental cannabis use.[29] Our cohort with a CUD diagnosis likely reflects a patient population with clinically recognizable use, which limits generalizability to recreational or intermittent cannabis users. Similarly, our control cohort most likely contains recreational cannabis users, which can cause underestimation of the true effect. Although cohorts were matched for mental health disorders, the unmeasured use of psychotropic medications (eg, antidepressants or antipsychotics) remains a potential confounder due to their potential effects on urinary function. Due to the nature of the available TriNetX data, residual confounding is possible through unmeasured confounders such as family and peer environment, socioeconomic status, genetic predispositions for CUD and LUTS, and cannabis frequency/dosage.

These findings suggest that diagnosed CUD is associated with increased risk of LUTS in young adults, a population not typically considered at elevated risk for urologic disease and warrants further investigation. As cannabis legalization expands, understanding non-neuropsychiatric sequelae of chronic cannabis use becomes increasingly important for patient counseling and relevant for public health policy, affecting both primary care and urology.

Given the limitations of the TriNetX database, these findings are hypothesis-generating. Future work could potentially include prospective studies that collect data on dose, potency, duration, and mode of use, including whether cannabis is consumed or inhaled (smoked, vaped, etc.). Further, future research utilizing discrete interval analyses would provide deeper insight into the longitudinal evolution of LUTS, specifically determining whether the incidence of LUTS remains continuously elevated for years following a CUD diagnosis or if the overall burden is predominantly driven by the acute 0-1 year period.

CONCLUSION

In a large cohort of previously healthy young adults, our findings indicate a longitudinal association between a diagnosis of CUD and the development of new LUTS compared to matched controls. Future

prospective studies are warranted to elucidate the underlying pathophysiological mechanisms and determine if these effects are ameliorable or reversible with cessation.

Disclosures

None.

CRediT authorship contribution statement

Andrew J. Cohen: Writing – review & editing, Supervision, Methodology, Investigation, Conceptualization. **Andrew T. Gabrielson:** Writing – review & editing, Validation, Methodology, Investigation, Conceptualization. **Jack A. Campbell:** Writing – review & editing, Methodology, Investigation, Formal analysis, Conceptualization. **Aurora J. Grutman:** Writing – original draft, Methodology, Investigation, Conceptualization. **Emma Giarracco:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Devin M. Dishong:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

None.

IRB Statement

This study was deemed exempt by the Johns Hopkins Institutional Review Board for its use of deidentified patient data.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.urology.2026.06.022.

References

1. Solmi M, Radua J, Olivola M, et al. Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. *Mol Psychiatry*. 2022;27:281–295. https://doi.org/10.1038/s41380-021-01161-7
2. Gorelick DA. Cannabis-related disorders and toxic effects. *N Engl J Med*. 2023;389:2267–2275. https://doi.org/10.1056/NEJMra2212152
3. Hedlund P. Cannabinoids and the endocannabinoid system in lower urinary tract function and dysfunction. *Neurourol Urodyn*. 2014;33:46–53. https://doi.org/10.1002/nau.22442
4. Tambaro S, Casu MA, Mastinu A, Lazzari P. Evaluation of selective cannabinoid CB (1) and CB(2) receptor agonists in a mouse model of lipopolysaccharide-induced interstitial cystitis. *Eur J Pharmacol*. 2014;729:67–74. https://doi.org/10.1016/j.ejphar.2014.02.013
5. Patwardhan AM, Jeske NA, Price TJ, Gamper N, Akopian AN, Hargreaves KM. The cannabinoid WIN 55,212-2 inhibits transient receptor potential vanilloid 1 (TRPV1) and evokes peripheral antihyperalgesia via calcineurin. *Proc Natl Acad Sci U S A*. 2006;103:11393–11398. https://doi.org/10.1073/pnas.0603861103
6. Akopian AN, Ruparel NB, Patwardhan A, Hargreaves KM. Cannabinoids desensitize capsaicin and mustard oil responses in sensory neurons via TRPA1 activation. *J Neurosci Off J Soc Neurosci*. 2008;28:1064–1075. https://doi.org/10.1523/JNEUROSCI.1565-06.2008
7. Christie S, Brookes S, Zagorodnyuk V. Endocannabinoids in bladder sensory mechanisms in health and diseases. *Front Pharmacol*. 2021;12:708989. https://doi.org/10.3389/fphar.2021.708989
8. Aizawa N, Hedlund P, Füllhase C, Ito H, Homma Y, Igawa Y. Inhibition of peripheral FAAH depresses activities of bladder mechanosensitive nerve fibers of the rat. *J Urol*. 2014;192:956–963. https://doi.org/10.1016/j.juro.2014.04.008
9. Taylor C, Birch B. Cannabinoids in urology. Which benign conditions might they be appropriate to treat: a systematic review. *Urology*. 2021;148:8–25. https://doi.org/10.1016/j.urology.2020.10.024
10. Pham MN, Hudnall MT, Nadler RB. Marijuana, lower urinary tract symptoms, and pain in the urologic patient. *Urology*. 2020;139:8–13. https://doi.org/10.1016/j.urology.2020.01.029
11. Xie L, Yu Z, Gao F. The association between recent cannabis use and urinary incontinence in women: a population-based analysis of the NHANES from 2009 to 2018. *World J Urol*. 2022;40:3099–3105. https://doi.org/10.1007/s00345-022-04193-y
12. Zhu S, Wang Z, Tao Z, Wang S, Wang Z. Relationship between marijuana use and overactive bladder (OAB): a cross-sectional research of NHANES 2005 to 2018. *Am J Med*. 2023;136:72–78. https://doi.org/10.1016/j.amjmed.2022.08.031
13. Fantus RJ, Riedinger CB, Chang C, Helfand BT. The association between tetrahydrocannabinol and lower urinary tract symptoms utilizing the National Health and Nutrition Examination Survey. *Urology*. 2019;123:120–125. https://doi.org/10.1016/j.urology.2018.06.054
14. Grutman AJ, Gumma ME, Page N, Gabrielson AT, Clifton M, DiCarlo H. Cannabis use is associated with lower urinary tract symptoms in pediatric patients-a large claims database study. *Urology*. 2025;205:187–195. https://doi.org/10.1016/j.urology.2025.07.014
15. Nedumaran B, Rudra P, Gaydos J, et al. Impact of regular cannabis use on biomarkers of lower urinary tract function. *Urology*. 2017;109:223.e9–223.e16. https://doi.org/10.1016/j.urology.2017.08.011
16. Boyle P, Robertson C, Mazzetta C, et al. The prevalence of lower urinary tract symptoms in men and women in four centres. The UrEpik study. *BJU Int*. 2003;92:409–414. https://doi.org/10.1046/j.1464-410x.2003.04369.x
17. Huang J, Chan CK, Yee S, et al. Global burden and temporal trends of lower urinary tract symptoms: a systematic review and meta-analysis. *Prostate Cancer Prostatic Dis*. 2023;26:421–428. https://doi.org/10.1038/s41391-022-00610-w
18. Wei JT, Dauw CA, Brodsky CN. Lower urinary tract symptoms in men: a review. *JAMA*. 2025;334:809–821. https://doi.org/10.1001/jama.2025.7045
19. Doggett A, Belisario K, McDonald AJ, Ferro MA, Murphy JG, MacKillop J. Cannabis use frequency and cannabis-related consequences in high-risk young adults across Cannabis legalization. *JAMA Netw Open*. 2023;6:e2336035. https://doi.org/10.1001/jamanetworkopen.2023.36035
20. Maserejian NN, Curto T, Hall SA, Wittert G, McKinlay JB. Reproductive history and progression of lower urinary tract symptoms in women: results from a population-based cohort study. *Urology*. 2014;83:788–794. https://doi.org/10.1016/j.urology.2013.12.016
21. Kinjo M, Nakamura Y, Taguchi S, et al. Sex differences in prevalence and patient behavior regarding lower urinary tract symptoms among Japanese Medical Checkup Examinees. *Urology*. 2021;151:24–30. https://doi.org/10.1016/j.urology.2020.05.065
22. Aizawa N, Gandaglia G, Hedlund P, et al. URB937, a peripherally restricted inhibitor for fatty acid amide hydrolase, reduces prostaglandin E2 -induced bladder overactivity and hyperactivity of bladder mechano-afferent nerve fibres in rats. *BJU Int*. 2016;117:821–828. https://doi.org/10.1111/bju.13223
23. Walczak JS, Cervero F. Local activation of cannabinoid CB_1 receptors in the urinary bladder reduces the inflammation-induced sensitization of bladder afferents. *Mol Pain*. 2011;7:31. https://doi.org/10.1186/1744-8069-7-31
24. Tyagi V, Philips BJ, Su R, et al. Differential expression of functional cannabinoid receptors in human bladder detrusor and urothelium. *J Urol*. 2009;181:1932–1938. https://doi.org/10.1016/j.juro.2008.11.078
25. Maggirwar SB, Khalsa JH. The link between cannabis use, immune system, and viral infections. *Viruses*. 2021;13:1099. https://doi.org/10.3390/v13061099
26. Wang ZY, Wang P, Bjorling DE. Treatment with a cannabinoid receptor 2 agonist decreases severity of established cystitis. *J Urol*. 2014;191:1153–1158. https://doi.org/10.1016/j.juro.2013.10.102
27. Bjorling DE, Wang ZY. Potential of endocannabinoids to control bladder pain. *Front Syst Neurosci*. 2018;12:17. https://doi.org/10.3389/fnsys.2018.00017
28. Graves BD, Mowbray O, Aletraris L, O'Shields J. An analysis of 16-year trends in cannabis use disorder treatment: predictors, barriers, and utilization patterns. *Subst Use Misuse*. 2025;60:1540–1549. https://doi.org/10.1080/10826084.2025.2505773
29. Gorelick DA. Cannabis-related disorders and toxic effects. *N Engl J Med*. 2023;389:2267–2275. https://doi.org/10.1056/NEJMra2212152